NEWS OF THE ME RESEARCH YOU ARE HELPING TO FUND

breakthrough

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FEATURES

Neurological biomarkers

The genetics of pain

Real experience of fatigue

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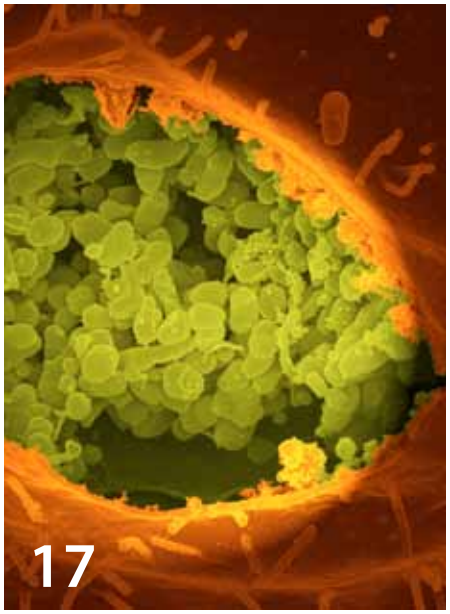
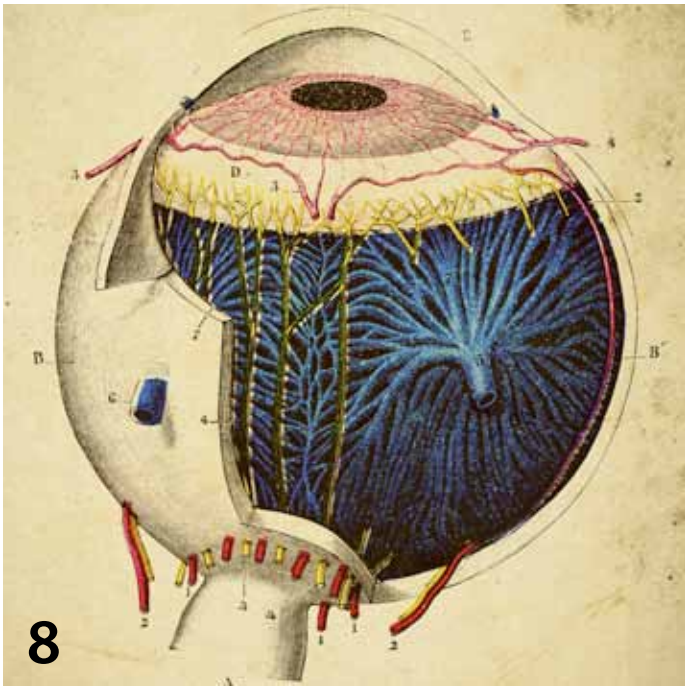
ME RESEARCH UK





Welcome

Breakthrough magazine is published by ME Research UK, a Scottish Charitable Incorporated Organisation that funds research into Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (also known as ME/CFS). The charity has an international remit, and its principal aim is to commission and fund high-quality scientific (biomedical) investigation into the causes, consequences and treatment of ME/CFS. It also aims to energise ME research by identifying potentially important areas for future biomedical research, producing high quality professional reviews and reports, and presenting research at meetings and conferences. *Breakthrough* is an open access publication and, with the exception of images and illustrations, the content may be reproduced free of charge, subject to the terms and conditions found at:

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In the spotlight

What's happening in the world of ME research and funding

Prof. Leonard Jason from DePaul University

Digging deeper

The real experience of fatigue in ME/CFS

Fatigue is a disabling aspect of many chronic diseases, but the word *fatigue* doesn't begin to describe the real experiences of ME/CFS patients. Many point out that their major problem is not the fatigue *per se*, but the conjunction of post-exercise severe fatigue, malaise, pain and other symptoms. We also know that the fatigue in ME/CFS patients can be more severe than in many other diseases.

This was shown in an ME Research UK-funded study by Prof. David Jones and colleagues at Newcastle University, who examined data from 600 people across five chronically ill disease groups: non-alcoholic fatty liver disease, vasovagal syncope, primary sclerosing cholangitis, primary biliary cirrhosis and ME/CFS. Fatigue severity was much higher in ME/CFS patients, and interfered with many other aspects of life.

Clearly, there is something very different about the experience of fatigue in ME/CFS, yet studies focusing on how fatigue impacts on patients and their lived experiences are rare. That's why a recent study published in the journal *BMJ Nursing* is particularly valuable: it lets the patients have their say, and classifies their experiences comprehensively.

Eva Stormorken (Oslo University) and Leonard Jason (DePaul University, Chicago) explored the experiences of Norwegians diagnosed with a post-infectious fatigue syndrome akin to ME/CFS. These people had been ill for four years following infection with the parasite *Giardia lamblia*. In total, 26 adults were recruited from patients seen at Haukeland University Hospital in Bergen. Each had a face-to-face interview using an interview approach that allowed for the maximum amount of information to be garnered. Content analysis of the interviews enabled a number of fascinating themes to be identified.

A major theme was the extensive and pervading nature of the patients' fatigue – a whole-body experience described as "all-pervasive", "feeling old" and being "out of control" that greatly reduces the person's ability to function personally or professionally.

Digging deeper, the researchers identified less well-recognised aspects, such as emotional fatigue (impatience, lowered stress intolerance, etc.); a state in which the mind is working overtime even though the body is not; cognitive fatigue characterised by difficulties finding words, concentrating or remembering; and weird body experiences, such as hypersensitivity to noise or light, vision and hearing problems, temperature regulation difficulties, and pins and needles. The participants also reported fatigue on waking up, with a prolonged waking process, and feeling drowsy and unrefreshed. As the authors point out, fatigue

Eva Sormorken from the University of Oslo

"The term fatigue does not capture patients' experiences, which are accompanied by a considerable symptom burden."

on awakening is rarely recognised by healthcare professionals, but should be.

Illness, malaise and a flare up of symptoms after even mild exertion was a prominent feature, with relapses due to overexertion lasting for hours, days or even months. Patients also reported a lack of endurance and stamina; being unable to multitask, or even do several things in the same day; and taking much longer to do things than normal. One of the most unusual findings was *beyond time* feelings, described as a state of mind when time passes with no awareness of what is going on. Indeed, several participants reported substantial gaps in their memory of the preceding four years.

The investigator's key point is that the term fatigue does not capture the participants' experiences "which are accompanied by a considerable symptom burden that contributes to the illness experience and the severe disability."

In fact, the patients' fatigue was multidimensional and far removed from the everyday tiredness experienced by healthy people. This central fact needs to be brought home to the general public, and medical staff and other healthcare professionals in particular, if the real, lived experiences of people with ME/CFS are ever to be understood and taken seriously.

What about the young?

Very poor quality of life in young patients

A decade ago, a postal survey of GP practices in the UK uncovered significant numbers of 5 to 19-year-olds with "unexplained severe fatigue", most of whom had a diagnosis of ME/CFS. These youngsters definitely exist, but you wouldn't know it from the TV or the newspapers, and their families are usually left to cope with the situation as best they can.

In Norway, the NorCAPITAL project ran for several years in order to explore ME/CFS in young people. All 20 paediatric departments in Norwegian hospitals, as well as many general practitioners, were invited to refer their patients to a central department of paediatrics for further investigation. Several scientific reports have already been published from the project data, and the latest, from the Institute of Nursing in Oslo, describes the health-related quality of life of 120 adolescents with ME/CFS compared with a group of healthy young people.

The investigators found that the average length of illness was 21.4 months, while school absence was 65% in the patients compared with only 2.1% in healthy children. Quality of life was dramatically worse in youngsters with ME/CFS: on a scale 0 to 100, they scored a full 44 points lower overall than their healthy peers. As regards specific aspects,

the ME/CFS patients scored 60 points lower than healthy children for physical functioning, 52 points lower for school functioning, 28 points lower for emotional functioning, and 27 points lower for social functioning.

Given their chronic illness, it was not surprising that the young ME/CFS patients had a much higher risk of depression-associated symptoms than did their healthy peers. However, statistical modelling of the data revealed that lower quality of life was associated with having ME/CFS rather than with being depressed *per se*. As the authors say, "Experiencing difficult thoughts and sad feelings (depressive symptoms) might not be surprising, considering the consequences of the disease, such as reduced school attendance and time with peers."

Meet our ambassador

Tracey Wilson

My daughter, Kelsey, was diagnosed with ME five years ago, when she was just 17. Since then my family has learned a lot about the illness, and have made many friends with other ME patients.

In 2014, I was organising one of my regular fundraising events for ME Research UK. Sue Waddle, the Vice Chair of the charity, was there, and she asked if I would be interested in applying to becoming an Ambassador. I didn't have to think twice! I was flattered that my contributions had been recognised but, more importantly, I wanted to raise awareness of ME and raise funds for research.

My most recent success has been to get my local Sainsbury's store to make ME Research UK its charity of the year. We have had collection tins at the checkouts, and had a table outside to raise further funds and awareness. I've also been involved in the annual Walk For ME scheme. The idea is that friends and family undertake a sponsored walk on behalf of their loved one who has ME. Kelsey and I have done a sponsored walk/wheelchair push in each of past 3 years, raising £1,350 in total.

These Norwegian researchers had previously investigated health-related quality of life in youngsters in remission after acute lymphoblastic leukaemia, and in children who had undergone renal transplantation. Crucially, they found that quality of life was more impaired in the young ME/CFS patients than in the patients with these two other conditions – a finding which chimes with ME Research UK-funded work at the University of Dundee (see page 13).

An important aspect of a dramatically reduced quality of life is the social isolation it brings, as the NorCAPITAL project found when it explored adolescents' own experiences of living with ME/CFS. The lack of participation at school and social gatherings with other teenagers made them feel like outsiders. As the researchers say, the young people "experienced loss of a normal life and the changes in friendships difficult, leading to loneliness and isolation". Cruelly, this concatenation of events happens at a particularly vulnerable time of life when disruption to education and family life has the severest consequences.

ME Research UK-funded researchers:
Prof. Jo Nijs, **Dr Faisel Khan** , **Dr Clive Carter**, **Prof. Lionel Lubitz**, **Dr Erinna Bowman**, **Victoria Strassheim** and **Prof. Julia Newton**

Coming together

2015 Research Collaborative conference

Fruitful and encouraging is how we would sum up the second Research Collaborative (CMRC) conference in Newcastle in October 2015. The aim of the CMRC – the first of its kind in the world – is to promote the highest quality of scientific research into ME/CFS by bringing together working researchers, national agencies and ME/CFS charities. This year, many of the main presentations were livestreamed, so people with ME and their families could watch the proceedings from home. Conference numbers were impressive, with over 105 delegates registered for the conference.

Prof. Stephen Holgate, Chair of the CMRC, began by welcoming delegates. He was particularly enthused by the reports published in the USA by the Institute of Medicine and the National Institutes of Health in 2015 which pointed up the significant functional impairment and disability caused by ME/CFS, and recommended increased funding. Prof. Holgate believes that rapid scientific discovery is within reach, after years of minimal funding for scientific research.

The major keynote lecture was by Prof. José Montoya of Stanford University who stated his "wish and dream that medical and research societies in the

Easyfundraising

Easyfundraising is a convenient way to access some of the UK's largest and best retailers through a single easy-to-use site. You have 2,700 top retailers at the click of a mouse, and each company will make a donation to your favourite charity.

Most high street stores are represented: M&S, John Lewis, Tesco Direct, Next, Sainsbury's, Boots and more. Also, the site offers amazing, exclusive deals, and major insurance companies, travel agents and mobile phone companies are all part of the scheme.

Just register with the site (www.easyfundraising.co.uk), and choose ME Research UK as your cause, to start shopping and donating to us. It doesn't cost you a single penny, and it helps us fund research studies.

Focus on funding
Hidden fundraising

Think of fundraising, and events such as street collections, sky-dives and coffee mornings come to mind. All these are important and we're glad that our supporters do them, but there are other 'hidden' ways to help us fund research projects that you might not have thought about. In fact, there's enormous scope to tap into the charitable giving of **companies** and **organisations**. The hard part is getting a foot in the door, and that's where you can help.

If your **workplace has charity days**, why not suggest ME Research UK? We can help with some promotional materials and literature (and even t-shirts and balloons).

If you are already fundraising for us or make regular donations, does your employer have a **matching giving scheme**? More and more companies are offering these as a tax-effective way of boosting their employees' charitable donations.

If you see a company, such as a supermarket or a building society, asking for **nominations for charity donations**, why not suggest us? It only takes a minute to put our name forward, but it can bring in a big donation.

It is more difficult to fundraise for research than for community-based projects, so every avenue is important – even the 'hidden' ones.

Dr Erinna Bowman inside the biobank

USA apologise to ME/CFS patients" for their attitudes in the past. He also described the 2015 Institute of Medicine report as a step forward, particularly in its recognition that ME/CFS is a physical illness. He outlined the large programme of work now underway at Stanford, which includes randomised clinical trials, longitudinal and case-control studies, and pilot investigations. The evidence over the last 33 years, he explained, is that ME/CFS is often triggered by infection leading to a neuro-inflammatory process. Fortunately, there is now "a precious opportunity to crack the most exciting scientific mystery".

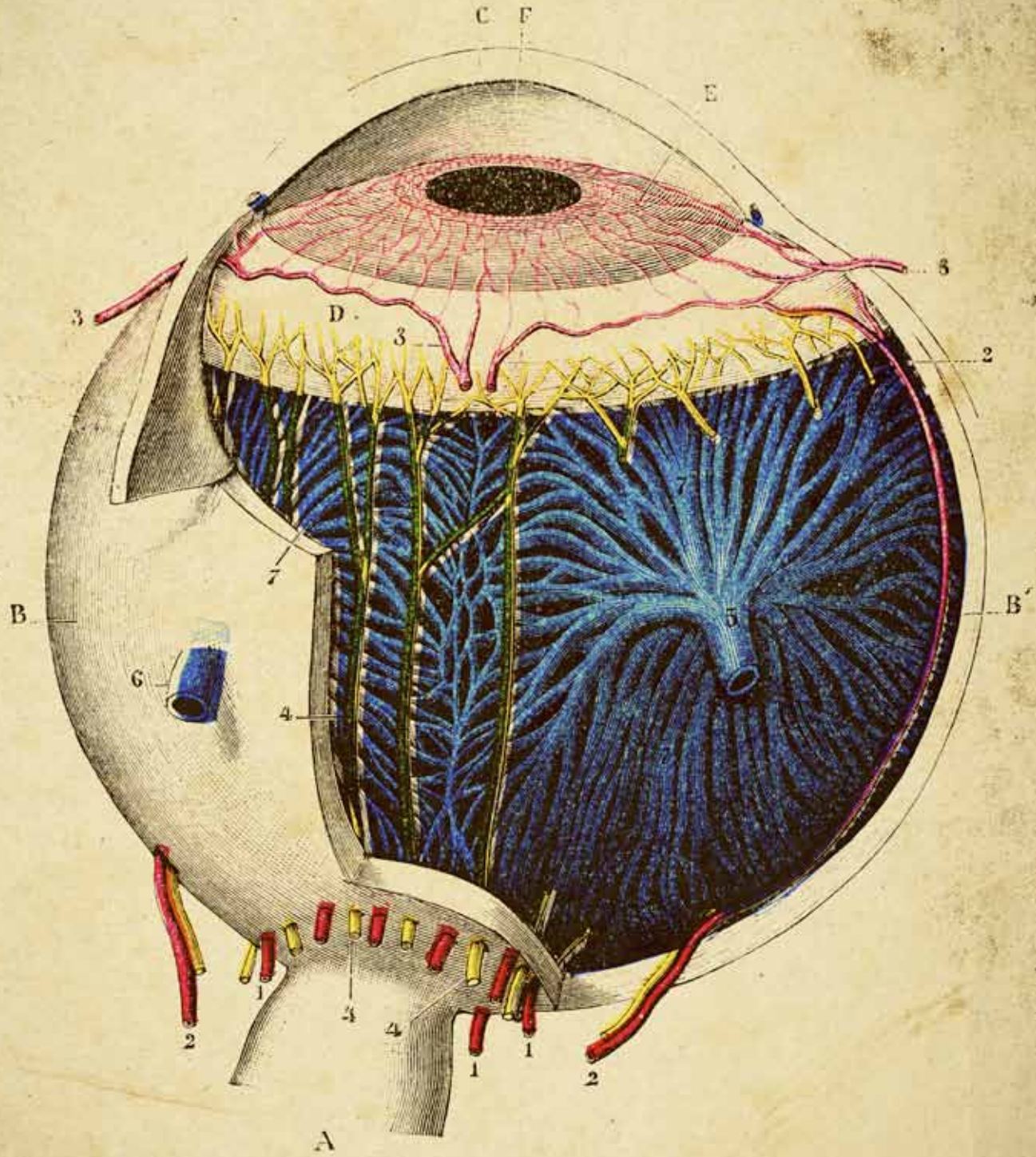
"[The CMRC is] bringing together working researchers, national agencies and charities"

There were also keynote lectures by a range of experts, including Prof. Jo Nijs who described his work on pain and the autonomic nervous system, Dr Øystein Fluge who reviewed his studies on rituximab, and Prof. George Davey Smith who discussed the need for 'big data'.

We were fortunate to have quite a few of our funded researchers in attendance giving shorter presentations. For instance, Prof. Julia Newton discussed cardiac aspects of ME/CFS, and her group is undertaking imaging of the heart to explore whether nervous input to the heart underlies the autonomic system problems seen in some patients. Also, Drs Strachan and Carter from Leeds described some early results from their study comparing B cell subsets in ME/CFS patients, breast cancer patients and healthy controls.

Many of the poster presentations brought scientific work to a wider audience. For example, the poster from our UK ME/CFS biobank described the progress to date. It has recruited 390 participants (245 ME/CFS cases, 101 healthy controls and 44 MS patients), and 22,500 aliquot samples are stored and will be available to research groups very soon.

The conference was sponsored by the MRC, Wellcome Trust and Arthritis Research UK, and the 2016 conference is in Newcastle in September – a date for your diary.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in and out of focus

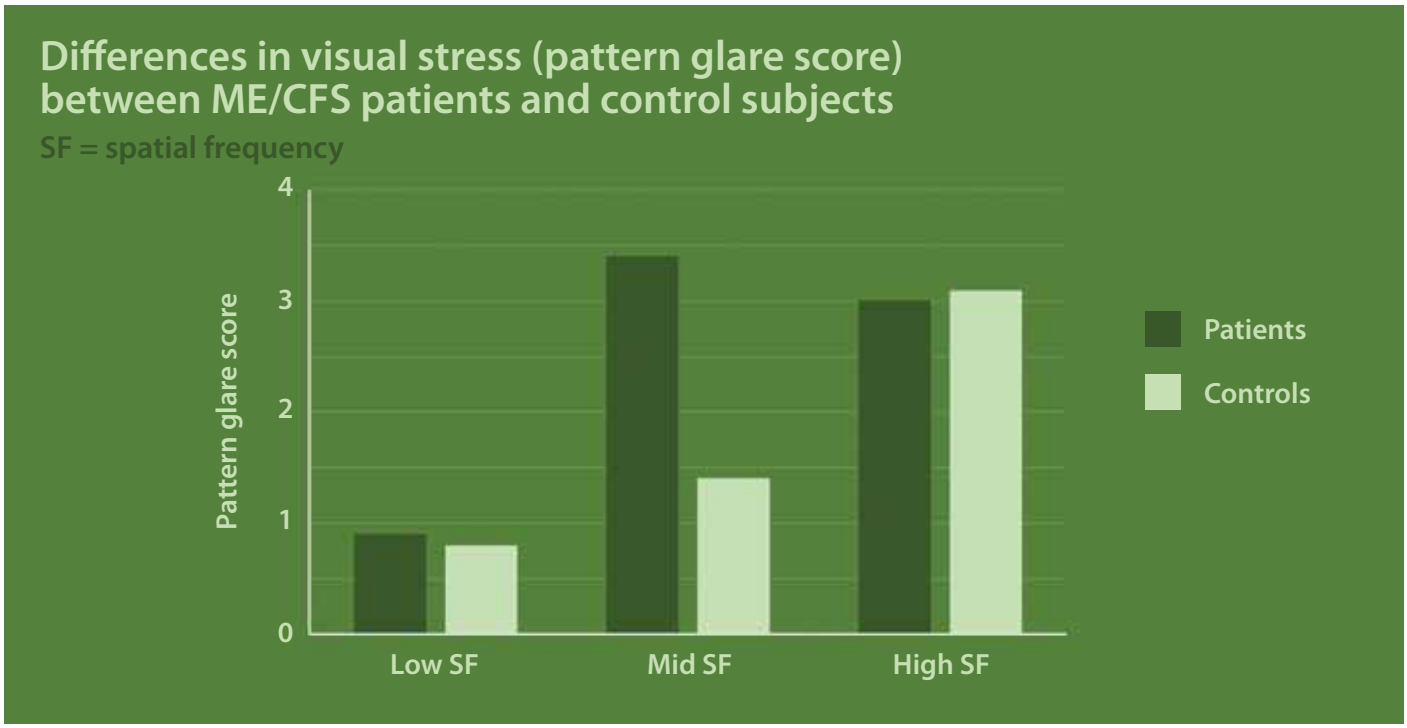
Researchers in Leicester explore the link between visual stress and **discomfort during reading** in ME/CFS patients

Problems with eyes and vision occur in around three-quarters of people with ME/CFS, yet these symptoms are rarely mentioned in scientific reports. Since 2012, Dr Claire Hutchinson and colleagues at the Vision and Language Research Group, University of Leicester have been working to identify and quantify vision-related problems in the disease. The Leicester programme was initiated with funding from ME Research UK and the Irish ME Trust, and has resulted in three robust scientific papers showing that ME/CFS patients perform worse than matched controls across three specific aspects of vision – scanning, keeping attention on a target, and moving attention towards it. Patients also had a problem with eye movement itself, and vision-related symptoms (sensitivity to bright lights, problems focusing, and eye pain) were shown to be significant clinical features which were severe in more than 30% of patients.

Pattern-related visual stress

In 2014, we gave additional funding to the team to investigate visual discomfort during reading, a common activity which is important for optimal quality of life but which many people with ME/CFS find difficult. The first short report from this project has now been published in the journal *Perception*.

The research team aimed to determine whether ME/CFS patients experience "pattern-related visual stress", a form of visual hypersensitivity to patterns, such as a page of words. This is also known as Meares-Irlen syndrome after the two researchers who first noticed a connection between reading difficulties and the glare of a white page. Typically, this visual stress causes distortions of print, including text that appears to jump, swirling effects, and letters that can double, fade or blur. Pattern-related visual stress is associated with symptoms such as difficulty focusing, poor



"Cortical abnormalities may be involved in the visual stress experienced by ME/CFS patients."

depth perception, and reading-related headaches, all of which seem relatively common in ME/CFS.

Pattern Glare Test

In the current investigation, 20 ME/CFS patients and 20 control subjects took the standardised Pattern Glare Test, which involves reporting the number of visual distortions experienced when looking at three repetitive striped patterns of different levels of detail: low, mid or high spatial freqency (SF). The basic findings were that few visual distortions were reported by either group at the low SF pattern where distortion is relatively mild, while both groups reported distortions at the high SF pattern where distortions are relatively extreme.

It was in the mid SF pattern that differences between the groups were observed, indicating increased susceptibility to visual stress (see the graph above). Also, the differences in the pattern glare score between mid and high SFs were significantly higher in the patients than in the controls. In effect, patients with ME/CFS experienced the kind of distortions in the mid SF pattern that healthy people experience at the high SF pattern.

Cortical abnormalities

So, why do ME/CFS patients experience visual stress? Dr Hutchinson and colleagues speculate that cortical abnormalities in the brain may be involved, based on observations of visual stress in other neurological illnesses including stroke and migraine (see page 17 of this issue of *Breakthrough*). If neurotransmission in the visual cortex is impaired, as seems possible, it would chime with the views of some scientists that chemical neurotransmission is abnormal in this disease.

This report adds to the growing body of evidence that problems with eyes and vision are important in ME/CFS. Dr Neil Abbot said in the Leicester University press release: "Dr Claire Hutchinson and her team have previously confirmed the existence of eye movement difficulties in ME/CFS patients, and that symptoms, including eye pain, can be severe. Her new report in *Perception* extends these findings and raises the possibility that vision anomalies, including pattern-related visual stress, may come to have a diagnostic role in the disease." In fact, it may be time to include these symptoms in clinical and diagnostic guidelines, such as the NICE Guideline in the UK. ●

MPhil student, **Rachel Wilson**, flanked by her supervisors **Dr Claire Hutchinson** and **Dr Kevin Paterson** from the University of Leicester

What do we already know?
Signs and symptoms in the eyes

Despite the impact of visual problems on ME/CFS patients' quality of life, before Dr Hutchinson started her research in 2012, only a small number of studies had been conducted in this area.

Two papers were published in the early 1990s reporting ocular symptoms in ME/CFS. The first was a survey that found a range of eye-related symptoms in ME/CFS patients, including functional problems, neurosensory symptoms (such as headaches and light sensitivity), entoptic phenomena (such as floaters) and anterior segment abnormalities (related to tears). In the second study, patients reported a range of eye symptoms, the most common being abnormalities of the pre-ocular tear film and ocular surface, reduced accommodation for age, and dry eyes.

Later in the decade, two more reports appeared. One reported symptoms ranging from mild accommodation dysfunction to debilitating disability, while the other reviewed the visual and ocular signs and symptoms of ME/CFS patients, and discussed several management options.

Two further reports appeared between 2000 and 2010, the first describing significant eye impairments in patients compared with controls, including foggy/shadowed vision and sensitivity to light, as well as problems of eyeball movement and tear deficiency. The second noted vascular pathology of the eye and dystrophic pathology in a significant proportion of ME/CFS patients.

These six relatively small reviews and studies probably represent the sum total of observations and research on visual dysfunction in ME/CFS before 2012, even though eye symptoms are a great concern for most patients.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WINDOW ON THE YOUNG

A new study searching for **neurological biomarkers** is investigating the response to mental exertion in youngsters with ME/CFS

Illness in youngsters has a particular poignancy; the transformation of a bright, active child into one who is unable to go to school or play with friends is something that touches everyone. There are few, if any, good estimates of the numbers of children and young people with ME/CFS, but it is likely that many thousands in the UK and USA have this diagnosis. The famous report to the Chief Medical Officer of England in 2002 pointed out that the illness "represents a substantial problem in the young" and "potentially threatens physical, emotional, and intellectual development of children and young people, and can disrupt education and social and family life, at a particularly vulnerable time of life".

For these reasons, scientific investigations of ME/CFS in young people are urgently needed, and may well result in important findings. ME Research UK-funded researchers at the University of Dundee, for example, have found biomedical anomalies in children with ME/CFS – increased oxidative stress and increased white blood cell apoptosis (or programmed cell death) – similar to those seen in adults with the illness. They also found that the children's quality of life was profoundly reduced compared with their healthy peers, and was worse than the quality of life reported in children with type 1 diabetes or asthma.

Neurocognitive difficulties

We already know that adults with ME/CFS have difficulties with memory, with processing information, and with concentration or attention. The memory problems include difficulties with visual or verbal memory, short-term and long-term recall, and mental clouding (so-called "brain fog"). These have significant effects on daily functioning at home or work, as most patients know. However,

Dr Sarah Knight of the Murdoch Children's Research Institute, Melbourne, Australia

much less is known about these neurocognitive difficulties in youngsters, particularly the role of mental exertion in worsening these symptoms. In fact, advanced structural and functional neuroimaging techniques have only rarely been applied to understanding the impact of ME/CFS on the function of the developing brain.

For this reason, ME Research UK has awarded funding to Dr Sarah Knight and her colleagues of the Murdoch Children's Research Institute in Melbourne, Australia, to examine how the brain responds to mental exertion in adolescents with ME/CFS, using neuroimaging techniques including fMRI (see below).

Functional neuroimaging

Professor Knight and colleagues lead a growing paediatric ME/CFS clinical research programme – the only one of its kind in Australia, and one of the very few in the world – which is dedicated to improving the lives of these children and adolescents. For this study, 25 adolescents with ME/CFS (diagnosed using the Canadian Clinical Criteria adapted for paediatricians) and 25 matched healthy control subjects will undergo functional neuroimaging, followed by 90 minutes of structured effortful thinking and learning activities similar to school work or home work, after which another brain scan will take place.

The aim is to combine sophisticated brain imaging techniques with cognitive assessments to examine the underlying brain function in these adolescent patients who are suffering from ME/CFS at a critical time in their development, and are at risk of significant long-term consequences affecting their academic and social activities. ●

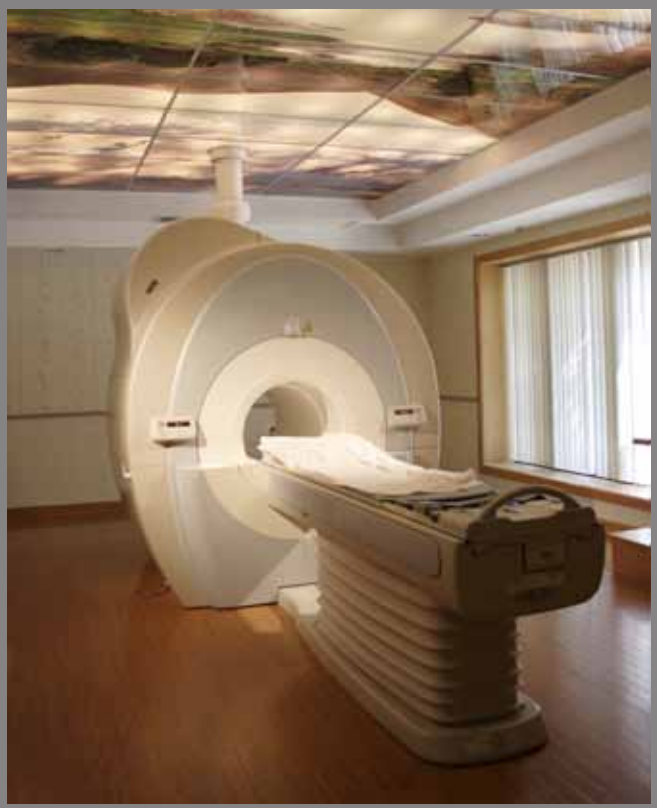
In more depth
What is functional magnetic resonance imaging (fMRI)?

Standard structural imaging uses various techniques to picture directly or indirectly the 'hardware' of the brain, such as the skull and cranial tissue. It is useful in the diagnosis of larger-scale diseases such as tumours or intracranial head injuries.

By contrast, functional imaging allows direct visualisation of the processing of information by the brain. fMRI works by detecting changes associated with blood flow; specific areas of the brain increase their metabolism (and their blood flow) when the brain is processing information, and these can be seen to 'light up' on the scan.

This makes the technique useful for identifying changes associated with stroke or more subtle metabolic disorders, although its major use is in medical research for measuring and mapping brain activity in health and disease.

fMRI has rarely been used in ME/CFS research, but the few controlled studies conducted (all of them on adults) have revealed that brain activation during mental exertion is increased or more widespread in patients than in healthy people.



the right connection

More new research investigating the **genetics of pain**

Chronic pain is debilitating and very common. Between 80 and 90% of people with ME/CFS report severe pain and/or muscle or joint pain. In recent years, it has become clearer that the inhibition of pain by the brain – something that occurs naturally every time we move – is impaired in people with ME/CFS. This is in line with the view that hypersensitivity of the central nervous system is involved in the disease, a phenomenon called central sensitivity.

To unravel the mechanisms of the pain associated with central sensitivity, we need to examine factors known to increase it. One such factor is brain-derived neurotrophic factor (BDNF), a protein which is produced by a variety of cells, including sensory neurons, motor neurons, and immune cells (i.e. white blood cells). In general, BDNF is a key regulator of connections (synapses) between nerve cells in the peripheral and central nervous system (i.e. spinal cord and brain regions such as the hippocampus and cortex), and increases the sensitivity of pain pathways.

Epigenetics

Genetics is concerned with changes to sequences of DNA which are then inherited. However, a relatively new discipline, epigenetics, has shown that changes in gene expression (the way information from a gene is used to make proteins) can be affected by other factors and processes, including childhood development, drugs, diet or the aging process. In particular, epigenetic modifications (DNA methylation, for example) can affect the function of genes over the long term, and may be involved in a range of illnesses, such as diabetes and cancer.

Prof. Lode Godderis from the University of Leuven

Epigenetic research is in its infancy in ME/CFS, but one recent analysis of epigenetic modifications of DNA found immune cell regulation to be different in ME/CFS patients and healthy people. Applying an epigenetic perspective to the understanding of pain may well be fruitful and lead to new strategies for treating pain in this illness. ME Research UK has funded a cross-disciplinary team of researchers, including Prof. Lode Godderis at the University of Leuven and Prof. Jo Nijs at Vrije Universiteit Brussels, to investigate the presence of epigenetic changes in the BDNF gene, and determine whether these changes are more prevalent in ME/CFS patients.

Given the current understanding of BDNF's role in central sensitization, their hypothesis is that epigenetic activation of the BDNF gene is related to the pain that people experience. All study participants (20 ME/CFS patients and 20 healthy controls) will attend the university hospital for two consecutive times in four days for epigenetic analysis blood sampling. They will also complete outcome measures for the quantification of pain inhibition and facilitation, and for the assessment of real time physical activity and symptoms. In addition, differences in epigenetic methylation pattern and stability over time will be related to changes in pain and symptom fluctuations.

Research bites

Our round-up of recent research from around the world

Problems standing upright

Eyskens et al., Journal of Rehabilitation Research & Development, 2015

One of the key difficulties that ME/CFS patients face is standing (orthostasis), particularly standing still. For them, simply being upright can trigger a cluster of symptoms, such as dizziness, altered vision, nausea, fatigue, headache or sweating. This orthostatic intolerance can have many causes, and researchers at Antwerp University Hospital decided to test whether a lack of endurance in the muscles of the trunk, which maintain the upright position, may be involved.

For the study, the investigators recruited 72 women with ME/CFS, 30 with osteoporosis (who also have standing problems) and 55 healthy women. All underwent a timed-loaded standing test which measures how long a person can hold a 1-kg dumbbell in each hand with straight arms. This test assesses combined trunk and arm endurance, and is intended to simulate the performance of the torso during everyday activities. As expected, timed-loaded standing was significantly shorter in patients with osteoporosis (84.5 seconds on average) than in the healthy women (165 seconds). In women with ME/CFS, however, timed-loaded standing was significantly shorter (50 seconds) than in either of these groups. The authors note that ME/CFS patients' problems with standing upright and physical activity is similar to the experiences of patients with osteoporosis, in that both groups of patients have problems keeping their spines vertical. This, and the specific biomechanical weakness the researchers identified in the women with ME/CFS, needs urgent investigation.

A link with migraine?

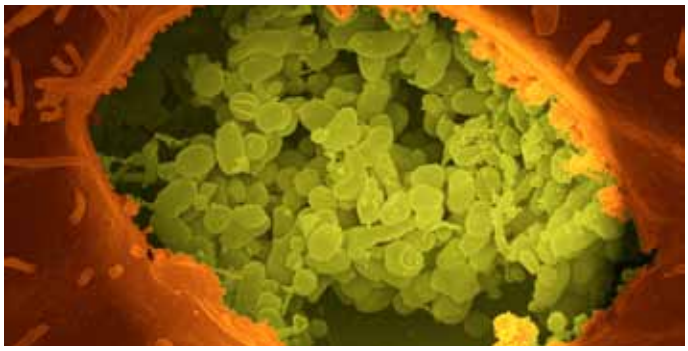
Lau et al., Journal of Psychosomatic Research, 2015

New-onset headaches, including migraines, are relatively common in ME/CFS. But what is the link between the two, and does the presence of migraine increase the risk of having ME/CFS? To explore the issue, researchers interrogated the Taiwanese National Health Insurance Research Database, identifying 6,902 newly diagnosed migraine cases and 27,608 migraine-free people for comparison. Overall, the risk of having ME/CFS was 1.5-fold higher in those with migraine, and was greatest in people aged 65 or older. To the researchers, this small but significant association points to an overlap between the two apparently distinct disorders, possibly involving mitochondrial dysfunction or hypersensitivity of the central nervous system.

Diagnosis from the face?

Chen et al., Computers in Biology and Medicine, 2015

Can ME/CFS be diagnosed from the face? Traditional Chinese medicine experts identified features which they thought might do this – vertical striped wrinkles on the forehead, puffiness of the lower eyelid, greyness of the forehead, less red cheeks and nose, and a mouth sloping downwards at the edge! The technique was put to the test by the Guangdong University of Technology using facial images of 294 ME/CFS patients and 297 healthy controls – and was 89% accurate. Of course, the technique is most likely to be assessing the facial characteristics of any group of chronically ill people, and mood and character will also be involved. If only making a diagnosis *was* as simple as reading a photo electronically!



Long-term illness after infection

Limonard et al., Epidemiology and Infection, 2015

Q fever is caused by the bacterium *Coxiella burnetii* and is linked to intensified goat farming. It is also a well-recognised cause of an ME-like illness, particularly in Australia and Canada. There was an outbreak of Q fever in the Netherlands in 2007, and Dutch researchers have been following the progress of infected patients ever since. Their latest report shows that four years after the primary infection, 35% of patients still have severe symptoms, and half have a severely affected quality of life. Follow-up studies like this are important because they confirm that simple contact with bacterial and viral pathogens really can lead to protracted, chronic, ME-like illnesses in significant numbers of people.

CBT not the answer

Patient survey, ME Association, 2015

The specialist care recommended by the NICE Guideline consists mainly of cognitive–behavioural therapy (CBT) and graded exercise. Many ME/CFS patients have since been prescribed courses involving these NICE-endorsed therapies. Thanks to the Illness Management Survey conducted by the ME Association recently, we now have an idea of how useful these courses have been. Overall, CBT courses made little or no difference to the severity of illness in most cases, while graded exercise was associated with a worsening of symptoms. Neither resulted in significant reductions in claims for state benefits. These findings reiterate that the main therapies recommended by NICE are not an answer for the great majority of people with ME.

ME/CFS as an infectious disease?

Underhill et al., Medical Hypotheses, 2015

In many people, ME/CFS develops suddenly, most commonly after a viral or bacterial infection, and is the start of a long period of chronic illness. This is why it is often considered an infectious disease, and a valuable new review by Dr Rosemary Underhill has brought together the clinical, immunological and epidemiological evidence supporting that view. It weaves together evidence from historical cluster outbreaks with recent studies on the sporadic cases most often seen today. The review points out that, in sporadic cases, immunological changes (including Th2 responses and defects in cell-mediated immunity) resemble the changes found in other infectious diseases, such as tuberculosis or cytomegalovirus infections. Also, there is evidence of transmission from person to person, including within families, although only a minority of close contacts of patients develop the illness. As Dr Underhill explains, "The clinical picture and course of the illness in outbreak and sporadic patients… is characteristic of an infectious disease which becomes chronic in some patients. The chronicity of the illness suggests a persisting pathogen." Finding that pathogen remains the Holy Grail.

Impact on brothers and sisters

Velleman et al., Clinical Child Psychology and Psychiatry, 2015

We all know that ME/CFS has a profound impact on the lives of youngsters, but what effect does it have on their brothers or sisters? Researchers at the University of Bristol sent standard questionnaires to the siblings of young patients, and compared the results with the general population of children. The siblings' quality of life was not affected, and nor were they more depressed, although they had higher levels of anxiety than adolescents of the same age. Nine siblings were interviewed in more depth, and all described "restrictions on family life" as a problem for their family, while most mentioned the personal impact of "changes of role or focus" and emotional reactions such as worry or frustration.

Vaccination questions

Magnus et al., Vaccine, 2015

A few people with ME/CFS say that their illness started following vaccination or immunization, including vaccination against influenza. There was a mass vaccination programme in Norway during the 2009 influenza A (subtype H1N1) pandemic in 2009, and the data collected has given researchers in Oslo a unique opportunity to compare the risk of ME/CFS after influenza and after vaccination itself. The people who developed influenza during the peak pandemic period were twice as likely as others to go on to develop ME/CFS. However, pandemic vaccination itself was not associated with an increased risk of the illness – welcome news at the population level since millions of doses of the vaccine were delivered during the outbreak.

"The clinical picture and course of the illness… is characteristic of an infectious disease"

Erectile dysfunction

Chao et al., Andrology, 2015

Chronic illness can affect sexual function in men, so researchers at the China Medical University examined erectile dysfunction in ME/CFS. In total, 1,976 male patients (newly diagnosed between 2003 and 2006) were compared with 7,898 healthy men, and the data cross-matched with patients diagnosed with organic erectile dysfunction. After excluding from the analysis other conditions associated with erectile problems, such as cardiovascular disease or depression, men with ME/CFS were almost four times more likely to have a diagnosis of organic erectile dysfunction than controls. Male sexual function is linked with the autonomic nervous system, of course, and autonomic problems are known to feature prominently in ME/CFS.

A case of intracranial hypertension

Higgins et al., Journal of Neurological Surgery Reports, 2015

Misdiagnosis remains a problem in ME/CFS. Researchers at Addenbrooke's Hospital, Cambridge examined a 49-year-old woman with "a long and debilitating history" of post-viral ME/CFS who was having specific investigations for headache. After lumbar puncture and cerebrospinal fluid drainage, she was diagnosed with borderline idiopathic intracranial hypertension, and further investigation showed narrowing at the transverse sinuses which allow blood to drain from the head. The authors say that treatment resulted in a remission of symptoms lasting at least two years. The report reiterates the need for ME/CFS patients to have proper clinical examinations, and for the diagnosis to be reassessed regularly.

Ed Dunkerley still looking fresh after his mountain marathon

Friends united

Some of the many activities undertaken by our supporters to raise funds for ME research.

Ed – the mountain king

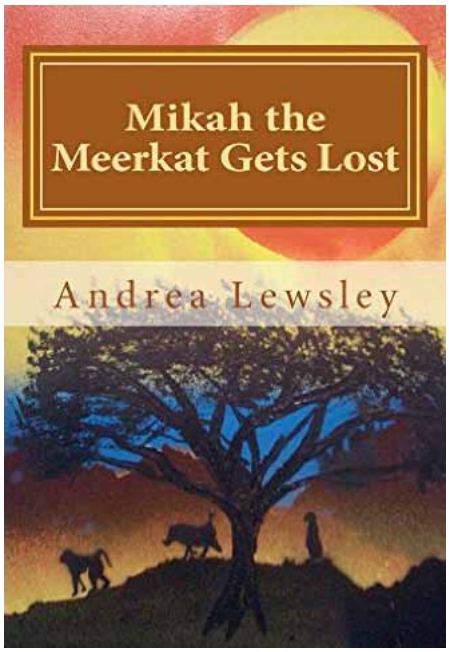
Glencoe was the scene of a famous massacre in 1692, but it now hosts one of the toughest marathons: 26.2 miles over a very challenging terrain, with a cumulative ascent of 1.6 km including a gruelling 500-metre climb over the fearsome Aonach Eagach Ridge. But ME Research UK Trustee, Ed Dunkerley, rose to the challenge, training by bagging a Munro and doing a 20-mile run that included the Devils Staircase. On the day, he successfully completed the mountain marathon in 4 hours, 48 minutes, finishing in the top 100 runners from all over the world.

All the right notes

One of the North's finest organists, Greg Smith, gave an organ recital at St Columba Church, Topcliffe in October. Greg has performed in many venues including the Royal Festival Hall, and the audience was treated to a wonderful programme of music on a magnificent Willis organ, including works by Bach, Buxtehude and Walton. Entrance was free, but ME Research UK Ambassador, Alan Nuttal, had arranged for donations received to come to the charity.

Emily's elves

Emily's Elves were running as a team in Morrison's Great South Run in memory of "the beautiful, kind and vibrant Emily Gregg" who lived with ME for many years. Emily was herself an enthusiastic runner, and taking part was a great way of paying tribute to her life. The elves raised many thou-



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01 Read more about Mikah and friends by **Andrea Lewsley**

02 Emily's Elves show off their well-deserved medals

03 Greg Smith at the keyboard for a programme of Bach, Buxtehude and Walton

04 Manny Vidi shortly after crossing the finishing line

sands of pounds, and say, "If Emily was still here, she'd have been running with us, and would certainly have beaten everyone to the finish line."

"Simples"

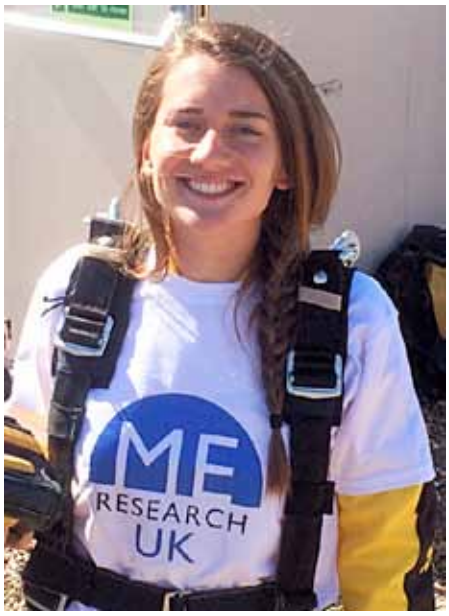
Author Andrea Lewsley has kindly agreed to donate a proportion of the royalties from her book *Mikah the Meerkat Gets Lost* to ME Research UK. The story revolves around Mikah and newly discovered friend Tilly as they face puff adders, lions and "hoomans". Andrea has penned this enchanting tale of friendship and adventure for children aged 5 to 8 years, but the book can be enjoyed at any age, and is available in paperback and Kindle editions.

Bristol to Bath marathon

Manny Vidi recently ran the Bristol Half Marathon for us, a personal challenge as he was recovering from a ruptured Achilles tendon. Then he went an extra 13 miles by completing the Bristol to Bath Marathon – in a time of 4 hours 24 minutes, far better than he ever expected. As he says, "Until 4 years ago, I had never run more than a couple of miles without gasping for breath, so I'm quite proud." Manny is a friend of Naomi Whittingham, whose brother Tom has made a moving film about the illness that can still be seen on YouTube.

More tea?

Enjoying the summer sun and, incidentally, some very nice looking strawberry fancies, friends and family of Kim Wellens gathered for a Tea for ME event on our behalf – and a great time was had by all. Holding a Tea for ME event is a great way to raise awareness of ME, enjoy some good cake and help our cause. The Tea for ME page on our website has some fabulous ideas and a few mouth-wateringly good recipes to help your event reach High Tea level.



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05 Lucinda Inman is a mixture of nerves and excitement as she looks forward to her 15,000-ft dive

06 More controlled falling as **Dan Hanslow** completes the Highland Fling

07 Nicholas Pearson completes the cycling leg of the London Triathlon

08 Inspired by **Kim Wellens**' Tea for ME event? Why not organise your own?

Highland Fling

Billed as the most spectacular scenic Bungee jump in the UK, the Highland Fling is a once-in-a-lifetime free-fall experience heading towards water at over 50 mph! Dan Hanslow, husband of Ambassador Rochelle, threw himself into fundraising for us at Killiecrankie, the scene of the famous Perthshire battle in 1689. Rochelle, with Dan's help, also organised a craft fayre at the Macrobert Art Centre, University of Stirling, and we were on hand to sell our range of Christmas cards.

London pride

Nicholas Pearson and team mate Rob 'Molerat' Thurmott completed the 2015 London Triathlon in support of ME Research UK. The triathlon involved a 1,500-metre swim, 40-km bike ride and 10-km run. Nicholas told us, "I'm happy to say that I completed the event in 2 hours, 37 minutes and 18 seconds, well beyond anything I thought I was capable of. Without a doubt, the generosity of the supporters who sponsored me helped drag me over the line. I gave it everything!"

Lucinda's skydive

The recent Guinness World Record attempt to grab back the tandem skydiving record was unfortunately scuppered by the weather. However, ME Research UK supporter and ME sufferer Lucinda Inman (who is a student at the University of the West of England) was undeterred. She re-booked at Dunkeswell Aerodrome in East Devon, and made the jump from 15,000 feet, the highest you can go without using an oxygen supply. Lucinda certainly looks like she enjoyed the experience.

Standing Order Form

To allow us to press ahead with our mission to Energise ME Research globally, please consider setting up a Standing Order by completing this form and sending it to: **ME Research UK, The Gateway, North Methven Street, Perth PH1 5PP**.

Name of account holder(s)

Address

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Telephone number

Name of Bank or Building Society

Branch address

Branch postcode

Instruction to your Bank or Building Society

To the Manager, Please arrange to debit my/our account with the amount detailed below, once every month until further notice.

Account number

Branch sort code

Debit amount (£)

Payment date each month

Date of first payment

Pay to: Clydesdale Bank, 158/162 High Street, Perth PH1 5PQ, UK, Account: ME Research UK, Account no: 50419466, Branch code: 82-67-09

☐ ***Tick*** *if you would like us to treat this, any future donations to ME Research UK (SC036942), and all payments in the previous 4 years, as Gift Aid donations, meaning your donation can increase in value by a quarter at no extra cost to you. You confirm that you are a UK taxpayer and understand that if you pay less Income Tax and/or Capital Gains Tax than the amount of Gift Aid claimed on all your donations in that tax year it is your responsibility to pay any difference. Please notify us if you wish to cancel this declaration, change your name or home address, or no longer pay sufficient tax on your income and/or capital gains. If you pay Income Tax at the higher or additional rate and want to receive the additional tax relief due to you, you must include all your Gift Aid donations on your Self-Assessment tax return or ask HM Revenue and Customs to adjust your tax code.*

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