



**Multiple System
Atrophy Trust**

20th ANNIVERSARY

Research Strategy

Multiple System Atrophy Trust

From April 2014



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Foreword

The Multiple System Atrophy Trust is the main funder in the UK of research into the degenerative brain disease, multiple system atrophy (MSA).

The Trust's Vision is a world free of MSA - this is our aspiration and goal. We hope one day to find a cure for this devastating disease.

In March 2017, the Board of Trustees agreed that the review of the Research Strategy in March 2017 by Professor Clare Fowler and Karen Walker indicated that the Strategy continued to reflect the trust's ongoing commitment to research and that it was not appropriate at this time to alter the strategic priorities. The Board of Trustees will continue to review the research Strategy regularly to ensure it meets the Trust's agreed focus for research.

As the charity has grown over the past few years, we have steadily increased our research funding commitment. The 2012 and 2013 grant rounds each took a sixth of our annual income. Our intention, where funds allow, is to continue to increase this spend, and as per the 2014 grant round to spend a minimum of £150,000 in each grant round so we can build on the excellent work already underway within the MSA research community. Our commitment to continuous funding demonstrates the importance we place on this area of the Trust's work. It also reflects the wishes of our members as recorded in our 2013 survey where over 70% believe MSA research should be an essential priority for the Trust.

To ensure we are funding the very best research in the field, we have revised our grants process to make it more robust and compliant with criteria laid down by the research standards body, the Association of Medical Research Charities (AMRC). As part of this, our independent Scientific Advisory Panel, whose membership includes experts in the field and people whose lives have been affected by MSA, will help us to rigorously evaluate and monitor grant applications to realise the ambitions laid down in this research strategy.

MSA is an extremely complex disease that is difficult to diagnose, and research to find the cause and

ultimately a cure is equally complex and may take many years. However, every research project is one step closer towards realising our aim.

The Trust remains committed to funding the very best research.

Darcy Hare

(Retired 2015)

David Burn

Trustee, Chair of the Trust's Scientific Advisory Panel, Professor of Movement Disorder Neurology, Newcastle upon Tyne

Clare Fowler

Trustee and Emeritus Professor of Uro-Neurology

Huw Morris

Professor of Neurology and Neurogenetics

Niall Quinn

Emeritus Professor of Clinical Neurology

Karen Walker

Chief Executive

Research Committee, Multiple System Atrophy Trust

April 2014, reviewed March 2017

Our research priorities

Historically the Trust's research activities have concentrated on funding grants (see pages 9 & 10).

This, the Trust's second Research Strategy, will increase the charity's research grant spend of **£150,000** and, at the same time, actively encourage engagement between scientists, the pharmaceutical industry and other organisations with an interest in MSA both in the UK and overseas. The Trust believes collaborative partnerships are crucial in order to maximise funding and resources for this "orphan" disease.

Our Research Strategy, March 2017 Will consider:

1.

Funding research grant projects aimed at:

- Finding the cause of MSA, and
- Improving treatments for people with MSA through drug discovery and translational studies including, for example, the treatment of important symptoms in MSA

2.

Seeking collaborative partnerships with other organisations involved in neurodegenerative research to increase research capacity, share resources and generally raise the profile of the disease.

Our research priorities over the next three years

3.

Encouraging engagement with the pharmaceutical industry, in particular around target identification and drug discovery, working in collaboration with the Trust-funded MSA UK Network: The Network will provide a biobank, enabling sharing of samples amongst the MSA research community, and will ultimately facilitate the participation of patients in clinical trials.

4.

Developing interest amongst clinical and non-clinical scientists to undertake MSA research by demonstrating the on-going commitment of the Trust to funding research, and by building links with existing research structures, for example, NIHR DeNDRoN, thereby organically growing the MSA scientists and clinicians of the future.

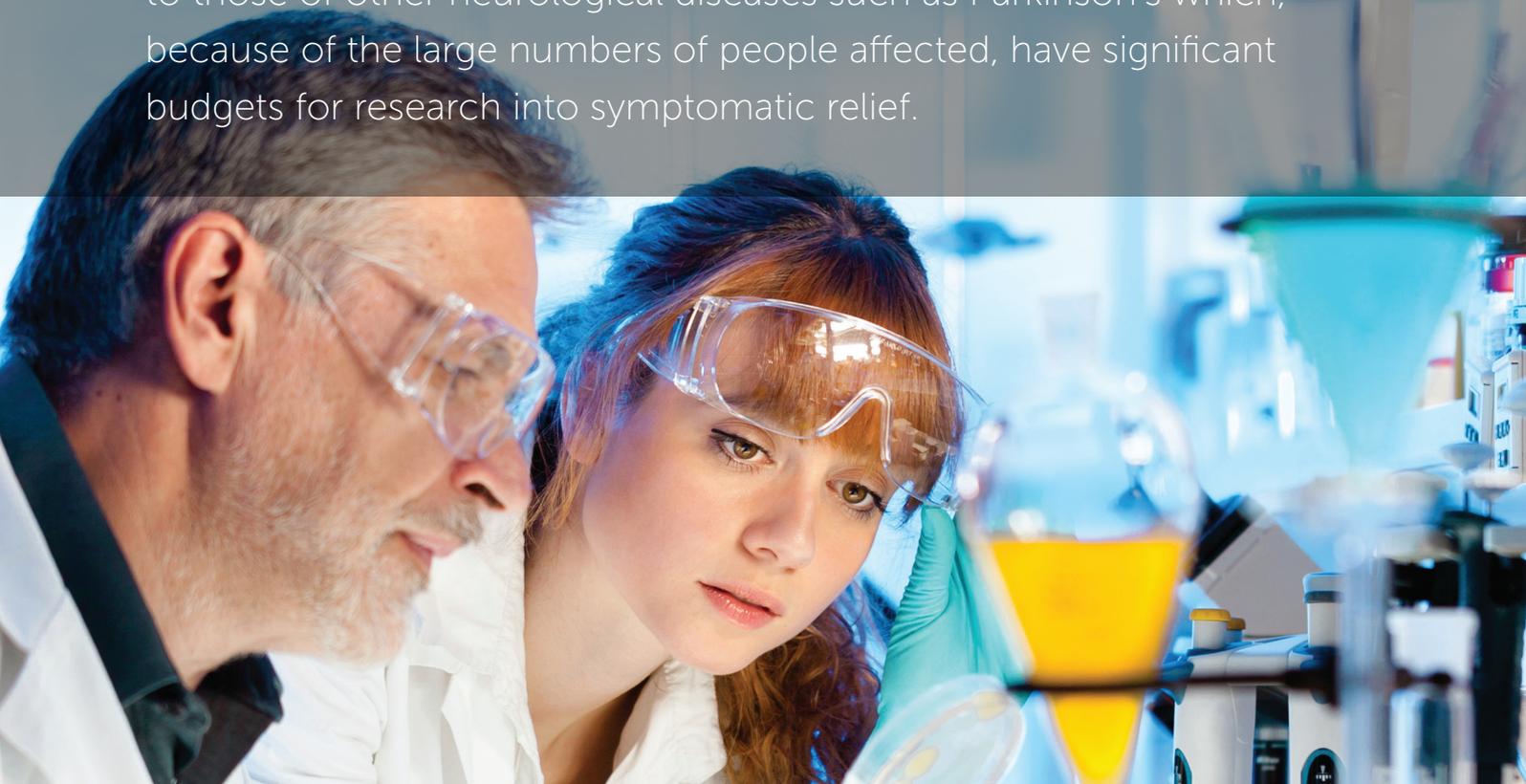
5.

Supporting international scientific collaboration, enabling participation in European initiatives and considering overseas grant applications from researchers with a demonstrable link to a UK-based Principal Investigator (PI) or institution.

Visit the Trust's website for more information of research activities within the MSA community (www.msatrust.org.uk).

Translational research and treatment

Many of the symptoms experienced by people with MSA are similar to those of other neurological diseases such as Parkinson's which, because of the large numbers of people affected, have significant budgets for research into symptomatic relief.



The Trust's limited funds are considered to be more effectively used to support work looking at the cause of MSA and translational treatments, seeking to work collaboratively and symbiotically wherever it can with organisations with larger funding resources.

Translational research means that discoveries generated in the laboratory are applied to studies in people over a four phase stage. The first phase takes a basic discovery into a clinical application

(bench to bedside); following this, phase two takes the basic discovery into a clinical setting (bedside to practice). Phase three moves the evidence-based guidelines developed in phase two into health practice and phase four evaluates the "real world" health outcomes.

From translational research of this type, it is hoped that ground-breaking treatments may be developed by pharmaceutical companies to alleviate the symptoms of MSA.

Some of our 2013-17 grants

Dr Janice Holton and her research team, based at the Queen Square Brain Bank in London

Dr Holton received support from the Trust's 2013 grant round to investigate the role of the CoQ2 gene in MSA.

The Trust has been funding Dr Holton's projects, which have looked at the underlying mechanisms of disease in MSA, for five years. The CoQ2 project aims to further increase understanding of MSA and, importantly, explore a potential genetic link to MSA.

While research to-date has revealed that MSA is a sporadic disease and is not inherited, Japanese researchers¹ discovered that genetic susceptibility may play a part in some MSA cases.

Their results suggested that an abnormality in the CoQ2 gene could be involved; a genetic link to MSA has never been found in UK studies.

Dr Holton says: "The CoQ2 gene plays a key role in the body as it is involved in the generation of energy in cells by mitochondria which function as the 'batteries' of each cell in the body. If the gene has a role in MSA, it could suggest that abnormal energy production by mitochondria may contribute to causing MSA. This could lead to very exciting developments in finding the cause of MSA if a genetic element was discovered".

Most diseases involve many genes in complex interactions, in addition to environmental influences. An individual may have a genetic variant that gives them a higher risk of acquiring a particular disease. This is called genetic

predisposition or susceptibility. Discovering a potential genetic element to MSA will be invaluable in discovering the cause of the disease.

However, Dr Holton emphasised: "It needs to be stressed in the strongest terms, a genetic predisposition does not mean you will get the disease or that, if you have the disease, you will pass it on to your children."

Researchers at the Queen Square Brain Bank are ideally placed to carry out this research because they have one of the largest samples of MSA brain tissue in the world.

When a patient makes the decision to donate their brain² it is usually after very careful discussion and fact-finding. It is a sensitive subject and personal to the individual. However, this particular research project is a very good example of how research into finding the cause and cure of MSA would not be able to take place without brain donation. It is a precious gift that will contribute to a world free of MSA and the suffering it causes.

¹ <http://www.nejm.org/doi/full/10.1056/NEJMoa1212115>

² The Trust has a fact sheet, A Guide to Brain Donation, which can be obtained from its information and support team on 0333 323 4591 or from the Trust's website, www.msatrust.org.uk.

Some of our 2013-17 grants

Professor Henry Houlden at the University College London (UCL):

The 2013 Trust grant round funded a research team, led by Professor Henry Houlden, to set up a UK MSA Network.

The Network will be the first of its kind in the UK. In simple terms it will be a longitudinal study looking at the progression of MSA and storing biological samples which will help in understanding the disease.

With their full consent, details will include patients' contact details, their MSA status, recent scans and blood and urine samples. These are important so the research team can quickly access all relevant clinical data about the patients. All data will be secure with access by authorised staff only. Key to the success of the project is the coordinator who will manage and monitor the database.

The database will offer significant value to researchers and pharmaceutical companies. Without it, should he currently be approached for, say, 20 eligible MSA patients in the UK to take part in a clinical trial, Professor Houlden, or others working

Professor Houlden says:

Pharmaceutical companies, who currently are not permitted to directly approach patients, need patient data and biological samples to develop essential biomarkers, in others words indicators of disease progression, in order to commence a trial of drugs that could slow or stop MSA. Our project is ethically approved, and a key element is collaboration between movement disorder clinics across the UK. The Network will play an important part in helping to prepare the MSA research community for clinical trials, and will help us to discover biomarkers.

For the first time in the UK, we will have the ability to look at an aggressive disease similar to Parkinson's disease. We hope that in the future this kind of database will be part of the NHS to encourage rare disease research.

in the field, would be unable to provide information quickly and effectively. His only option would be to undertake the time-consuming task of going back through patient records, and this would not be the best way to access patients with symptoms for a particular trial. However, once the MSA Network is set up, researchers will be able to locate patients by searching the database.

Professor Houlden's regret is that this project was not put in place ten years ago as it would have meant a decade of valuable MSA data would be available today.

While there are currently no active studies recruiting patients in the UK, Professor Houlden believes this could change once the Network is established. He says the pharmaceutical industry sees MSA as a far more aggressive form of Parkinson's disease, and therefore the efficacy of drugs trialled on MSA patients will be visible in a shorter frame time.

Trust funded research grants (2001 – 2013)

Dr Tim Young, Clinical Research Fellow at Imperial College.

Awarded **£50,000** for a three year Research Fellowship to carry out studies, including “effects of water and carbon dioxide in MSA”.

Dr Anette Schrag, Reader in Clinical Neurology at the Institute of Neurology, University College London (UCL).

Awarded **£31,000** for a two year project, “Quality of Life Survey for MSA patients/carers”.

Dr Nin Bajaj, Consultant Neurologist at Nottingham University.

Awarded **£10,000** for a study into “Imaging Patients”.

Following establishment of the Trust’s Research Advisory Panel in 2005

Professor Tamas Revesz, Professor of Neuropathology and **Dr Janice Holton**, Honorary Consultant and Reader in Neuropathology, both at UCL Institute of Neurology.

Awarded **£60,000** (the Margaret Watson Memorial Grant) for a one year study into “The role of p25a in GCI formation”.

Professor Henry Houlden, Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, UCL.

Awarded **£109,410** for a three year study into “Comprehensive characterisation of those genetic risk factors that predispose the development of MSA and those that lead to predominantly parkinsonian, cerebellar and/or autonomic features in this disorder”.

Dr Janice Holton, Honorary Consultant and Reader in Neuropathology at UCL Institute of Neurology.

Awarded **£179,502** for a three year grant looking at the “Central role of oligodendroglia in the pathogenesis of multiple system atrophy”.

Trust funded research grants (2001 – 2013)

Dr Shahin Zibae, Post-doctoral Research Associate at the Cambridge Centre for Brain Repair, University of Cambridge.

Awarded **£30,000** for a one year study "Testing a prion-like 'strain' concept for the alpha-synuclein filaments in glial cytoplasmic inclusions of MSA".

Dr Chris Kobylecki, NIHR Clinical Lecturer in Neurology at the University of Manchester.

Awarded **£50,448** for a two year project "A study of structural and metabolic correlates of neuropsychological dysfunction in patients with MSA and IPD".

Dr Janice Holton, Honorary Consultant and Reader in Neuropathology at UCL Institute of Neurology.

Awarded **£100,000** for a two year project "Neuro-inflammation in MSA: A neuropathological study".

Dr Janice Holton, Honorary Consultant and Reader in Neuropathology at UCL Institute of Neurology.

Awarded **£72,441** for an 18 month project "The role of CoQ2 in MSA".

Professor Henry Houlden, Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, UCL.

Awarded **£96,630** for "The UK MSA Network: A longitudinal clinical, imaging, biomarker study and future resource for MSA".

Professor John Hardy, Professor of Neuroscience at the Institute of Neurology, UCL.

Awarded **£55,535** for a three year project "Development and characterization of a human induced pluripotent stem (iPS) cell derived oligodendrocyte model of MSA".

Glossary

Biomarkers

A reliable biomarker for MSA could contribute to the diagnosis, treatment and disease modification of MSA by improving diagnostic accuracy, defining disease progression and providing an objective measure of the response to disease modifying interventions.

Longitudinal Study

Is an observational research method in which data is gathered for the same subjects repeatedly over a period of time. Longitudinal research projects can extend over years or even decades.

In a longitudinal cohort study, the same individuals are observed over the study period. Cohort studies are common in medicine, psychology and sociology, where they allow researchers to study changes over time.

NIHR DeNDRoN

The Dementia and Neurodegenerative Diseases Research Network (DeNDRoN) is part of the National Institute for Health Research (NIHR) Clinical Research Network (CRN), supporting research to make patients, and the NHS, better.

DeNDRoN's Aims and Objectives are to: Ensure patients and healthcare professionals from all parts of the country are able to participate in, and benefit from, clinical research; integrate health research into patient care and treatment; improve the quality, speed and co-ordination of clinical research and increase collaboration with industry partners and ensure that the NHS can meet the health research needs of industry.

Orphan Disease

Is a rare disease that affects a small percentage of the population.

Translational Research

Helps turn early-stage innovations into new health products, advancing the innovation to the point where it becomes attractive for further development by the medical industry or healthcare agencies.



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Information, support, education and research

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The Trust is funded entirely by voluntary donations.