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Oxford Parkinson's Disease Centre

NEWSLETTER

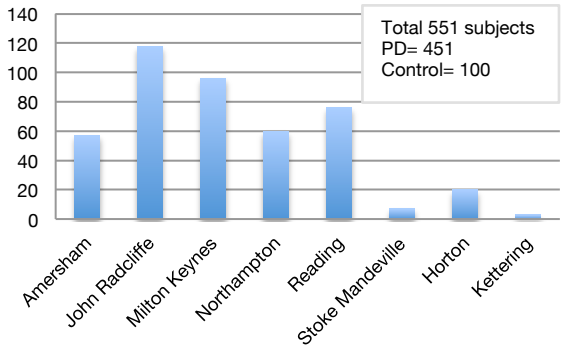
November 2011, Issue 2

Thames Valley DeNDRoN
Dementias & Neurodegenerative Diseases Research Network

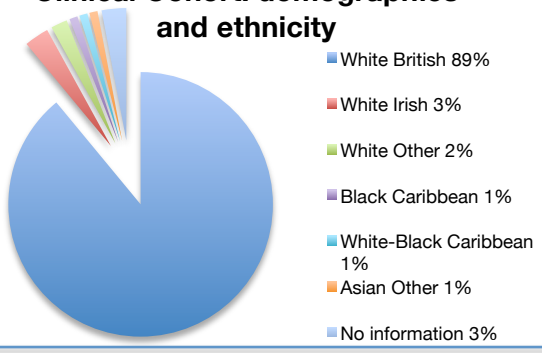
Introduction

- **What is the Oxford Parkinson's Disease Centre (OPDC)**
  - We are an interdisciplinary research center investigating the causes of Parkinson's and the earliest changes in the disease.
  - Our researchers come from areas of science which are central to Parkinson's research: molecular genetics, stem cell research, brain cell biology, brain imaging and clinical medicine.
  - We are funded by a £5m Monument Trust Discovery Award from leading research charity Parkinson's UK, granted in 2009.
- **Our aims**
  - Our mission is to accelerate progress towards finding a cure for Parkinson's.
- **In this Newsletter**
  - We present the aims of our research as well as an update on recent results of our research into stem cell models, brain imaging, the Parkinson's Brain Bank, and clinical biomarkers in Parkinson's.

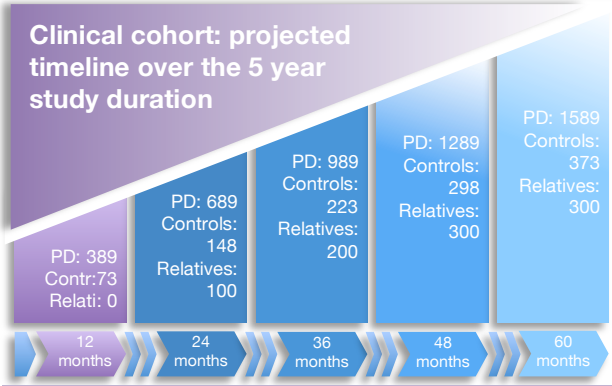
Recruitment according to site



Clinical Cohort: demographics and ethnicity



Clinical cohort: projected timeline over the 5 year study duration



For more information on taking part contact: Kathryn Lucas, Tel: 01865 234310, Fax: 01865 234609, email: k.lucas@nhs.net or check our website: www.opdc.medsci.ox.ac.uk

The Thames Valley Parkinson's Cohort- discovering new biomarkers in Parkinson's – Dr Michele Hu

- **What is a biomarker**
  - Biomarkers are biological markers like proteins or molecules that can be measured to diagnose and monitor conditions like Parkinson's
- **What we aim to do**
  - We are looking for early biomarkers, which will indicate the differences between people with Parkinson's and healthy people (called controls) by looking at blood results, genetic make-up and brain scans, which can then be compared and contrasted with specific clinical features.
  - Biomarkers have the potential to be used in drug trials to develop new potential protective treatments and to help predict the rate and pattern of progression of Parkinson's.
- **How to achieve it**
  - We aim to get together a group of 1500 people with Parkinson's, 300 healthy control subjects and 300 relatives of people with Parkinson's.
  - We examine our participants during a two hour clinic visit which includes taking a blood test.
  - The most accurate and consistent indicators for Parkinson's will then be selected for development as a potential disease biomarker.
- **What have we achieved**
  - We have recruited 550 Parkinson's and control participants in total from 8 participating hospitals (figure)
  - We are opening our 9th site by the end of 2011 in Heatherwood and Wexham Park Hospital
  - We anticipate a steady increase in research participants as shown in the figure.
- **How can you help**
  - Join our research if you were diagnosed with Parkinson's within the last 3 years and live in the Thames Valley. If there are several people with Parkinson's in your family, and you are able to travel to one of our clinics from within the UK, we would also like to hear from you.
  - Ask your partner or friends to consider volunteering for the control group
  - Ask your brothers or sisters who don't have Parkinson's to consider volunteering for the relatives group

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Taking part in our research

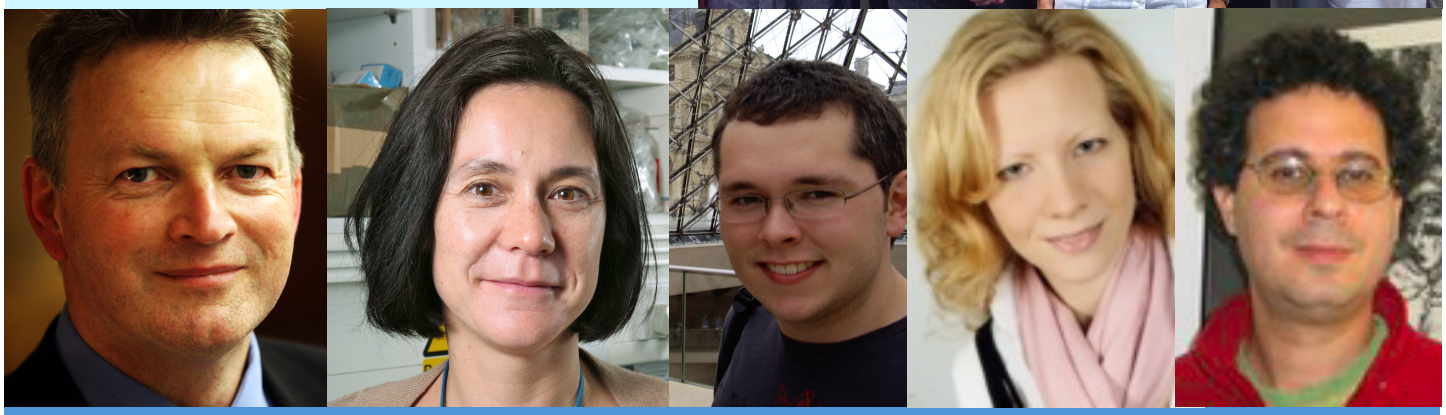
- We are very grateful to everyone who has generously given their time and effort to help us with the research so far
- Many individuals have told us they found taking part a rewarding experience
- Paul Beadle, 58, who has Parkinson's and is a member of Parkinson's UK's local Banbury group has already taken part: "I spent half an hour filling in the questionnaire at home. It asked in-depth questions about my health, symptoms, and possible environmental factors that may contribute to Parkinson's developing."
- "Then I was invited along to my nearest centre in Banbury. The whole process took about two hours. A painless blood test was taken and then motor skills tests like balancing on one foot, how well I could manipulate my hands, and also a fascinating smell test, because loss of sense of smell can be an early warning sign of Parkinson's. There was also the option to take a brain MRI scan and donate a sample of skin or spinal fluid."

Meet Lucy

- This is Lucy, she is 39, and recently moved to Oxfordshire with her husband and two cats. She was diagnosed with Parkinson's ten months ago. Lucy is taking part in the Discovery Study and has just completed her first visit.
- "I decided to take part in the study because I felt I just had to, and an overwhelming responsibility to help. In thirty years' time I don't want to be complaining that there is still no cure for Parkinson's, knowing that I could have taken part and didn't."
- "The experience has been fascinating and thorough, and has helped me understand my condition a bit more, as I am still getting used to it. All of the staff were positive and friendly, and having recently moved to the area, taking part provided another means of support."
- Interview was conducted by Sarah Murphy, Dendron research nurse.

Meet the clinical team

- Successfully running a research project of this size depends on a team of research nurses, doctors and scientists. Here we introduce you to some of them:
- Left to right: Wendy Barrett (research nurse), Dr Kannan Nithi (neurologist), Jo Glennon (research nurse), Dr Konrad Krolikowski (neurologist), Dr Michele Hu (neurologist), Dr Paul Tomlinson (neurologist), Lesley Catterall (research nurse)



- The clinical team is lead by Dr Michele Hu and Professor Kevin Talbot, Consultant Neurologists.
- Sam Evetts is our Research Technician who looks after the skin and blood samples we collect in the lab. Ricarda Menke is an imaging scientist based in the Oxford Centre for Functional MRI of the Brain (FMRIB) who analyses the brain scans. Professor Yoav Ben-Shlomo is a statistician working with us to design the study, and then interpret and analyse the data we collect.

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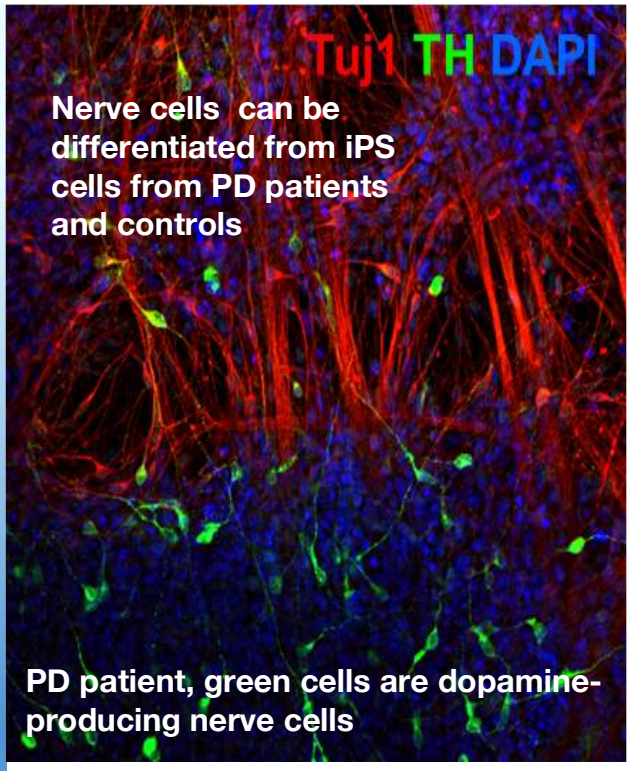
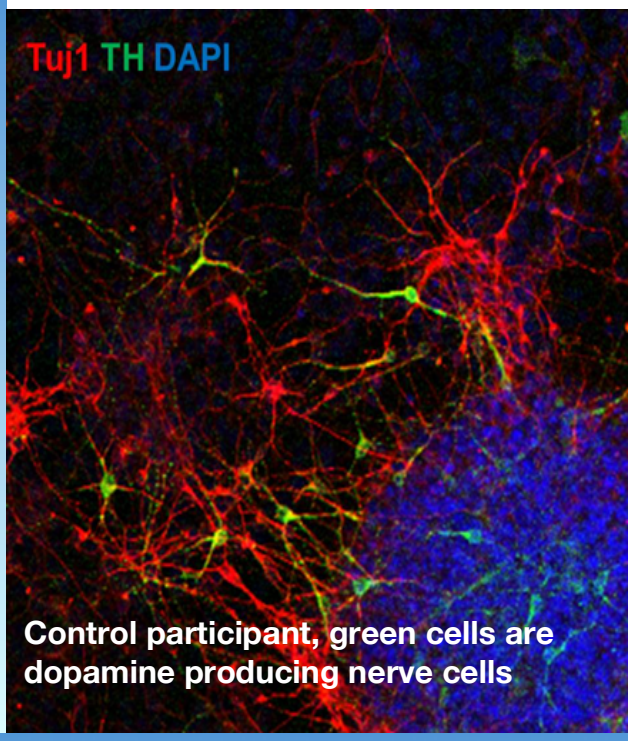
Induced Pluripotent Stem cells: Converting Skin into Brain Cells – Sally Cowley

- **What we aim to do**
  - Understand early changes in the affected brain cells of people with Parkinson's
- **How to achieve it**
  - Brain cells (neurons) most affected in Parkinson's, called dopaminergic neurons, reside deep in the brain and are not accessible while a person is alive. It has long been assumed that mature human cells like brain cells or skin cells cannot normally turn into any other cells. Only Pluripotent Stem cells in the embryo were thought to be able to develop into any cell type within the body.
  - Four years ago a revolutionary discovery gave us the opportunity to 'reprogramme' adult human cells, by delivering a cocktail of 4 genes. The transformed cells are called Induced Pluripotent Stem cells (iPS cells) and give us a unique opportunity to grow and study Parkinson's brain cells in the lab.
- **What have we achieved**
  - This year, 20 people with Parkinson's and controls have kindly donated skin biopsies.
  - We are in the process of reprogramming these skin cells to iPS cells. It takes over a month to this, and requires great care and attention. So far we have succeeded in making stem cell lines from 4 people with Parkinson's and 3 controls. As these cell lines can multiply indefinitely, they will be an incredibly valuable resource for research for years to come.
  - In the next step, Liz Hartfield, a researcher at the OPDC, is turning the iPS cells into the dopamine-producing brain cells that are damaged in Parkinson's The process takes over a month of careful nurturing. The cells that emerge are impressive, projecting long extensions that interact with each other.
  - Liz has already shown that the brain cells produce dopamine and are able to transmit nerve signals along their length. Differences between people with Parkinson's and controls should shed light on what is going wrong in the early stages in Parkinson's and may lead to improved treatments.

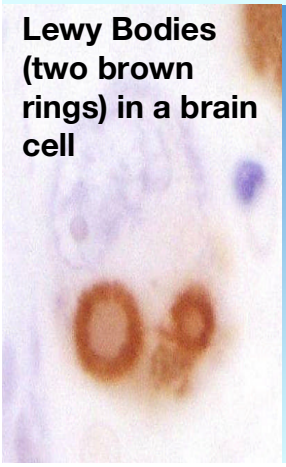


Nerve cells can be differentiated from iPS cells from PD patients and controls

PD patient, green cells are dopamine-producing nerve cells



Control participant, green cells are dopamine producing nerve cells


Lewy Bodies (two brown rings) in a brain cell

The importance of human brain tissue in Parkinson's research – Laura Parkkinen

- Many important advances in PD research including drug treatments such as levodopa have come from the study of human brain tissue
- Individuals recruited to our study will be invited to consider brain donation after death through the existing Parkinson's UK Brain Bank scheme (http://www.parkinsons.org.uk).
- Tissue generously donated in this way allows us to study the earliest changes in the brain in PD in the hope of developing a treatment that would slow disease progression.
- Brain cells in Parkinson's accumulate abnormal protein, shown here as two brown ring-like structures inside the cell called Lewy bodies.
- Our scientists at the OPDC are looking at how this protein accumulation leads to cell death in PD, and ways to reverse this process.

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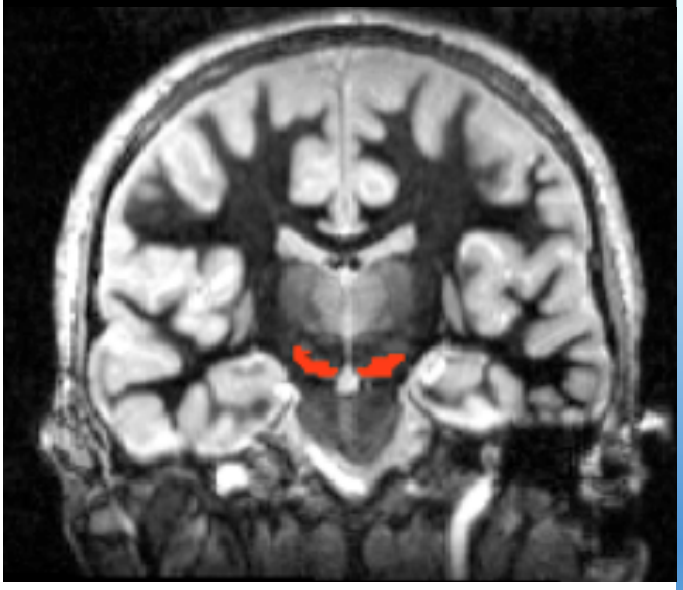
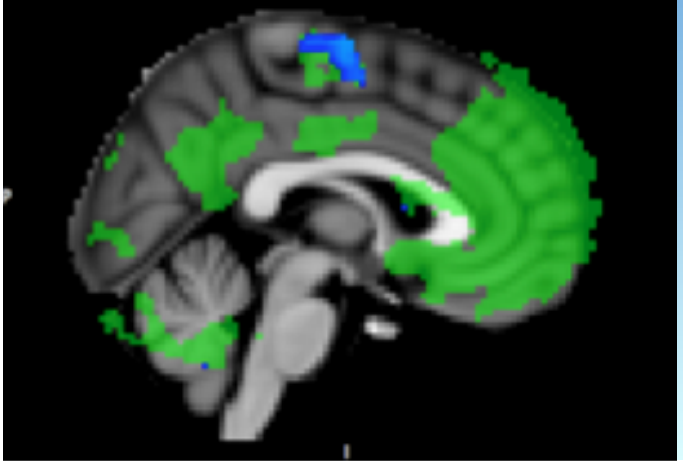
Substantia nigra, shown in red, has reduced volume in PD patients



Supplementary motor area, shown in blue, is disconnected from the rest of the network, shown in green



Brain Imaging and Parkinson's – Ricarda Menke, Konrad Krolikowski, Clare Mackay

- **What we aim to do**
  - Development of an early diagnostic test for Parkinson's using Magnetic Resonance Imaging (MRI) of the brain.
- **How to achieve it**
  - Dopamine brain cells particularly affected in Parkinson's are located deep in the brain in an area called the substantia nigra.
  - Recent MRI scanning techniques can show this area with good precision. There are three particularly promising ways of showing changes in Parkinson's:
  - Looking at iron content in the substantia nigra can help assess degeneration of the dopamine neurons.
  - Cell damage and changes in connectivity between remote brain areas can be seen with a technique called Diffusion Tensor Imaging.
  - Resting state functional MRI gives a glimpse of brain activity changes over time and how they may be influenced by disease.
- **What have we achieved**
  - 20 people with early stage Parkinson's agreed to be scanned along with 13 healthy controls.
  - Initial analysis shows:

    1) Shrinkage of the substantia nigra

    2) Increased iron levels

    3) Parts of the brain responsible for movement coordination seem to be functionally disconnected from their normal networks, confirming that the abnormalities affect distant parts of the brain
  - In the next 12 months we plan to scan more participants to confirm our initial findings.

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Editors: Michele Hu, Kevin Talbot, Konrad Krolikowski. Tel: 01865 231893.

Information on all our current research activities can be found on our website www.opdc.medsci.ox.ac.uk and via the 'Current Research' section of Parkinson's UK website http://www.parkinsons.org.uk.
For more information on taking part in our research contact Kathryn Lucas:
Tel: 01865 234310, Fax: 01865 234609, email: k.lucas@nhs.net.