NIHR Dementia Translational Research Collaboration

Engaging with NHS and industry to advance dementia research

www.nihr.ac.uk/trc-d
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Cover image:
PET scan using the radiotracer [11C]PIB overlaid on a MRI scan showing the distribution of beta amyloid plaque in a patient with Alzheimer’s disease.

(Image provided courtesy of Franklin Aigbirhio, Tim Fryer, Young Hong, James Rowe and John O’Brien of the University of Cambridge, undertaken as part of the NIMROD study funded by the Cambridge Dementia Biomedical Research Unit).
Foreword

Dementia is a growing problem that affects over 44 million people globally.

With approximately 800,000 people currently living with dementia in the UK, at a cost to our society of over £20 billion a year, patient numbers are expected to double within the next 30 years.

In direct response to the Prime Minister’s 2012 call for improved research in dementia, the UK government established the NIHR Dementia Translational Research Collaboration.

This Collaboration brings together the nation’s world-class dementia researchers to drive the translation of discoveries from basic science into the clinic and through to real benefits for patients.

Effectively addressing dementia’s main research questions requires drawing on a wide range of scientific areas and specialist expertise.

Partnership with industry plays a crucial role in the development of new treatments for dementia and is therefore a major focus of the Collaboration. Improving collaborations between academia, the NHS and industry, with greater mutual transparency, is vital, and the opportunity for such collaboration has never been greater.

I invite the life sciences industry to engage with the NIHR Dementia Translational Research Collaboration and to work with us on the development of new approaches to tackle the global problem of dementia.

This booklet introduces the Collaboration and outlines some of the many capabilities hosted within it.

Professor Simon Lovestone
NIHR Dementia TRC Director
Professor of Translational Neuroscience
About the NIHR Dementia Translational Research Collaboration

Comprising four NIHR Dementia Biomedical Research Units (BRU) and six NIHR Biomedical Research Centres (BRC) with dementia-related research themes, the NIHR Dementia Translational Research Collaboration (TRC-D) is managed and staffed by expert translational researchers.

Its research activities are underpinned by expertise in biomarker discovery and validation, and by platforms for research including large patient populations, biobanks and other bioresources.

Aims of the NIHR Dementia Translational Research Collaboration

The UK Government established the NIHR Dementia Translational Research Collaboration to pull new discoveries in dementia research from basic science into the clinic.

TRC-D members will work closely together on questions of early diagnosis, patient stratification, phase I and phase II experimental medicine and proof of concept trials.

The TRC-D is a key contributor to the development of the UK Dementias Research Platform.

NIHR Office for Clinical Research Infrastructure (NOCRI)

The NIHR Office for Clinical Research Infrastructure (NOCRI) provides coordinated access to the Dementia Translational Research Collaboration for life science industry partners.

For information about NOCRI visit www.nocri.nihr.ac.uk
Expertise and Strengths

The NIHR Dementia Translational Research Collaboration’s range of expertise includes:

- Late-onset dementias, including Alzheimer’s disease, Vascular disease and Lewy body dementia
- Young-onset dementias
- Frontotemporal dementia with motor neuron disease
- Parkinson’s disease, including progression to dementia
- Neuroinflammation
- Huntington’s disease

It brings together internationally recognised strengths in:

- Patient stratification through identification and validation of diagnostic and prognostic biomarkers of disease and genetic markers of susceptibility
- Discovery, development and delivery of innovative disease modifying therapies, which include those discovered through the longitudinal study of genetically at-risk cohorts
- Identification of new disease-causing genes and subsequent development of clinical testing
- Extrapolation of discoveries in young onset dementia to older patient groups
- Detection, prevention and treatment of protein misfolding and aggregation in dementia
Members and Capabilities

Cambridge

The NIHR Cambridge Biomedical Research Centre has research themes focusing on dementia and neurodegeneration. The BRC Dementia and Neurodegeneration research theme is led by Professor Roger Barker.

The NIHR Cambridge Dementia Biomedical Research Unit brings together pipelines for preclinical and clinical discoveries relevant to dementia.

The BRU combines a group of internationally-recognised researchers harnessing a rich inter-disciplinary interface to solve problems impeding effective classification and treatment of dementia.

Director of the NIHR Cambridge Dementia BRU is Professor Peter St George-Hyslop.

Key expertise and capabilities in Cambridge:

- Advanced cell-based systems for therapeutics discovery
- Molecular neuroimaging, MRI and PET imaging
- Cognitive neuroscience and assessments of cognitive impairment
- Epidemiology of dementia
- Autophagy in relation to neurodegeneration
- Genetics of dementia.
Members and Capabilities

**Imperial**

The NIHR Imperial Biomedical Research Centre’s Neuroscience theme focuses on neurodegenerative disorders including Alzheimer’s and Parkinson’s diseases, late cognitive and behavioural consequences of traumatic brain injury or stroke and neurodegeneration in neuroinflammatory disorders. The BRC Neuroscience theme is led by Professor Paul Matthews.

Dementia research is more broadly coordinated within the cross-faculty Imperial College Dementia Interest Group (ICDI), chaired by Dr Robert Perneczky.

ICDI includes input from the following activities:

- The Drug Discovery Group led by Doctors Matthew Fuchter and Ed Tate in the Institute of Chemical Biology
- The Neurotechnology Initiative led by Dr Simon Schultz and Professors Bill Wisden and Paul Matthews
- The Neuroepidemiology and Ageing Research (NEA) Unit at the School of Public Health led by Professor Lefkos Middleton and Dr Robert Perneczky.

**Key expertise and capabilities in Imperial:**

- Internationally recognised expertise in epidemiology of late life disease, clinical trials design and healthcare technology assessment
- Advanced PET and MRI Imaging and host institution for Imanova, the specialist Imaging company owned by London universities and MRC
- UK Parkinson’s and Multiple Sclerosis Brain Bank
- CHARIOT, one of the UK’s largest registries for rapid recruitment into dementia clinical drug trials and other research studies
- An integrated Academic Health Sciences Centre that has strong partnerships with two major community and mental health trusts (Central and Northwest London NHS Foundation Trust and the West London Mental Health NHS Trust)
- The Data Science Institute, a centre for Big Data healthcare studies and advanced imaging visualisation.
Members and Capabilities

Newcastle

The **NIHR Newcastle Biomedical Research Centre** focuses on the complex healthcare needs of the older person, based on an advanced understanding of the ageing process and age-related disease and aims to deliver personalised medicine for the older patient. Professor Ian McKeith is the Ageing Brain research theme lead.

The **NIHR Newcastle Dementia Biomedical Research Unit** focuses on Lewy body dementia, including Parkinson’s disease patients who later develop dementia. Newcastle is a recognised world-leader in research into Lewy body dementias. These complex and disabling conditions affect around 160,000 older people in the UK. They are the most common form of dementia after Alzheimer’s disease.

Director of the NIHR Newcastle Dementia BRU is Professor David Burn.

Key expertise and capabilities in Newcastle:

- Well characterised patient cohorts in Parkinson’s disease and Lewy body dementia
- Gait metrics and activity monitoring exploring gait as a new biomarker
- Basic research on mechanisms of ageing including systems biology of ageing
- High quality clinical trial facilities for experimental medicine
- Track-record in pathophysiology and treatment of dementia, in particular non-Alzheimer’s types.
The NIHR Oxford Biomedical Research Centre focuses on multidisciplinary translational research for patients with dementia and on the development and application of interventions to promote healthy ageing.

Oxford BRC’s dementia-related research themes include:
- Dementia & Cardiovascular Disease theme led by Professor Peter Rothwell and Dr Sarah Pendlebury
- Functional Neuroscience & Neuroimaging theme led by Professor Peter Brown
- Cognitive Health programme led by Professors Kia Nobre and Heidi Johansen-Berg.

Professor Simon Lovestone is Professor of Translational Neuroscience and chairs the Dementia Translational Research Collaboration.

Key expertise and capabilities in Oxford:
- Multi-modal structural and functional brain imaging, MRI and magnetoencephalography
- Induced pluripotent stem cells
- Genomics and state of the art sequencing technologies
- Well characterised patient cohorts in presymptomatic patients individuals in vascular dementia, Parkinson’s and Lewy body dementia
- Clinical trials and experimental medicine
- Biomarker discovery in neurodegeneration, blood and cerebrospinal fluid studies, cognitive testing and imaging
- Clinical informatics and bioinformatics
- Use of connected devices and mobile computing for health
- Effects of physical exercise and cognitive training on enhancing neural plasticity and cognitive health.
Members and Capabilities

South London and Maudsley

The NIHR South London and Maudsley Biomedical Research Centre focuses on four main areas:

- Early detection and intervention of psychiatric disorders
- Personalisation of treatments based on genomics, biomarkers and psychological traits
- Experimental medicine to provide proof-of-concept for innovative medical and psychological treatments
- Exploring the mental-physical health interface for more effective treatments.

The NIHR Dementia Biomedical Research Unit accelerates the translation of dementia research from basic science to early phase clinical trials. The BRU focuses on the three common late-onset dementias: Alzheimer’s, Vascular and Lewy body dementia and Frontotemporal dementia with Motor Neuron disease.

Director of the NIHR South London BRC is Professor Matthew Hotopf. Interim Director of the Dementia BRU is Professor Clive Ballard.

Key expertise and capabilities in South London and Maudsley:

- Exploratory clinical biomarker studies utilising imaging and molecular technologies
- Genomics and proteomics
- MRI and PET neuroimaging
- Electronic medical records, bioinformatics and biostatistics
- Induced pluripotent stem cells.
University College London

The NIHR Queen Square Dementia Biomedical Research Unit focuses on Young-Onset dementias and development of new methods of diagnosis and treatment.

These and other degenerative dementias often occur on an autosomal dominant inherited basis, with the same clinical features as sporadic disease. Identification of the mutated genes causing the dementia, and longitudinal study of individuals who carry the gene, create a window on the disease process.

Director of the Queen Square Dementia BRU and NIHR National Director for Dementia Research is Professor Martin Rossor.

Professor Nick Wood at University College London Biomedical Research Centre leads a neuroscience research theme in dementia. Successes from within this theme include:

- identification of a gene responsible for Alzheimer’s disease
- discovery of two genes responsible for Dystonia
- development of a new ultra-sensitive test to measure mutant Huntington’s disease representing a fundamental step in developing rational and robust biomarkers.

Key expertise and capabilities in UCL:

- Diagnostic MRI, including advanced image analysis of serial brain MRI to measure rates of tissue loss
- Cerebrospinal fluid, CSF analysis for markers of Alzheimer’s disease and neurodegeneration
- Induced pluripotent stem cells
- Genetics of dementia
- Well characterised patient cohorts
- Expertise in prion biology in relation to neurodegenerative disease.
Projects and Activities

NIHR-MRC Dementia Deep and Frequent Phenotyping Study
NIHR and MRC have jointly funded a feasibility study for intensive phenotyping of early Alzheimer’s disease patients. Led by NIHR Dementia TRC Director Simon Lovestone from Oxford, and involving several industry collaborators, the study was launched at the 2013 G8 Summit on Dementia.

The aim is to identify a multi-modal marker for preclinical or prodromal disease for use in stratification or selection for clinical trials or for use in monitoring change. The study is in pilot phase; testing the feasibility in a multicentre trial and acceptability to participants of very complex repeated measures including imaging, electrophysiology and molecular measures as well as many other potential biomarkers. This pilot will lay the foundation for a larger follow-on study.

Establishing such biomarker signatures will enable relatively short and cost-effective clinical trials for new drugs at an earlier stage of disease. This will revolutionise the landscape for drug development. By allowing drug developers to make earlier and better informed decisions on whether drugs are likely to be effective, costs and risks for the development of new drugs will be reduced, and ultimately will provide real benefit for patients.

Parkinson’s Disease Biomarker Study
Parkinson’s UK has provided the TRC-D with funding to search for elusive Parkinson biomarkers in blood and cerebrospinal fluid using proteomics – both mass spectrometry based technologies and arrays. Identifying reliable biomarkers would transform the diagnosis and management of Parkinson’s and would also speed up research to develop the next generation of treatments to slow or stop the progression of the condition.

Researchers from NIHR Biomedical Research Centres and Units in Cambridge, Oxford, London and Newcastle, in collaboration with leading UK and US biotechnology companies, are using blood samples and information collected through the largest ever in-depth study of people with Parkinson’s. The Tracking Parkinson’s study is also funded by Parkinson’s UK and has recruited over 2,000 people with Parkinson’s across 70 UK study centres.
Projects and Activities

Dementia TRC work streams
The Dementia Translational Research Collaboration has established a number of work streams to develop shared resources and consistent experimental practices in key areas of dementia research:

MRI Protocol Sharing
- Led by Dr Claire Mackay (Oxford BRC) and supported by Nick Fox (UCLH BRC)
- Development of a consistent informatics platform across all the TRC-D centres to allow sharing of MRI images, image analysis methods, protocols and QC processes. It will establish consistent MRI capabilities and sharing of image databases at a national level.

Induced pluripotent stem cells (iPSCs)
- Led by Professor Martin Rossor (Queen’s Square UCL BRU)
- Use of induced pluripotent stem cells (iPSCs) in neurological disease.

PET Imaging
- Led by Franklin Aigbirhio (Cambridge BRU)
- Best practice and use of PET-imaging capabilities across the TRC-D to facilitate delivery of multi-centre studies, including standardised protocols and image analysis.

Bioinformatics
- Led by Simon Lovestone (Oxford BRC)
- Roll-out and use of the Clinical Record Interactive Search (CRIS) System to enable the use of electronic medical records for research at TRC-D centres.
The NIHR Dementia TRC and the UK Dementias Research Platform

The MRC UK Dementias Research Platform (UKDP) is a multi-million pound public-private partnership, developed and led by the Medical Research Council with support from the National Institute for Health Research and other partners. It is directed by Dr John Gallacher at the University of Cardiff, together with an executive team of investigators drawn from seven universities (Cambridge, Edinburgh, Imperial College London, Oxford, Newcastle, University College London and Swansea).

The aim of the UKDP is to accelerate research progress and develop knowledge leading to new drug treatments and other therapies that could prevent or delay the onset and progression of dementias. Its activities are aimed at improving early detection, treatment and ultimately, prevention, of dementias.

Specifically, the UKDP is creating the world’s largest population study for use in dementias research, bringing together two million participants aged 50 and over, from 22 existing study groups within the UK.

Included are people from the general population, people known to be at risk of developing dementia, and people diagnosed with early-stage dementia.

The NIHR Dementia Translational Research Collaboration and the UKDP are distinct initiatives with shared objectives.

Drawing on its key experimental medicine infrastructure and capabilities, the TRC-D embarks on research projects such as the Deep and Frequent Phenotyping Study that tackle key questions in dementia research and directly support the development of the UKDP.
The NIHR Office for Clinical Research Infrastructure (NOCRI) simplifies access to the UK’s world-leading clinical research infrastructure in dementia through the NIHR Dementia Translational Research Collaboration.

For further information visit:
• www.nihr.ac.uk/trc-d
• www.nihr.ac.uk/nocri

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