The University Of Sheffield.

SITraN
Sheffield Institute for Translational Neuroscience

Briefing Notes May 2015

SITraN

Sheffield Institute for Translational Neuroscience

A centre of excellence for basic and clinical research into

Motor Neurone Disease

Contents

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Motor Neurone Disease (MND)

"There is no worse disease than MND." - Dame Cicely Saunders OM DBE FRCP, founder of the modern hospice movement.

What is MND?

Motor neuron disease (MND) has first been described by the French neurologist Jean-Martin Charcot in 1869. MND is a term used for a group of diseases which are caused by the death of motor neurons in the brain and spinal cord leading to progressive muscle paralysis. MND is also known as Lou Gehrig's or Charcot's disease or Amyotrophic Lateral Sclerosis (ALS), the most common form of MND.

What happens when motor neurones die?

Motor neurons initiate and control our muscle movements. When motor neurons die, the muscles stop working and waste away. MND often starts with walking problems, followed by the loss of arm and hand movements, until swallowing, talking and finally breathing are affected. Patients die from weakness and paralysis of their breathing muscles on average 2 to 3 years after the onset of symptoms. MND is a progressively debilitating and fatal condition. Only 1 out of 10 diagnosed MND patients survives longer than five years. Many doctors regard MND as the worst disease in medicine.

Who has MND?

Any adult can get motor neurone disease, at any age. In over 90% of cases the cause for the disease is unknown, only 5-10% of cases are inherited forms linked to certain genes, e.g. SOD1, C9orf72, TDP43, FUS. In the UK over 5,000 people suffer from MND, and 5 people die from MND every day. Worldwide over 750,000 people suffer from MND, men are more often affected than women. The longest known MND survivor is the eminent physicist Stephen Hawking. Other well-known MND patients include Mao Zedong, former England Manager Don Revie and the actor David Niven.

What are the treatment options?

As yet, there is no cure and no effective treatment for MND. Current treatment is based predominantly on symptom management and palliative care e.g. assisting breathing and nutrition and improving other disease related symptoms. At present, only one drug (riluzole) has been proven to slow the progression and modestly extend survival of MND patients by several months. Non-invasive ventilation (NIV) has also been shown to extend survival, as well as improving quality of life for some people with MND who experience problems with breathing.

What are the challenges to finding a treatment?

Due to its generally rapid course from diagnosis to death, the prevalence of MND in the population is only 6-8/100.000. MND is therefore regarded as a relatively rare "orphan disease" and as a consequence, there is limited interest in government or private sector funding for therapy development. This leaves academic institutions with a major role in developing new treatments for MND. Widely now regarded as a disease of ageing, it is expected that more cases of MND will be seen in our ageing population which further stresses the need for an effective treatment.

MND is a complex disease

Today, MND is regarded as a multisystem disorder not purely affecting motor neurones, although these specialised neurones tend to be affected earliest and most severely. At least 15 genes have so far been identified to be associated with MND and in up to 70% of inherited "familial" cases the gene causing the disease is known. What causes motor neurones to die in MND is not yet fully resolved and is best understood in the subtype of MND linked to a faulty SOD1 gene. A defective SOD1 gene is the known cause of 20% of inherited cases and approximately 2% of all MND cases.

For more information on MND visit: www.mndassociation.org or NHS choices: MND.

SITraN

The Sheffield Institute for Translational Neuroscience

A Centre of Excellence for Research into MND & Neurodegenerative Diseases

SITraN is the first and only European Institute dedicated to and directly linking basic and clinical research into motor neuron disease (MND) and related neurodegenerative diseases. Our aim is to accelerate therapy development and offer new treatments to patients with neurological disorders.

A Unique Research Facility with a Unique History

SITraN is the result of an unprecedented fundraising initiative set in motion by patients and supporters of Professor Pam Shaw for a research institute dedicated to research into MND and related neurodegenerative disorders including Parkinson's and Alzheimer's disease. SITraN was officially opened in November 2010 by The Queen and Prince Philip.

Visionary Leadership, Wide-ranging Expertise and Collaborative Spirit

SITraN founder and director Professor Pamela Shaw has attracted and directs a multi-disciplinary team of eminent doctors and scientists working and collaborating in SITraN under one roof. SITraN scientists combine wide-ranging skills and expertise in clinical neurology, pathology, neuroscience, gene therapy, cell and molecular biology, genetics, biochemistry, bioinformatics, imaging including MRI, stem cell technology, disease modelling, pharmacology, drug screening and development, drug trialling, as well as clinical trials and applications.

Translating Research Discoveries into Benefits for Patients

SITraN is devoted to translational neuroscience – the rapid application of scientific research discoveries to the benefit and treatment of patients with neurological disorders. In order to accelerate the pace of therapy development, scientists and clinicians are working together closely with the added input and feedback from MND patients. Basic research is directed towards finding the disease causes and mechanisms, as well as testing the right targets to develop new and more effective treatments for patients.

Direct links to clinical research and patient care

The specialist MND Care and Research Centre for Motor Neurone Disorders established by Prof Shaw in 2003 in Sheffield serves as a focus of excellence for specialist patient care and clinical MND research, as well as a pivotal resource for the scientific research undertaken at SITraN.

Securing MND research excellence for the future

SITraN will provide a long-term international focus for research excellence in neurodegeneration by offering future clinicians and scientists highly specialised training. In addition to PhD training, two new Masters courses in Clinical Neurology and Translational Neuroscience have been established at SITraN with a combined intake of 40 students per year.

SITraN's success so far:

Since its opening in 2010, SITraN has grown immensely, now employing close to 100 staff, including 10 professors, and 90 postgraduate students. SITraN scientists have produced over 400 original peer-reviewed research publications and attracted over £17M in research funding for neurodegenerative diseases. The gene therapy for SMA and the drug S(+) apomorphine for MND have received "orphan drug designation" and are being further trialled, as is a promising drug for Parkinson's disease. While more potential therapies are being uncovered at SITraN a range of assistive technologies such as a customisable neck collar and an innovative telehealth system are being developed and trialled to ensure better care and quality of life for MND patients.

For more information on SITraN visit our homepage: www.sheffield.ac.uk/sitran

SITraN - Fast Facts

Name: Sheffield Institute for Translational Neuroscience, SITraN

Location: Sheffield, UK - within the central campus of The University of Sheffield

Opened: November 2010 by The Queen and Prince Philip

Founder and Director: Professor Dame Pamela Shaw DBE FRCP

Founding Patrons: Sheffield Institute Foundation and The University of Sheffield

Honorary Patron: The Duke of Devonshire KCVO CBE DL

USP: a dedicated centre of research into MND and related neurodegenerative diseases, purpose-built to allow unique collaboration of a multi-disciplinary team of clinicians and scientists under one roof to link pure science to clinical research and accelerate therapy development.

Purpose: Translation of scientific discoveries into new therapies for patients

Current Staff: >100 staff, including 30 faculty academic staff

Postgraduate Students: > 40 MSc students in 2013/14, > 50 PhD students since 2010

Research funding since 2010: > £17 mio

Publications of SITraN researchers since 2010: > 400 peer reviewed original research articles

SITraN pipeline: "Orphan drug designation" for ReSagen (SMA), and S(+) apomorphine (MND)

Scientific Disciplines: SITraN hosts 10 Professorships in
Neurology – Pamela J Shaw; Translational Neuroscience – Mimoun Azzouz;
Neuropathology – Paul Ince and Steve Wharton; Movement Disorders – Oliver Bandmann;
Clinical Neuropsychology – Annalena Venneri; Clinical Neurology – Markus Reuber; Cerebrovascular Neurology – Arshad Majid; Machine learning and Computational Biology – Neil Lawrence;
Bioinformatics and Computational Biology – Winston Hide;

Space: 2800m^2 of research laboratories, offices, conference and research training facilities.

Pivotal Resources:

- Sheffield Care and Research Centre for Motor Neurone Disorders established and directed by Prof Shaw with a clinical database of >1000 MND patients, and biobanks of human material and tissues donated for research.
- Host to Sheffield Brain Tissue Bank (SBTB) with material from > 1000 donors.
- Host to Public and Patient Research Advisory Groups for MND and dementia research
- Host Centre leading the UK Dementia (DeNDRoN) Clinical Studies Group for MND
- The Bateson Centre for Developmental and Biomedical Genetics with access to animal models e.g. zebrafish, drosophila (fruit fly)
- Access to facilities within University of Sheffield and Sheffield Teaching Hospitals
- National and international collaborations

Profile: Dame Pamela Shaw

Professor of Neurology, Director of SITraN, University of Sheffield

Dedicated to improving the lives of patients with motor neuron disease (MND)

Professor Dame Pamela Shaw has a worldwide reputation as an acclaimed Clinical Neurologist and Neuroscientist who has dedicated her life's work to the exemplary care of MND patients and the understanding and development of treatments to combat the disease. She is one of the most renowned and experienced specialist consultants for motor neuron disease worldwide and has been at the forefront of MND scientific and clinical research for the last two decades. She has played a crucial role in influencing and implementing policies, guidelines and infrastructures in the UK to improve care for MND patients and put MND on the national healthcare agenda. In addition to numerous scientific awards and accolades, Pam Shaw's services to Neuroscience were acknowledged by HM The Queen in the New Year's Honours 2014 with a Damehood.

Promoting MND research and specialist care for MND patients

After her very successful medical and specialist training in neurology, Pam Shaw took up a post as Honorary Consultant Neurologist in 1991 and directed a specialist MND care and research centre in Newcastle. She embarked on a major clinical and laboratory programme of MND research funded by the Wellcome Trust which she transferred to the University of Sheffield in 2000 accepting a Chair in Neurology. In 2003, with support from the MND Association, she established and continues to direct one of the major national Care and Research Centres for Motor Neurone Disorders in Sheffield which serves as a focus of excellence for MND care and clinical research. She continues to lead the systematic development of clinical research nationwide to tackle major problems faced by MND patients where new approaches and new evidence-based guidelines are required.

Putting motor neurone disease (MND) on the agenda - nationwide

Prof Shaw's influence has ensured that neurodegenerative diseases are included in the NHS Clinical Research Networks Initiative and she has helped to implement MND care guidelines by providing the required evidence through clinical research. Prof Shaw has taken part in more than 15 MND clinical trials and played a key role in promoting into clinical practice the only known MND treatments to prolong survival, riluzole and non-invasive ventilation. For 8 years she has led the Clinical Studies Group for MND within the NIHR Dementia and Neurodegenerative Diseases (DeNDRoN) network and helped to develop a high quality UK clinical research network (UKCRN) linking 19 MND Care and Research Centres and establishing a network of 10 UK centres experienced in MND clinical trials.

SITraN, a research centre to reach the ultimate goal: Finding a cure for MND

The opening of SITraN by Her Majesty The Queen in 2010 was the culmination of over a decade's work, for which Pam Shaw provided both the overarching vision and the relentless practical driving force. The unique research institute is dedicated to accelerating the therapy development and improving care and quality of life for patients with MND and other neurological disorders. Scientific research undertaken at SITraN is firmly linked to the clinical research at the specialist MND Care and Research Centre in Sheffield which also serves as a pivotal resource.

Professor Shaw has authored more than 350 publications of original research Google Scholar H-index 69), reviews and book chapters and has edited several books on MND. She has supervised the research training of more than 100 individuals from medicine and science including 30 PhD students and since 1983 has generated more than £50 million in research funding.

For more information on Professor Shaw, her research and biography,
visit: http://sitran.dept.shef.ac.uk/people/shaw

Images

A range of images can be downloaded from the SITraN image archive

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