

information

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The MEA Ramsay Research Fund explained

One of the many problems besetting ME/CFS research is the fact that research into the underlying physical cause of the illness has not been funded by the Medical Research Council – the government-funded body that plays a major role in stimulating and funding medical research activity in the UK.

Added to this is the fact that pharmaceutical companies do not generally regard ME/CFS as a useful avenue to pursue.

The result is that almost all research carried out so far into the underlying physical cause has had to be funded by charities or individuals.

The ME Association has always regarded the promotion and funding of medical research to be one of our key priorities. We do this through our Ramsay Research Fund – named after the late Dr Melvin Ramsay, the consultant in infectious diseases who brought ME to the attention of the medical profession following an outbreak at London's Royal Free Hospital in 1955.

WHAT SORT OF RESEARCH DOES THE RAMSAY RESEARCH FUND SUPPORT?

The Ramsay Research Fund (RRF) exists to fund research that will help to provide:

- a better understanding of the underlying physical cause of ME/CFS
- a diagnostic marker or test
- an effective form of treatment

Large-scale research studies may require funding for up to three years – involving substantial outlays for both staff and equipment.. This type of funding has to be considered very carefully by our trustees as it may mean using up a large amount of the money that we are able to raise over the same period.

We also have a facility for making small research grants of up to about £2,000. This is money that could be used for a variety of purposes connected to a research study – for example, the purchase of a specific item of equipment.

HOW DO WE RAISE FUNDS FOR RESEARCH?

Most of the money comes from MEA members in the form of individual or group donations, or money left to us in a Will.

HOW MUCH DO WE SPEND ON ADMINISTRATION?

The ME Association is very aware that people who give money to research want to see it spent on research – not swallowed up in administration.

So, in legal terms, the RRF is what is called a restricted fund. This means that all of the money given to us is used for research activity. It cannot be used for any other purpose.

Unlike most other research charities, we do not employ any extra staff at Head Office to deal with the routine administration of the RRF or the research we are funding.

This is a very cost-effective method of donating money to ME/CFS research.

WHAT SORT OF RESEARCH HAS THE RAMSAY RESEARCH FUND PAID FOR IN THE PAST FEW YEARS?

Over the past 20 years, The ME Association's research funds have paid for a considerable number of important research studies.

These include:

Professor Mina Behan, Dr Fiona Curtis and colleagues at the Department of Neurology, University of Glasgow.

This study examined the role of blood-brain barrier permeability in ME/CFS. The blood-brain barrier is a cellular barrier that helps to prevent viruses and toxins that may be present in the bloodstream from passing into the brain and cerebral nervous system.

This study and the results add further weight to the view that a disruption to the blood-brain barrier at the time of an acute infection or stressor could be an important factor in the development of neurological symptoms and complications in ME/CFS.

Professor Mina Behan became seriously ill towards the end of this study and sadly died. Preliminary results have been presented at scientific conferences in London (Physiological Society) and Germany (Third Symposium on Signal Transduction in the Blood-Brain Barrier) and, although not published, the results are available to the scientific community.

Professor Ronald Chalmers and colleagues at St George's Hospital Medical School, London.

This study investigated the role of diagnostic urinary markers, urinary and plasma organic acids and amino acids, and plasma and urinary carnitine in chronic fatigue syndrome. The three key conclusions from this study were:

- ◆ Chemical compounds/markers found in the urine of people with ME/CFS – termed CFSUM1 and CFSUM2 – are artefacts of the sample preparation procedure and the presence of these urinary markers should not be used for either diagnostic or assessment purposes in people with ME/CFS.
- ◆ There are no significant differences in the levels of plasma (blood) or urinary total, free or esterified (acyl) carnitine between people with ME/CFS and controls, or in the renal excretion (ie removal by the kidneys) of these compounds. This is relevant because carnitine is a substance that helps the muscle to produce energy and carnitine supplementation has been suggested as a possible form of treatment for ME/CFS.
- ◆ Analysis of plasma and urinary organic acids and amino acids provides further evidence of an underlying inflammatory process taking place in ME/CFS and a lowered threshold for micro-injury to muscle.

Publications:

Chalmers RA *et al.* CFSUM1 and CFSUM2 in urine from patients with chronic fatigue syndrome are methodological artefacts. *Clinica*

Chimica Acta, 2006, 364, 148 - 158.

Jones M G *et al.* Urinary and plasma organic acids and amino acids in chronic fatigue syndrome. *Clinica Chimica Acta*, 2005, 361, 150 - 158.

Jones M G *et al.* Plasma and urinary carnitine and acylcarnitines in chronic fatigue syndrome. *Clinica Chimica Acta*, 2005, 173 - 177.

Dr Evaline Georgiades and colleagues at the University of Glasgow.

Study that examined the function of various brain chemical transmitters – serotonin and dopamine – during rest, exercise and recovery, and their possible role in the production of central fatigue.

The study found significant differences in the activity of substances that are involved in modulating the activity of two important brain chemical transmitters known as 5-HT (5 hydroxytryptamine) and dopamine (a chemical that is involved in Parkinson's disease). Levels of free tryptophan (a rate-limiting 5-HT precursor) were significantly higher in ME/CFS patients at exhaustion, and during recovery. Levels of tyrosine (a rate-limiting dopamine precursor) were significantly lower at all time points in comparison to controls.

The results help to increase our understanding of how abnormalities in the levels of brain chemicals may be involved in the production of brain fatigue, other neurological symptoms, and the

increased sensitivity to drugs that affect these chemicals.

Publication: Chronic fatigue syndrome: new evidence for a central fatigue disorder. *Clinical Science*, 2003, 105, 213 - 218.

Professor John Gow and colleagues at the Institute of Neurological Sciences, University of Glasgow.

Study that investigated the role of antiviral pathways and markers (ie 2-5A Synthase/RNase-L) in the assessment of people with ME/CFS.

Results indicate that assays of antiviral pathway activation (ie the RNaseL blood test) do not provide a sound basis for a diagnostic test for ME/CFS. The ME Association does not therefore recommend that people spend money on having this test carried out in the private medical sector.

Publication: Gow J W *et al.* Antiviral pathway activation in patients with chronic fatigue syndrome and acute infection. *Clinical Infectious Diseases*, 2001, 23, 2080 - 2081.

Dr Derek Pheby and colleagues at the University of the West of England.

Study that looked at factors that may be involved in the development of severe ME/CFS.

The results indicate that a number of specific factors are (or are not) involved in the development of severe ME/CFS.

Publication: Dr Pheby presented the key results from this study to a meeting of the Melvin Ramsay Society in London in April 2007. The results have been prepared for publication in a scientific journal.

Dr Vance Spence and colleagues at the University of Dundee.

Study of the role of peripheral blood vessel dilation in ME/CFS.

The study found evidence of prolonged acetylcholine-induced dilation of blood vessels in ME/CFS – possibly due to a disturbance in a part of the blood vessel wall known as the endothelium, where this chemical acts. These findings might help to explain some of the heart and blood vessel symptoms – eg lowered blood pressure on standing/postural hypotension and orthostatic intolerance – that are characteristic of ME/CFS.

Publication: Prolonged acetylcholine-induced vasodilation in the peripheral microcirculation of patients with chronic fatigue syndrome. *Clinical Psychology and Functional Imaging*, 2003, 23, 282 - 285.

Professor Graham Whitehouse and colleagues at the University of Liverpool.

Study using magnetic resonance neuro-imaging to investigate the hippocampal region of the brain. This study found significantly reduced concentrations of N-acetyl-aspartate (NAA) in the right hippocampus. NAA is an important marker of neuronal function.

The hippocampus is a part of the brain that has a critical role in working (ie short-term memory, the storage of new information, and in the retrieval of long-term information). The abnormalities identified may help to explain why people with ME/CFS often have significant problems with short-term memory, concentration, attention span and information processing.

Publication: Brooks J C *et al.* Proton magnetic resonance spectroscopy and morphometry of the hippocampus in chronic fatigue syndrome. *British Journal of Radiology*, 2000, 73, 1206 - 1208.

Rhona Wilson and colleagues at St Bartholomew's Hospital, London.

Study by dietitians into the role of dietary modification – ie a low-sugar and low-yeast/anti-candida diet – in ME/CFS.

This study failed to demonstrate any benefits from using a low sugar/low yeast diet – an approach that often forms part of the popular 'anti-candida diet' in ME/CFS. These type of dietary restrictions, along with other anti-candida measures, cannot therefore be recommended as a routine form of treatment for ME/CFS.

Publication: Hobday R A *et al.* Dietary intervention in chronic fatigue syndrome. *Journal of Human Nutrition and Dietetics*, 2008, 21, 141 - 149.

WHAT STUDIES HAVE BEEN RECENTLY COMPLETED OR ARE CURRENTLY BEING FUNDED BY THE RAMSAY RESEARCH FUND?

● GENE EXPRESSION

The Ramsay Research Fund has recently finished funding a key phase in an important study into gene expression. This was carried out by Professor John Gow and Dr Suzanne Hagan at Glasgow Caledonian University.

The aim of the study was to identify specific genes in people with ME/CFS that have become under-expressed or over-expressed – an indication of whether they are activating or suppressing metabolic pathways and cellular activities under their control.

Preliminary results suggest that a number of significant abnormalities in gene expression are occurring in ME/CFS – findings that could eventually lead to specific diagnostic markers and treatments aimed at the underlying disease process.

Publication: A Gene Signature for Post-Infectious Chronic Fatigue Syndrome, *BMC Medical Genomics*, 2009, 2:38. Available as a downloadable pdf at www.biomedcentral.com/1755-8794/2/38

● MUSCLE ABNORMALITIES

Professor Julia Newton and colleagues at the University of Newcastle have been investigating the role of autonomic system dysfunction in ME/CFS and several papers from her research group relating to these findings have now been published.

Professor Newton has also been looking at possible explanations for the sometimes quite disabling fatigue that is reported by people with primary biliary cirrhosis.

The main emphasis of the new study being funded by The MEA's Ramsay Research Fund will be to look at whether there is a peripheral (ie muscular) component to exercise-induced fatigue in ME/CFS. This will be done by examining how skeletal muscle produces lactic acid during exercise and then removes the acid during the recovery phase.

The proposed study will take forward findings from small studies that have already examined this

aspect of muscle function. Some of these studies indicate that there is a defect in muscle energy metabolism/production, possibly due to mitochondrial dysfunction, and that this defect cannot be explained by the deconditioning/inactivity model – at least in a sub-group of people with ME/CFS.

This study is planned to start in 2009. More information on muscle research can be found in the research section of *ME/CFS/PCVS: An Exploration of the Key Clinical Issues* (published by The MEA, fourth edition, September 2008).

● POST MORTEM AND TISSUE BANK

Anyone following reports in our quarterly *ME Essential* magazine will know that we are keen to set up a permanent facility in a UK hospital that will be able to collect and store tissue (which could be obtained during a routine operation) and post-mortem material from people with ME/CFS. Tissue would then be made available to any research group that wished to make use of it.

We are at present discussing these proposals – which will involve a hospital building, staff, and the establishment of a database of willing volunteers – with a group of researchers who are also keen to see such a facility.

A specific fundraising initiative involves a walk from the source of the River Amazon in Peru to where it enters the sea in Brazil. This is now in its 16th month. Regular blogs about the walk can be read at www.walkingtheamazon.com

Post-mortem research is something that the Ramsay Research Fund already funds and helps to administer, but only on a small scale. A separate information leaflet on post-mortem research can be obtained from The ME Association.

● OTHER PLANS

We are also keen to fund studies that will help fill existing gaps in our knowledge about existing research

findings – for example, the role of immune system chemicals known as cytokines in the production of fatigue.

HOW DO RESEARCHERS APPLY FOR GRANTS FROM THE RAMSAY RESEARCH FUND?

We operate a flexible system that encourages researchers to first contact our medical adviser for an informal discussion.

We also publish occasional invitations in *The Lancet* to researchers to submit applications on specific topics. This is done when we have sufficient funds available to finance one or more major studies. We are planning to review our major grant application form. When this is ready, it will be available to download from The MEA website. We are very willing to consider new applications for small research grants.

HOW ARE DECISIONS MADE?

The process is based on guidelines produced by the Association of Medical Research Charities. This normally involves internal and external peer review.

Our internal peer review involves assessment of the application by trustees and the ME Association's medical advisers. External peer review involves the application being sent off to one or more independent experts in the area of research being proposed.

HOW CAN YOU HELP?

If you want to help with MEA-funded research, please make out a cheque to **The MEA Ramsay Research Fund** and send it to:

**The ME Association
7 Apollo Office Court
Radclive Road,
Gawcott, Bucks MK18 4DF.**