

NEWS OF THE ME RESEARCH YOU ARE HELPING TO FUND

breakthrough



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Breakthrough magazine is published by ME Research UK, a Scottish Charitable Incorporated Organisation with the principal aim of commissioning and funding high-quality scientific (biomedical) investigation into the causes, consequences and treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). We influence, inform and invest in ME research globally by identifying potentially important areas for future biomedical research, and by producing high quality professional reviews and reports. *Breakthrough* is an open-access publication and, apart from images and illustrations, the content may be reproduced free of charge, subject to the terms and conditions found at meres.uk/bt-terms.

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In the spotlight

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

Editorial

Welcome to the autumn 2023 issue of *Breakthrough* magazine. Last issue, I reported that we had reached £3 million in research funding since our inception as a charity. I am delighted that just six months later we have committed to fund eight new studies and our total research funding now stands at just over £4 million. A summary of our research funding to date and the new studies are included in this issue.

We have also just launched an initiative to identify and fund a research fellowship in collaboration with the Daphne Jackson Trust, adding further impetus to our drive to support new and existing researchers to enter and remain in the field of ME/CFS research. I hope we will be updating you with positive news on this initiative soon.

Of course everything we do is only possible as a result of your support and we are indebted for it. This issue has some wonderful examples of the fundraising activities undertaken allowing us to continue our work on your behalf. I also want to highlight the annual Big Give campaign, where every pound donated will be matched – potentially doub-

ling every donation made. This campaign raised almost £25,000 of much-needed funds last year, every penny of which is committed to research funding.

We have received Cort Johnson's latest 'Postcard from Nevada' in which he sets out a compelling case for our place in the ME/CFS research funding landscape – and says it far better than I could.

Finally, August saw the publication of the DHSC interim delivery plan on ME/CFS. We have set out the key elements of the plan and our views on it. We continue to be actively and constructively engaged in this process, and are doing our level best to effect positive change for everyone who has been affected by the disease. I urge you to engage in the consultation process, as we are (open until 4 October, using the link: bit.ly/3YvBycx).

Thank you for your continued support and I hope you enjoy this issue of *Breakthrough*. (PS Christmas is just around the corner and our 2023 range of cards is available to purchase online, by post or telephone!)

Jonathan Davies
Chair, Board of Trustees

Christmas cards 2023

Our Christmas cards are now available to order (for residents of GB, the Isle of Man and the Channel Islands only).

There's a great selection to choose from, and you can also order online at shop.mereseearch.org.uk. As always, the proceeds go to help support our work.

If you would prefer not to send a physical card, dontsendmeacard.com has a good selection of digital cards and allows you to donate to us.





The Big Give

The Big Give Christmas Challenge is the UK's largest matched-funding campaign, and ME Research UK is taking part again this year.

Supporters have already pledged £8,675, so the first £8,675 of donations made on the Big Give's website from midday on 28 November until midday on 5 December 2023 will be matched by the pledgers – potentially doubling every donation made.

We may also be chosen for Charity Champion funding, which would add a further £8,675 to the pledge pot.

Information on how to make a donation will be on our website and social media during the campaign. As always, all funds raised will be invested in ME research globally.



The full reality?

The DHSC interim delivery plan on ME/CFS

My full reality: the interim delivery plan on ME/CFS was published by the Department of Health and Social Care (DHSC) on 9 August 2023. Consultation on the plan is now open until 4 October.

The document was developed around three key themes: research, attitudes and education of professionals, and living with ME/CFS. Within each of the themes, the report summarises issues and makes recommendations for improvements.

While this plan provides a much-needed review of the global funding landscape for research into ME/CFS, it falls short in a number of areas, most significantly:

- The plan adds little new.
- There is no commitment to ring-fence dedicated funding

for ME/CFS research.

- There are no strategies to keep established researchers in the field or to encourage early career researchers to specialise in ME/CFS.

The box on the right sets out the major limitations of the plan relating to research in more detail.

There are positive aspects to the plan, which shows a welcome level of commitment to lay the foundations of advancing research into ME/CFS. However, unless there is a commitment to more funding, little will change.

While critical issues are highlighted, there is little new. The central issues facing ME/CFS biomedical research are already well known, and have been for decades. The Gibson Inquiry report highlighted them in 2006, and yet research remains under-



funded seventeen years later.

The plan suggests that failures in ME/CFS research are due largely to researchers themselves, rather than the chronic under-funding that has hampered them for years. The focus is on moulding new grant applications into a form that will achieve the MRC's standard for success, rather than providing reassurances as to the funds required to transform the research landscape.

In order to increase research capacity, there must be dedicated funding schemes, not only to retain highly regarded senior academics, but also to attract new and skilled scientists to the field of ME/CFS research.

That is the glaring omission in this interim delivery plan, and ME Research UK will continue to push for a commitment to more research funding when we respond as part of the consultation process.

Limitations of the plan

- While the plan reiterates important strategies for ME/CFS, such as ensuring that the voices of people with experience of ME/CFS are heard, and the need to educate healthcare professionals, it adds little new.
- The lack of high-quality research into ME/CFS is put down to a lack of capacity among researchers. However, no funding is announced to encourage new scientists to join the field of ME/CFS research. The plan sets out no strategies to keep established researchers in the field, and to help them build capacity through multidisciplinary collaboration, and no dedicated funding to encourage early career researchers to specialise in ME/CFS research.
- There is still much work to be done in identifying specific research opportunities, and lessons ought to be taken from similar processes currently underway worldwide.
- There is no commitment to ring-fence funding for biomedical research into ME/CFS to reflect the disease's prevalence and severity, nor any attempt to redress the historic imbalance in funding which has disadvantaged those affected by the disease for decades.
- Despite its higher prevalence, functional disability and impact on wellbeing, funding for ME/CFS still does not match that for other conditions.
- The rise in ME/CFS since the emergence of COVID-19, and its impact on both current prevalence and economic burden, is not fully acknowledged. Research funding available should reflect this, but at present does not.
- Education materials for healthcare professionals are key to improving care and reducing stigma. However, currently there is inadequate high-quality research on which to base these materials, and no dedicated funding to ensure this evidence is generated.



Conference season

Researchers present new findings in Berlin and Cambridge

ME Research UK staff represented the charity at two international ME/CFS research conferences in recent months, both bringing together researchers, clinicians and experts from across the world to discuss the latest evidence and findings related to ME/CFS.

“Understand, Diagnose, Treat: ME/CFS Conference 2023” took place at Charité Universitätsmedizin Berlin in May. Among the presenters were several researchers who have been supported by funds from ME Research UK.

The conference focused on the three key areas in its title, within which a number of important aspects were highlighted: the accurate and early diagnosis of ME/CFS, with early access to treatment; the identification of

distinct symptom profiles; individualised care which takes into account the needs and circumstances of individuals; a multi-professional team approach to care; and the need to increase health professionals’ knowledge of ME/CFS.

Presentations stressed the complex, multi-system nature of ME/CFS, and how this can lead to complications in researching and treating the disease, as well as the need for more targeted treatments based on specific groups of symptoms.

We also attended the 15th Invest in ME Research International Conference in June at Hinxton Hall Conference Centre near Cambridge.

The topics discussed here mirrored many of those in Berlin, and included: the diverse,

multifactorial and complex nature of ME/CFS; viruses, in particular viral reactivation and viruses in the gut microbiome; the need to look at all areas of research relating to ME/CFS in different groups – for example, by sex, age, and length of illness; and the need for collaboration, where researchers from different areas work together.

One of the common links that ran through the presentations was metabolism, and how altered metabolism in different systems of the body, such as the immune system, can lead to a disease state such as that seen in ME/CFS.

All presenters highlighted the need for more biomedical research to better understand the mechanisms underlying the disease process in people with ME/CFS.

Dr Roger Jefcoate

Founding patron receives honorary degree

ME Research UK was delighted to hear in June this year that our founding patron, Roger Jefcoate CBE DL, had been awarded the honorary degree of Doctor of the University by the University of Buckingham.

For over sixty years Roger has worked to enhance the use of technology for people living with a disability, starting with the ten years he spent at Stoke Mandeville Hospital. This included Possum, the world's first remote-controlled system for disabled people. Roger played a key role in its development, and was instrumental in ensuring it was available to all disabled people through the NHS.

Throughout his career, Roger has given his time, knowledge and resources as an independent advisor, often on a voluntary basis knowing the financial pressures already facing those needing his help the most.

For his services to disabled people, Roger was appointed CBE in 1998, and has further served as chairman of The Princes Trust between 1990 and 1997, and as Deputy Lieutenant of Buckinghamshire since 2011. He continues to provide support

to various causes through the numerous charities he has founded or supports through the Roger and Jean Jefcoate Trust.

Roger also worked on the development of independence enhancing technology for those severely disabled at Stoke Mandeville Hospital, and later at the National Spinal Injuries Centre. The team also developed the first adapted computer and the first portable speech aid.

His philanthropic initiatives include being co-founder of Medical Detection Dogs and Canine Partners; patron of Wheelpower (the national charity for wheelchair sport), the Sequal Trust and MK SNAP; and founding patron of ME Research UK.

Both inspirational and practical, Roger and his late wife Jean established The Roger and Jean Jefcoate Trust which has awarded millions of pounds to health and disability charities nationally – including to ME Research UK.

We congratulate Roger on the recognition of his contribution to charity over many years. Asked about receiving his honorary degree, he said it was “a great honour and a lifetime highlight”.



Christmas shopping

When you shop online for Christmas this year, you could also be raising funds for ME Research UK, at no extra cost to you.

Give as You Live gives a free donation with almost every purchase you make at over 6,000 stores, including John Lewis and Argos: bit.ly/3E7LBLE

You can also use easyfundraising.org.uk which hosts some of the UK's best online stores: bit.ly/47NfVIY

Do you need to get rid of unwanted presents? eBay allows sellers to give some or all of their sale proceeds to their favourite charities: bit.ly/45E4pOk



23 years of growth

ME Research UK reaches another milestone as we top £4 million of ME/CFS research projects funded

It has been 23 years since Dr Vance Spence and Bob McRae first had the idea for a charity focused specifically on funding high-quality biomedical research into ME/CFS, the illness that had blighted their own lives, and those of many others.

Now, thanks to the generosity and fundraising efforts of many hundreds of supporters, ME Research UK has reached another milestone in its growth – the charity has now funded more than £4 million worth of ME/

CFS research studies.

Over the page, we have tried to summarise the 70 projects supported across the globe, and representing many of the most important scientific areas relevant to ME/CFS.

2023 has been a particularly busy year for the charity, and from page 12 we are excited to present eight new studies that we have agreed to support this year – putting the fruits of our supporters' hard work to good use with new, high-quality research.

As Cort Johnson points out in his article on page 17, smaller funders such as ME Research UK play an important role in supporting innovative research that might not find funding elsewhere. Pilot studies that can provide the data for researchers to take to the larger funders.

So, thank you to Vance and Bob for their vision 23 years ago. And thank you to all those supporters who have helped grow the charity into what it is today. We're not stopping here!

70 PROJECTS IN 10 COUNTRIES



70
PROJECTS



AUSTRALIA



AUSTRIA



BELGIUM



CANADA



10
COUNTRIES



9
SCIENTIFIC AREAS



£4 MILLION
INVESTED

9 SCIENTIFIC AREAS



MUSCLE
FUNCTION



CELL
METABOLISM



PAIN & PEM





FRANCE



GERMANY



SPAIN



SWEDEN



UK



USA



BRAIN &
NERVOUS SYSTEM



DIAGNOSIS



HEART &
CIRCULATION



INFECTION &
IMMUNE SYSTEM



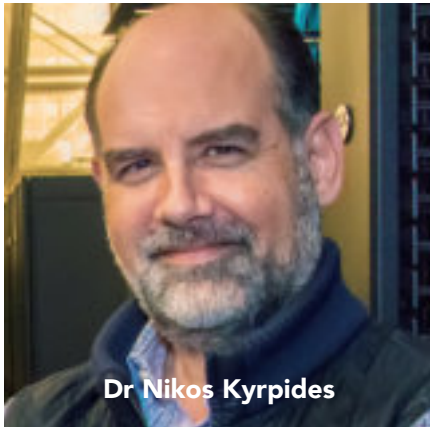
GENETICS



SYMPTOMS
& DISABILITY

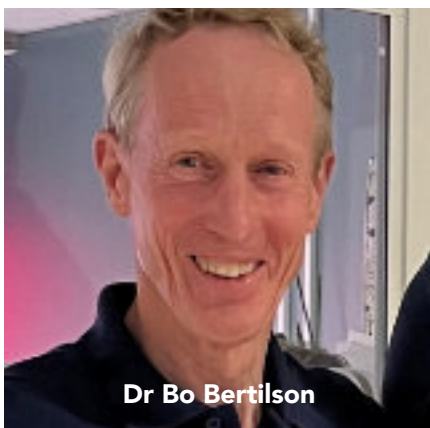
Identifying viruses in tissue and nerve samples from ME/CFS patients

- Researchers** Dr Amy Proal, Dr Nikos Kyrpides & Dr Michael VanElzakker
- Institutions** PolyBio Research Foundation, Medford; Berkeley National Laboratory, Berkeley; Massachusetts General Hospital, Boston, USA
- Aims** Dr Proal and her team are using new computer-based technologies to search for viruses in tissue and nerve samples from people with ME/CFS. The viruses most associated with ME/CFS – especially polio-type enteroviruses and herpesviruses – can infect nerves and ‘hide’ in tissue, and may therefore not clear from the body after the initial infection. The team plans to clarify if this viral activity contributes to the disease process in ME/CFS, and to identify which specific viral species are most involved. This may also help identify targeted treatments for the disease. (Financial support from the Gordon Parish Charitable Trust.)



Searching for ME/CFS biomarkers in blood and cerebrospinal fluid

- Researchers** Dr Bo Bertilson, Prof. Per Sjögren & Prof. Jonas Bergquist
- Institutions** Bragée Clinics, Stockholm; Uppsala University, Uppsala, Sweden
- Aims** Dr Bertilson and colleagues are using a technique called mass spectrometry to search for biomarkers of ME/CFS in blood plasma and cerebrospinal fluid samples from people with the disease. The team will use state-of-the-art methods to analyse proteins and metabolites in the samples, with the aim of identifying a profile of these molecules that is characteristic of ME/CFS and can help identify people with the disease. Proteins perform many critical roles in the body, while metabolites are produced during chemical processes. Identifying biomarkers of ME/CFS could improve diagnosis of the disease, as well as highlighting potential new treatment options.



Investigating spinal nerve cell function and the serotonin system in ME/CFS

Researchers Prof. Janet Taylor, Dr Christopher Latella & Prof. Anthony Blazeovich

Institution Edith Cowan University, Joondalup, Australia

Aims Reduced muscle strength in people with ME/CFS may be due to problems with the nerves that drive these muscles, specifically those nerves in the spinal cord that supply the muscle fibres and control our movements. Prof. Taylor and her team plan to record the electrical activity of these nerves during muscle contractions, comparing people with ME/CFS and control subjects. They will also look at whether any abnormalities are due to a reduced action of serotonin, a chemical that carries messages between nerves. The findings may help us better understand the muscle problems experienced by people with ME/CFS, and lead to more effective treatments.



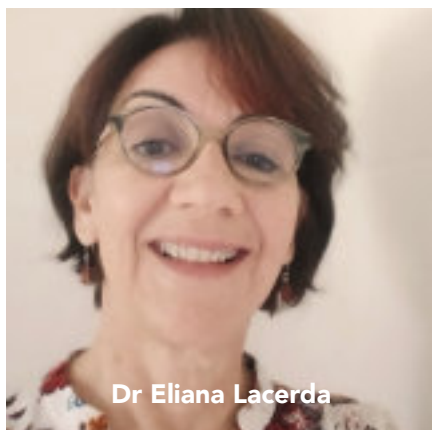
Prof. Janet Taylor

Exploring patterns of antibodies in moderate and severe ME/CFS

Researchers Dr Eliana Lacerda & Prof. Geraldine Cambridge

Institutions London School of Hygiene & Tropical Medicine; University College London, UK

Aims One potential explanation for many of the features of ME/CFS is that the body's immune system is attacking damaged proteins, some of which are involved in generating energy. These proteins may be damaged by an excess of toxic molecules (reactive oxygen species). An immune response is characterised by the production of antibodies, and Dr Lacerda and Prof. Cambridge plan to analyse the pattern of antibodies in samples from patients with moderate and severe ME/CFS, linking them to changes in specific proteins. Their results may form the basis of new diagnostic tools for the disease, including stratification of patients based on severity.



Dr Eliana Lacerda

Using MRI to assess brain neuroinflammation and the lymphatic system in ME/CFS

Researchers Dr Zack Shan, Prof. Jim Lagopoulos, Dr Peter Del Fante & Dr Richard Kwiatek

Institutions University of the Sunshine Coast, Birtinya, Australia

Aims Dr Shan and colleagues are conducting the world's first controlled study directly assessing neuroinflammation in the brains of people with ME/CFS. Neuroinflammation occurs when the brain's immune system is activated, and is believed to play an important role in ME/CFS. The team's advanced imaging techniques mean they can analyse several aspects of this, including microglia and astrocytes (the immune cells of the brain), the lymphatic system, and various neurometabolites. Their results will provide evidence of whether neuroinflammation is a factor in ME/CFS, and could point to treatments. (Financial support from the Davies Bequest.)



Do gut viruses have a role in the development of ME/CFS?

Researchers Prof. Simon Carding, Dr Penny Powell, Dr Jonathan Kerr & Prof. Elisa Oltra Garcia

Institutions Quadram Institute, Norwich, UK; Universidad Catolica de Valencia, Spain

Aims Our gut is home to many bacteria and viruses comprising the microbiome, which is vital for maintaining health, providing essential nutrients and vitamins, and boosting our immune system. Disturbances of the microbiome are seen in numerous diseases, including ME/CFS, but most studies have focused on the bacteria rather than the viruses (or virome). Prof. Carding and team plan an analysis of the gut virome in people with ME/CFS, to identify signature viruses that might be involved in the development of the disease, and could represent a new biomarker. They will also look at their response to microbiota transplantation. (Financial support from the Davies Bequest.)

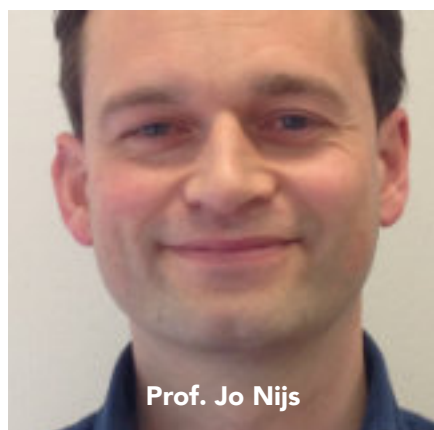


Links between mitochondrial function and the autonomic nervous system in ME/CFS

Researchers Prof. Jo Nijs, Prof. Julia Newton, Prof. Paweł Zalewski & Dr Andrea Polli

Institutions Vrije Universiteit Brussel, Belgium; Newcastle University, UK; Nicolaus Copernicus University, Poland

Aims Prof. Nijs and colleagues are investigating the relationship between two features of ME/CFS thought to contribute to its symptoms. Dysfunction of the mitochondria (responsible for energy production in cells) may be an important factor in the disease, while there is also evidence of abnormalities in the autonomic nervous system (which controls heart rate, circulation, etc.). This PhD project will compare mitochondrial function between ME/CFS patients divided according to their autonomic symptoms. As well as understanding the disease better, subgrouping patients could help improve diagnosis and treatment. (Financial support from the Davies Bequest.)



Prof. Jo Nijs

Investigating cognitive problems and brain structure and function in ME/CFS

Researchers Prof. François Jérôme Authier, Prof. Emmanuel Itti & Dr Nadia Oubaya

Institution Henry Mondor University Hospital, Créteil, France

Aims Cognitive problems (affecting memory, concentration, reading, etc.) are a common, disabling symptom of ME/CFS, and Prof. Authier and his team are investigating how these abnormalities are related to functional changes in the brain. The group will carry out a comprehensive neuropsychological evaluation and functional brain imaging in patients with ME/CFS, in order to look at the correlations between them. In particular, they are exploring whether a specific pattern of brain hypometabolism (seen in many neurodegenerative diseases) may be used as a biomarker for ME/CFS, and whether patients can be stratified according to the severity of impairment.



Prof. François Authier



Postcard from Nevada



In his latest postcard, **Cort Johnson** discusses how smaller funders provide a critical link in the ME/CFS medical research landscape

You might ask why private disease foundations fund medical research at all? Why not just let science take its course?

The big federal funders like the National Institutes of Health (NIH, with a \$45 billion budget in 2022), the European Commission (\$3.7 billion in 2016) and the UK's Medical Research Council (\$1.3 billion in 2016) bring billions of dollars or pounds to the table. Surely that's

enough?

Unfortunately, it's not. All you have to do is look at the many different private medical research foundations that exist. It's been said that if you want to make a difference, produce what's missing – and that's what private efforts do. They didn't just spring up out of the blue. They're there for a reason. They fill a gaping hole in our medical research landscape – and nowhere is that hole bigger and deeper than in diseases like ME/CFS.

The gap manifests itself in two ways: creativity and money. It may have sounded strange when Dr Walter Koroshetz, the head of the \$2.8 billion National Institute for Neurological Disorders and Stroke at the NIH, said that he didn't expect the answer for ME to come from the NIH. Even with the NIH's paltry ME/CFS funding (\$13 million per year), it's still far and away the biggest funder of ME/CFS research. So why wouldn't we expect the answer to come from it?



Cort Johnson

Big versus small funders

Because these big funders are fundamentally conservative and when it comes to ME/CFS, sometimes ignorant. The ‘expert committees’ they use to grade grant applications often don’t contain many ME/CFS experts. Because large amounts of money are at stake – a typical large NIH grant lasts 5 years and runs in the millions of dollars – they also tend to be risk averse. They want something that’s worked out.

Contrast that approach with an ME/CFS organisation that just wants answers. An organisation that intimately knows the suffering that ME/CFS imposes – that was in fact borne out of a desire to alleviate that suffering. Compare the stake that organisation has to the stake that volunteer experts on a review committee have, and you have an entirely different outlook.

You’re not willing to settle for the status quo. You’re willing to

take risks. You keep an eagle eye on the emerging research, and when something promising shows you pounce on it – and, in contrast to the federal funders, you do so quickly. You fund small pilot studies that

give researchers the data they need to approach the big boys.

How effective that approach is has been borne out in the many prominent ME/CFS researchers (David Systrom, Bhupesh Prusty, Chris Armstrong, Leigh Barnden, Amy Proal) and scores of young researchers who have been able to keep their ME/CFS work alive via small pilot grants.

Jarred Younger, though, perhaps best exemplifies how valuable this approach can be.

“An organisation that just wants answers... that’s not willing to settle for the status quo”


Younger’s first trick was to flip a small seed grant in 2011 into a multi-million dollar NIH grant to study immune functioning. Next, he turned a small ME/CFS grant on a new way to measure neuroinflammation into another big multi-year NIH grant. Now, with ME Research UK’s aid, he’s using a new technique to determine if immune cells from the body are making their way into the brain.

Younger’s last two pilot grants – the new way (thermography) to measure neuroinflammation and his immune cell tracking study – aren’t just moving the science of ME/CFS forward. They’re introducing new, cutting-edge techniques to the medical world at large and could have a profound effect on many diseases. It was no accident, though, that when Younger needed funding, he went to a private ME/CFS research foundation like ME Research UK – he knew he would get a good hearing there.

Exploring new worlds

In the private medical research world it really is about exploring new worlds and frontiers. Boldly going – could we say – where no one has gone before, and so it goes with ME Research UK’s recent grants.

Take Amy Proal’s viral nerve and muscle study, funded by ME Research UK. Viral studies in the blood are pretty much tapped out – but the nerves and the muscles, they are another



realm entirely. There's not a snowball's chance in you-know-where that a federal funder is going to pick up an exploratory study like that. Yet finding viruses nestled in tissues (something long speculated but never explored) could be a game-changer.

With a patient getting well using a TORC1 inhibitor and autophagy drawing interest in ME/CFS, Sarah Annesley's TORC1-mitochondrial study, also funded by ME Research UK, is right on the cutting edge of mitochondrial research.

Oxidative stress could be whacking cell membranes, disrupting signalling, beating up the mitochondria, etc. It is mentioned in virtually every mitochondrial study and was recently hypothesised as a possible cause of ME/CFS, yet we've seen very little on oxidative stress in ME/CFS over the past decade. Faisal Khan's ME Research UK-funded

***“It is the
private
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ME/CFS”***

ded oxidative stress study is the first in years to dig into this potentially crucially important area.

Leighton Barnden – the brainstem pioneer and another ME Research UK grantholder – is getting funded again. And guess who else is funding ME/CFS brainstem research? The NIH. There's no way that happens without Barnden's decade of work in that area.

Jarred Younger's immune cell study might just take the cake. Immune cells from the body, after all, are never supposed to end up in the brain, and when they do they can produce havoc – the kind of havoc that could explain the dreadful disability too often seen in ME/CFS. A positive finding could revolutionise what we know of the disease.

Symbiotic relationship

The private medical research efforts and the big federal efforts then feed each other. Neither works well without the other. The big medical research funders provide the funding for the really big studies needed to get the findings accepted. But they lack the creativity, the focus and the urgency of the private funders. It is the private funders like ME Research UK that are most likely to light the spark of the fire that eventually illuminates ME/CFS.

Research bites

Our round-up of recent research from around the world



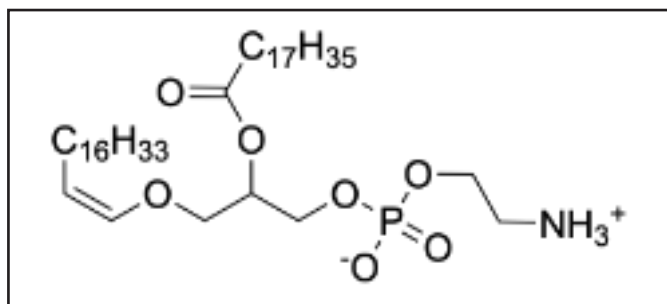
ME/CFS and Lyme disease

Bai & Richardson, Chronic Diseases and Translational Medicine, 2023

Lyme disease is a tick-borne illness caused by the bacteria *Borrelia burgdorferi*, which can usually be treated with antibiotics. However, up to 20% of cases do not resolve, leading to a collection of symptoms such as debilitating fatigue, muscle and joint pain, cognitive issues, and sleep difficulties. This is referred to as post-treatment Lyme disease syndrome (PTLDS). The underlying disease mechanism is unknown, but it is tempting to draw comparisons with ME/CFS, and this is what US researchers have done in this systematic review evaluating patients with PTLDS, and assessing overlap with ME/CFS symptoms.

The most common overlapping symptoms were

fatigue and brain fog, but 11 out of 18 studies also reported that people with PTLDS had joint pain, muscle pain and memory difficulties. In fact, most studies documented at least four out of six major ME/CFS symptoms, including post-exertional malaise and unrefreshing sleep. In one study, all participants fulfilled diagnostic criteria for ME/CFS. The authors also highlighted potential mechanisms of PTLDS which overlap with ME/CFS, namely increased levels of markers for inflammation as well as metabolic differences. This kind of approach does have its limitations, and further research is needed to validate the findings and understand the connections.



A role for plasmalogens?

Chaves-Filfo et al., Brain Res. Bulletin, 2023

Plasmalogens are a type of fat molecule which are involved in inflammation and immune processes. Reduced plasmalogen levels have been seen in people with ME/CFS, and a new study from Canada suggests that this oxidative stress may be causing damage to the plasmalogens and the structures that make them, peroxisomes. Peroxisomes are important in maintaining energy levels, so this disruption could lead to some of the key symptoms of ME/CFS. Plasmalogen replacement therapy may therefore have potential as a treatment.



Overlap with Sjögren's syndrome?

Kim et al., Journal of Clinical Medicine, 2023

Sjögren's syndrome is an autoimmune condition affecting the glands that produce fluids such as tears and saliva, but it also has other symptoms such as fatigue. This recent study from Germany investigated the symptom overlap between Sjögren's syndrome and ME/CFS, which might complicate diagnosis. While a subgroup of Sjögren's patients had more severe fatigue and pain, only four out of eighteen fulfilled Canadian Consensus Criteria for ME/CFS, largely because they didn't have post-exertional malaise that was triggered by physical activity.



Alcohol intolerance

Maciuch & Jason, World J. of Neurology, 2023

Some people with ME/CFS report an intolerance to alcohol, possibly due to autonomic dysfunction. However, attempts to investigate this have been hampered by methodological problems. Researchers from the USA recently used the DePaul questionnaire to properly identify those with alcohol intolerance. Alcohol intolerance was more common in ME/CFS patients, and symptoms (including post-exertional malaise, cognitive impairment and pain) were more severe in ME/CFS patients with alcohol intolerance than in those without.



Leaky gut

Uhde et al., Brain Behav. Immun. Health, 2023

The lining of the gut acts as a filter, allowing nutrients to enter the bloodstream but preventing harmful bacteria from making the same trip. It has been suggested that this lining could be compromised in people with ME/CFS – an idea called leaky gut syndrome. Scientists from the USA explored this possibility by looking at various markers of immune activity and intestinal damage in patients with ME/CFS. Their findings suggest increased gut damage and movement of antigens across the intestinal barrier, indicating a leaky gut that needs further investigation.

Oxidative stress in the brain

Hampilos et al., J. Clin. Transl. Sci., 2023

Oxidative stress is frequently cited as a potential mechanism of disease in ME/CFS (as well as many other conditions). Oxidative stress is an imbalance in the production of reactive substances (free radicals) and antioxidants in the body. Antioxidants can make free radicals less reactive and so less able to cause damage to tissues and organs. Researchers from the USA recently looked at whether levels of an antioxidant called glutathione are reduced in people with ME/CFS, leading to oxidative stress in the brain.

Using proton magnetic resonance spectroscopy, they measured levels of glutathione in the occipital cortex (a brain region involved in memory formation and visual processing) of 20 people with ME/CFS and 11 healthy control subjects. The patient group had lower levels of glutathione, but only in those with a specific genetic mutation: a C>T single nucleotide polymorphism (representing about 45% of the patient group). These results suggest that the presence of this mutation is associated with brain oxidative stress in ME/CFS, and that antioxidant therapy may be effective for this subgroup of patients, although the findings need to be validated in a bigger study.



A ferritin biomarker?

Yamamoto et al., J. of Clinical Medicine, 2023

Ferritin is a protein that stores iron and releases it as the body needs it, and ferritin levels are commonly tested in people with signs and symptoms of anaemia. But could it have any value in diagnosing ME/CFS? A new study from Japan found that serum levels of ferritin were significantly higher in long COVID patients who met criteria for ME/CFS than in those who did not, and levels also correlated with scores of fatigue. High ferritin levels are often found in infectious or inflammatory diseases, but the potential relationship with ME/CFS needs much further research.

Whole-body cryotherapy

Tabisz et al., British Medical Bulletin, 2023

Here's a novel approach to symptom management. Whole-body cryotherapy involves controlled exposure of the body to cold, and may have health benefits. Researchers from Poland recently reviewed the application of this therapy to a number of conditions including rheumatoid arthritis, chronic brain disorders and ME/CFS. They highlight that whole-body cryotherapy may have anti-inflammatory effects, and may therefore have value as an adjuvant therapy in conditions involving chronic inflammation. But studies so far have been of low quality, and proper clinical trials are needed.



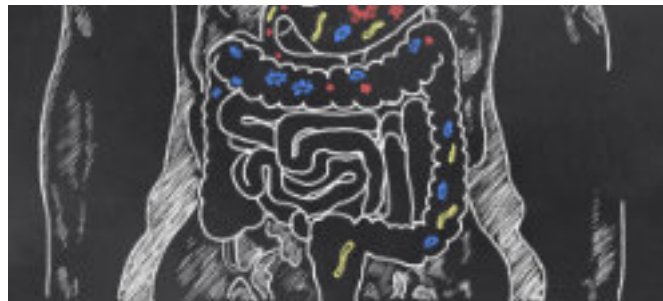
“Multiple measures of the gut microbiome were altered in ME/CFS”



Can microRNAs be used for diagnosis?

Soffriti et al., Int. J. of Molecular Science, 2023

Our last issue featured a study on the potential of microRNAs as a biomarker for ME/CFS, and here's another such study. MicroRNAs are molecules which help cells create proteins. Researchers in Italy and Latvia found significant differences in the levels of four microRNAs between patients and control subjects, and these levels were associated with more severe symptoms. Three of the microRNAs have also been found to be upregulated in ME/CFS in previous studies, but a lot more data is needed before we can make conclusions about their diagnostic potential.



Faecal microbiota transplantation

Salonen et al., J. of Translational Med., 2023

Elsewhere in this issue we have reported on a new study from Prof. Carding in Norwich, who is looking at gut viruses and their response to faecal microbiota transplantation. This treatment aims to rebalance the gut microbiome (comprising various bacteria and viruses) and may be an effective strategy for people with ME/CFS. This study from Finland didn't find any improvements in symptoms or quality of life following the therapy, but they included only a very small number of patients and so a trial such as Prof. Carding's in a larger sample is absolutely necessary.



Fundraising stories

Recent fundraising activities by our supporters.
To support ME Research UK, please visit our website for ideas.

I would walk 500 miles

Well, Rob Messenger is doing just that, with funds raised going to three charities. Over the course of 100 days, he will greet the sunrise on a daily 5-mile round-trip to the top of Paxton's Tower. By the end of his challenge he will have climbed the equivalent of twice the height of Mount Everest. Rob and his wife are full-time carers for their son, who is very severely affected by ME. Follow his progress: tinyurl.com/37ayrhd9

Island Trek

Another multi-day walk was recently completed by Alan Avis with friends John and 'Pinch', hiking from Ryde Pier to the Needles in the Isle of Wight over three days. The sights included 1,500 yachts competing in the annual Round the Island Race. Alan's daughter has been severely disabled with ME for half of her life, and so the friends were walking to raise funds for ME Research UK, in the hope of a cure one day.

The final route

The Celtic Wiseman cyclists are a team of ME Research UK's foremost fundraisers, and they recently completed the final route in their series of gruelling (but often picturesque) routes, with a 126-km ride in Brittany through idyllic villages and up a mist-capped mountain. Joining the team in France was Martin Wiseman himself, the original inspiration for the challenge. Thank you so much to the whole team for their incredible efforts



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01 Ali McAuley and friends with a piece of the art on display

02 Rob Messenger is getting to know Paxton's Tower really well

03 The amazing Celtic Wiseman cycle team

over the years, in which they have smashed their fundraising target.

Coffee and cakes

Fundraising for ME research doesn't have to involve exercise. There's always cakes! Many thanks to David Baxter who organised a coffee morning and raffle for North Lanarkshire Council, raising funds and

sharing information about the charity's activities.

Art exhibition

We are also grateful to artist Ali McAuley and Linden Ross who organised a charity art exhibition to raise money. "We will continue to host events and pray that one day doctors and scientists will come up with a cure." Thank you to Ali and Linden, and

everyone who donated art and bought paintings.

A decade of fundraising

Another of ME Research UK's valued fundraisers is Rob Saunders. Over more than a decade – from his 40th birthday to his 50th earlier this year – he has kept his fundraising page open for donations. Thank you, Rob, for a decade of support.



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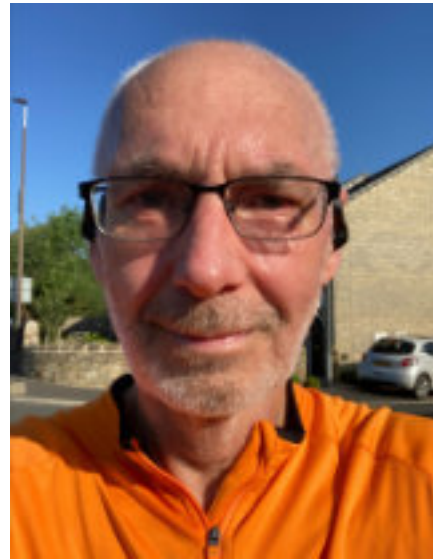
Ultra marathon

Lizzy Hodcroft ran the Yorkshire Wolds Ultra Marathon on 29 July, to raise funds for ME research, and in honor of her sister. As Lizzy says, “Running an ultra marathon is an incredibly challenging and rewarding experience. It is much longer than a standard marathon and can involve climbing mountains, navigating rugged terrain, and running in hot, cold, and wet conditions.” Congratulations and thank you so much to Lizzy for

her support, and for a fantastic sum raised for ME research.

Football fundraiser

Many thanks to the 2009 boys’ team of Motherwell Phoenix Football Club who played against a team of coaches and referees on 21 May at Ravenscraig Sports Centre, all in aid of ME Research UK. The event was inspired by Anna who has severe ME, and who loved to watch her brother, Nathan, play before she became bedbound.



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01 Motherwell Phoenix Football Club

02 Yorkshire Wolds: the setting for **Lizzy Hodcroft’s** ultra marathon

03 **Richard Heywood** sets off on a training ride

Triathlon in York

Richard Heywood took part in the UK Triathlon York event on 20 August 2023. The event involved a 400 m swim, 18 km cycle ride and finishing with a 5 km run, so in training his aim was to do 2 bike rides and 2 runs per week up until the event. Richard totally smashed his fundraising target, so many congratulations to him on a herculean effort, and thank you for your support and the amazing sum raised.

Standing Order Form

To support our work, 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**

☐ Please tick this box to indicate you are happy for us to collect and store your personal information, in accordance with our Privacy Policy at meresearch.org.uk.

Name of account holder(s)

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

Address and postcode

Debit amount (£)

Payment date each month

Telephone number

Date of first payment

Name of Bank or Building Society

Pay to: Virgin Money, St John's Centre, Perth, PH1 5UH, UK, Account: ME Research UK, a/c no: 50419466, Branch code: 82-67-09

Branch address and postcode

☐ **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.

Signature

Date



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ME Research UK
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