

DEMENTIA RESEARCH CENTRE

NEWSLETTER

Summer 2013

A very big thank you to all our patients and carers who have been involved in the various research projects and without whom none of our research would be possible.

A summary of our progress this year is provided below:

In October 2012, Professor Martin Rossor stood down as Director of the Dementia Research Centre, handing over to Professor Nick Fox. Martin is still a Consultant and Principal Investigator at the Centre and is as involved as ever. He is now Director of the new Queen Square Biomedical Research Unit in dementia, which includes researchers from the Centre who will be partly located in a new unit recently completed on the fifth floor of 8-11 Queen Square. This much needed additional space will enable us to continue to expand our research activity. The Biomedical Research Unit is one of only four in England awarded by the National Institute of Health Research to advance research in dementia for patient benefit.

This year we have been pleased to welcome Linda Molloy (Research Nurse) and Amanda Haines, (Clinical Nurse Specialist) along with the clinicians, Dr Rebekah Ahmed, Dr Catherine Slattery, Dr Ross Paterson, Dr Camilla Clark, Dr Chris Lane, Dr Zeinab Abdi, Dr Ione Woollacott and Dr Phil Weston to the Centre. We were also delighted to welcome back Dr Susie Henley, as our new Clinical and Research Psychologist. Susie worked with us prior to obtaining her PhD and undertaking clinical training. Felix Woodward and Kirsty Macpherson, both Research Assistants have also joined the psychology team on a part-time basis and will be assisting with research assessments. We also welcome Leonie Figov, who will be covering for Dee Patel our Research Patient Co-ordinator, whilst she is on maternity leave.

We are pleased to report that Dr Colin Mahoney won the Alzheimer's Association International Conference - Alzheimer's Imaging Consortium for the Best Oral presentation which was titled *"The Neuroimaging Phenotype of Frontotemporal Dementia With the C90RF72 Hexanucleotide Repeat Expansion."*

Trials: The clinical trial team has had a busy year under the lead of Dr Cath Mummery. We have welcomed Linda Molloy, clinical research nurse and Dr Chris Lane, clinical research associate, to the team.

We have a number of trials running in mild to moderate Alzheimer's disease including a study examining the safety and efficacy of MABT5102A, a monoclonal antibody (an antibody that binds to one of the proteins involved in Alzheimer's disease in order to dissolve it) in the treatment of mild to moderate Alzheimer's disease. This study involves monthly infusions and regular MRI scans and psychology testing. This study will finish in July 2013 and then patients enrolled will be invited to continue in an open label extension study.

We are currently in the set-up stages of several new studies - one study looking at an oral treatment tablet in fronto-temporal dementia and two studies looking at treatment (an oral drug and an infusion drug) in mild to moderate Alzheimer's disease. Once we are ready to recruit we will be contacting eligible patients on our database and advertising the trials. Finally and very excitingly we are in the early stages of setting up a trial in at-risk individuals with a genetic marker for familial Alzheimer's disease. Our support group for familial Alzheimer's disease has continued to grow – providing support and a forum for people at risk of, or affected by, familial AD, and also for their families.

Frontotemporal dementia (FTD): FTD is a dementia where personality or language can be affected early on and the memory is often preserved until much later in the disease course. Diagnosis can be delayed, because personality changes are difficult to quantify and measure. For her PhD project, Dr Camilla Clark is conducting research into tasks that could potentially be affected early on in the disease and, if changes are in fact demonstrated, using these changes to understand where in the brain the damage is occurring. Dr Clark's research involves the use of psychology testing using manipulated images and sounds with functional imaging which allows us to look beyond the structure of the brain and into its ability to think. Dr Clark's first study is on sense of humour as we know that this is affected early in the disease but is very difficult to measure. Dr Clark has therefore devised an experiment looking at how our brains work out if a picture is a joke or not in an attempt to quantify sense of humour. If you are interested in finding out more about any of these projects please feel free to get in contact through email (camilla.clark@ucl.ac.uk) or phone 0203 448 3193 and ask to speak to Dr Camilla Clark.

The Genetic Frontotemporal dementia Initiative or GENFI has now entered its second year. This study has seen us form a collaboration with twelve other research centres studying genetic FTD across Europe and Canada. So far almost 200 people have been seen across the different sites and we hope to increase this further over the next few months. The

study is of people from families with genetic mutations in one of three genes, progranulin, tau or C9ORF72, and includes people who are currently well who are first-degree relatives of people who have symptoms, as well as people who have developed FTD. The study involves coming for 1 or 2 days per year for psychology tests, an MRI scan, blood tests and in some people a lumbar puncture. We hope to take this study into a new phase later this year with the aim of developing a platform for future drug trials. If you are interested in being in the study please email Dr Jonathan Rohrer (j.rohrer@ucl.ac.uk).

We have also seen the recent launch of a support group for people with genetic FTD. The familial FTD support group had its first meeting in March and we heard talks from Rachel Taylor a genetics nurse specialist at the hospital, as well as Selina Wray, a neuroscientist at UCL working on stem cells in FTD. Our first newsletter and a website will be produced soon and a further meeting will occur later in the year, open to all carers or family members of people with genetic FTD. Please let us know if you would like to come along by emailing Dr Jonathan Rohrer at j.rohrer@ucl.ac.uk.

Young Onset Alzheimer's Disease: Later this year we will be recruiting individuals to a new study into early onset Alzheimer's disease (individuals with symptoms before the age of 65 years without a known genetic cause). We already know that Alzheimer's disease can cause different problems in individuals with symptom onset at an early age compared with those whose symptoms begin later on in life: in particular we know that some patients with young onset Alzheimer's disease have much more prominent problems with vision rather than day-to-day memory. We suspect that there are other such variants and this study will allow us to explore the clinical and neuropsychological features, brain imaging signatures and cerebrospinal fluid (CSF) profiles of Young-onset Alzheimer's disease. This study, funded by Alzheimer's Research UK through a very generous donation from Iceland Foods, will be one of the largest carried out to date and we hope will allow us to gain unique insights into how young onset Alzheimer's disease affects individuals and their families. More generally we hope that this research will help us understand better the biological processes that cause Alzheimer's disease. Drs Catherine Slattery and Ross Paterson are the researchers who will be running this study, supervised by Dr Jonathan Schott and Professor Nick Fox. For more information about the study, please contact us by email (c.slattery@ucl.ac.uk; r.paterson@ucl.ac.uk) or by telephone (0203 448 3856).

Posterior Cortical Atrophy (PCA): PCA is a variant of degenerative disease characterised by early difficulties in visual processing (knowing where things are and what they are), calculation and spelling, due to loss of brain tissue at the back of the brain. In July 2012 Dr Sebastian Crutch brought together a multi-disciplinary group of PCA research and clinicians

to form an international working party, with a meeting held prior to the Alzheimer's Association International Conference. Eighteen researchers attended the meeting and another 30 researchers representing a total of 25 institutions in ten countries have agreed to participate. This working party allows important issues, such as consensus on definitions of PCA and whether there are subtypes of PCA, to be discussed. It is also a catalyst for collaborative projects; plans for a genome-wide association study to identify genetic risk factors with data from a number of research groups are already underway.

Here at the DRC we are joined by Silvia Primativo a PhD student from Rome who is visiting to undertake research including improving the characterisation of spelling abilities in PCA. We have also been visited by Aida Gonzalez and Aparna Dutt who conduct research into PCA in Spain and India respectively. Our longitudinal study of PCA continues, with particular projects aiming to facilitate reading and improve our understanding of eye movement deficits in PCA.

Dr Pirada Witoonpanich, an Honorary Research Assistant to Dr Jason Warren, has investigated olfactory processing in patients with posterior cortical atrophy (PCA), which is an important variant of Alzheimer's disease. This project includes a behavioural and neuroanatomical study of olfactory function in patients with PCA compared with patients with typical Alzheimer's disease. Hopefully, this will lead to a better understanding of olfactory processing in the brain and the pathological process underlying PCA.

The PCA Support Group (www.pcasupport.ucl.ac.uk) continues to grow, providing support for patients and carers to meet others in a similar situation; previously all meetings have been held in central London, but this year saw the first regional meetings in Croydon and Worthing. Later this year we hope to see meetings in the North West and Cambridge so those who live further from London will be able to take part and share their experiences with others from their region.

Imaging remains a core part of our research at the DRC giving valuable information about the structure, function and pathology of the brain in dementia.

Our imaging research has produced both exciting new tools to investigate brain changes in Alzheimer's disease and other dementias as well as providing important insights into disease processes. It has long been understood that more brain tissue is lost over time in those people with Alzheimer's disease compared with healthy subjects of the same age. Some of our recent work has shown that in specific areas of the brain this loss accelerates during the early stages of Alzheimer's disease. Although this acceleration is relatively small, it provides

some insight as to how and when tissue loss moves from levels seen at normal ageing, to those seen in Alzheimer's disease.

Low levels of brain tissue loss are evident in the brains of healthy elderly people. We have recently published an article which shows that those healthy elderly with higher amounts of Alzheimer's pathology have higher amounts of brain tissue loss over time. Further, those subjects who show some evidence of vascular disease in their brain, also have higher amounts of tissue loss. These results suggest that a number of diseases are having an effect on the brain tissue even though the people experience no overt symptoms. This information may give scientists and clinicians a window of opportunity to find and treat diseases before individuals experience any problems.

Imaging of the human brain does not only give a picture of the brain structure, but diffusion imaging can give information about the structural integrity of the brain. These changes may be occurring earlier than tissue loss can be observed. We have recently developed and published new methods to assess how this structural integrity changes over time within a subject. This development will allow small areas of the brain to be assessed more accurately and in more detail. We have also used diffusion imaging to investigate the earliest changes in an inherited form of Alzheimer's disease revealing that damage to the brain cells may occur before symptoms. Diffusion imaging has also revealed alterations in the networks of brain regions in dementia patients with language problems. These alterations differ according to the specific language problem experienced by the patients and demonstrate that different parts of the language network in the brain are vulnerable to degeneration.

DRC researchers have featured in a number of news stories or programmes, most notably when we hosted the visit of the Prime Minister, David Cameron, when he launched his Prime Minister's Challenge on dementia. The Prime Minister met a patient and his wife as well as some of the researchers at the DRC and also visited the MRI scanner.

The DRC also featured in a range of other programmes from explaining on Radio 4's Women's Hour why certain neuropsychological tests are used, to discussing progress towards trials in presymptomatic familial Alzheimer's disease.

Brain donation: The Dementia Research Centre works closely with the Queen Square Brain Bank for Neurological Disorders, and we are very grateful to the patients who have donated their brains for research after death, and to their families. If you would like more information on brain donation please contact Katy Judd (telephone 020 3448 3540, email katy.judd@uclh.nhs.uk) or Suzie Barker (telephone 020 3448 3218, email suzie.barker@ucl.ac.uk).

Support for our research: The Dementia Research Centre receives support from a number of grant-giving bodies including a number of charities. These include Alzheimer's Research UK, the Alzheimer's Society, and The National Brain Appeal. We are very grateful for their assistance and if you wish to support these charitable bodies, their contact details are below and we are sure they would be pleased to hear from you.

Alzheimer's Research UK

Website address: <http://www.alzheimersresearchuk.org>

Telephone: 01223 843899

Email: enquiries@alzheimersresearchuk.org

Alzheimer's Society

Website address: <http://alzheimers.org.uk>

Email: enquiries@alzheimers.org.uk

Telephone: 020 7423 3500

The National Brain Appeal

Website address:

<http://www.nationalbrainappeal.org/>

Email: leigh.stanger@uclh.nhs.uk

Telephone: 020 3448 4724

Once again, may we thank you very much for your continued support.

Professor Nick Fox, Professor Martin Rossor, Mrs Katy Judd, Dr Cath Mummery, Dr Jonathan Schott and Dr Jason Warren