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Please help us make *Progress* even better by filling in our short survey online at parkinsons.org.uk/progressfeedback



Welcome

Welcome to the summer 2011 issue of *Progress*, Parkinson's UK's research magazine. I hope that this issue will give you a flavour of the key role that Parkinson's UK is playing in global research to improve care, treatments and services for people with Parkinson's. This research will ultimately move us closer to a cure for the condition.

One of the central themes of our research strategy is to develop models for Parkinson's that help us understand why nerve cells die and allow us to test new drugs quickly and effectively. This issue's cover feature (page 4) explains how we're developing and using animals like fruit flies and zebrafish, alongside human cells as tools to study Parkinson's, and how they're bringing us closer to a cure.

We also work hard to ensure that the projects we fund make a difference by helping researchers take the next step in their research. On pages 16–17 you can read about how studies funded by us have now led to the development of clinical trials testing new treatments for Parkinson's.

Finally, I would like to introduce you to our Research Support Network. This is a group of people who have a special interest in Parkinson's research. There are many opportunities for research supporters to help us. You could organise a research event, raise vital funds, take part in a clinical trial or volunteer your time to help ensure people affected by Parkinson's are involved in research. And there's also the research page on Parkinson's UK's online forum for you to post about your experiences and read about what others have been doing (see page 8). So, we'd love to hear from you if you are interested in getting involved.

I hope that you enjoy the magazine, and we look forward to receiving your feedback.

Best wishes,

NUCON.

Dr Kieran Breen Director of Research and Development



ROGRESS

ANIMAL MODELS OF PARKINSON'S:

why do we need them?

Setting the scene – our research priorities

Back in the summer 2010 issue of *Progress*, we revealed our groundbreaking five-year plan for research that will lead us closer to a cure. This identified four key priorities that will ultimately keep us focused on our goal of making a cure become a reality. Along the way, we will also work to find better treatments to improve the lives of people with Parkinson's. The four research priorities are:

- understanding why nerve cells die in Parkinson's
- developing new animal models of Parkinson's
- faster, better drug screening
- finding 'biomarkers' for early diagnosis

In this issue of *Progress*, we are focusing on priorities two and three, to uncover how developing new animal models of Parkinson's can lead to faster and better drug testing.

What is an animal model?

A model is a living, non-human animal that is used in medical research to mimic aspects of a human medical condition. This allows researchers to test treatments or ideas and find out if they might work and are safe before they are tried on humans.

Why use animal models?

Many important advances in science have been made using animal models. In fact, of the 98 Nobel Prizes that have been awarded for physiology or medicine, 75 were associated with research carried out using animals. These studies have led to major breakthroughs in our understanding of Parkinson's. Arvid Carlsson, the Swedish scientist who won the 2000 Nobel Prize for medicine, used an animal model to show that the chemical dopamine plays vital role in Parkinson's.

Arvid was able to show that dopamine acts as a chemical signal in the co-ordination of movement, and that the loss of dopamine in certain areas of the brain leads to the movement or motor symptoms that are characteristic of Parkinson's.

Choosing the right model

Parkinson's is a complex, progressive condition that develops over time. It is caused by the death of dopamine-producing nerve cells in the part of the brain called the substantia nigra.

What we don't know is what causes the nerve cells to die. It's likely that multiple factors are involved. These are made up of a combination of genetic and environmental factors. Less than 5% of people with Parkinson's inherit it directly. However, there are likely to be many genes that will increase a person's risk of developing the condition. To learn more about the recent discovery of five new genes linked to the development of Parkinson's, see page 19.

While animal models are important for us to understand how Parkinson's develops over time, at the moment it is very difficult to mimic the condition. But our current models are useful for the development of therapies that treat the symptoms. We need to develop better animal models to bring us closer to treating the Parkinson's, rather than its symptoms.

Researchers have used animal models to show that defects in the energy-producing mitochondria inside nerve cells could be associated with Parkinson's. Mitochondria are like the batteries within nerve cells. If they don't work properly, the cells are more fragile and likely to die. Researchers have also confirmed these findings in humans using post-mortem brain tissue. (You can read about the Parkinson's UK-funded Brain Bank on page 19.)





Researchers currently have a choice of several animal models to work with, including mice, rats, flies, worms and zebrafish. However, we don't yet have a model that completely reproduces what happens in the nerve cells of people with Parkinson's. So we need to develop a variety of complementary models. This is achieved by doing things like changing an animal's genetic makeup, or treating them with certain chemical agents that may start a slow, progressive nerve cell death.

Zebrafish: modelling Parkinson's

In 2008, we awarded Dr Oliver Bandmann at the Sheffield Institute for Translational Neuroscience (SiTRaN) a three-year research grant worth £184,287 to see if there are any drugs that could repair damaged mitochondria in cells.

He describes his research:

"In Parkinson's, there appears to be something wrong with the mitochondria, not only in the brain, but also in other cells, such as the skin cells. However, the nerve cells appear to be more vulnerable. In this study, we have taken skin biopsies from people with an inherited form of Parkinson's. We'll grow these skin cell samples in the lab and use them to screen different drugs. We believe that if any of the drugs have an effect in Parkinson's skin cells, they may also protect nerve cells."

Based on his initial results from this study, Oliver has been awarded a further grant to continue this research. You can find further details on page 9.

After certain promising drugs have been shortlisted, they will be tested in the zebrafish, which is an important new model for Parkinson's. Cells grown

in the lab can tell us a lot about what happens in Parkinson's. However we need to remember that nerve cells don't exist alone and they interact with other cells in the brain. This is why we need to take our findings into a whole animal model of Parkinson's.

Oliver tells us:

"Zebrafish are quite closely related to humans and it's also relatively easy to change them genetically. We can modify them so that certain nerve cell start to die. They also contain many of the genes that are associated with the development of Parkinson's.

"In this project, we'll remove the parkin gene, a gene associated with the development of Parkinson's. We will then look at the difference this makes to the nerve cells as the animal grows, and how the gene defect can influence the death of nerve cells. This work will be carried out using a Parkinson's UK three-year research grant of £239,593 that I was awarded in 2009.

"Ultimately, we want to use the zebrafish models in the initial screening of new drugs that could slow down or halt the progression of Parkinson's."

Fruit flies are helping us to screen for drugs

Another animal model that can be used is the fruit fly. They reproduce rapidly and can be used to test more new drugs over shorter periods of time. The genetic make-up of these flies can also be easily modified to cause nerve cells to die. Dr Frank Hirth at King's College London started a three-year project, worth £184,696 in 2008 to develop a fruit fly model of Parkinson's.

"A fruit fly has dopamine-producing nerve cells in its brain – similar to those that die in people with Parkinson's. So we can use fruit flies to study why the nerve cells die and search for ways to prevent this from happening.

"In Parkinson's, failure of the mitochondria means that nerve cells may not have enough energy to survive. We've developed a new fruit fly model that has faulty mitochondria, and their dopamine-producing brain cells die with age.

"We can use a number of techniques to screen for ways to prevent the death of the nerve cells. One way is to use a 'gene therapy' approach. So we can add certain genes into the cells to see whether we can rescue the mitochondria. Another approach is to add drugs to the flies' food, so that we can screen for chemicals that may protect the damaged mitochondria in the nerve cells.

"As a result, our fruit fly model enables us to identify possible therapies to prevent the death of specific nerve cells. But we can also find out why dopamine-producing nerve cells die in the first place."

Nerve cells grown from people with Parkinson's

Ultimately, only human nerve cells are affected by Parkinson's, so we will need to test any new drugs on these cells. One way to do this is to use stem cells. Stem cells are like blank cells that can turn into any type of cell within the body, such as the nerve cells inside the brain.

Recently, researchers have found a way to transform skin cells into stem cells. These cells, called 'induced pluripotent stem cells' or iPS cells (see image on the right), can then be transformed into any cell type within the body, including nerve cells.

In 2009, Dr Tilo Kunath at the University of Edinburgh was awarded a career development award worth almost £380,000 to create iPS cells from skin cells. He spoke to Progress about his research:

"My study will investigate whether iPS cells derived from people with Parkinson's could create an ideal model of the condition. This will help us to understand why nerve cells die in Parkinson's and may allow us to replace those that have died. It will also help to develop an invaluable tool to screen for potential new protective drug molecules."

But, Tilo cautions:

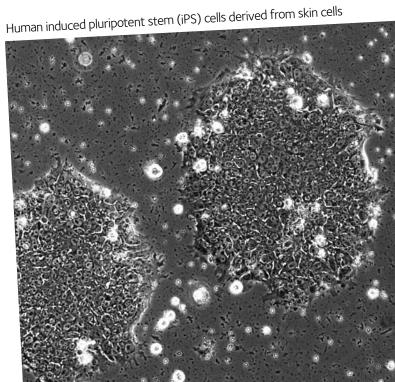
"There's still a long way to go. We don't know what the longer term effect of the transformation of the cells will be."

Tilo and his team are also trying to produce iPS cells from people with the inherited form of Parkinson's. Due to them having a specific gene associated with the condition, their cells may be more fragile and are more likely to die. So, they can screen a number of drug compounds that have been made in the lab, to see which ones can protect the nerve cells.

Find out more about our research strategy

If you would like a copy of Our plan to cure Parkinson's: The Parkinson's UK research strategy 2010-2014 you can by download it from parkinsons.org.uk/researchstrategy. On this webpage there is also a film about our strategy.

You can also request a free copy of the research strategy by calling our distributor on 01473 212 115 or by emailing resources@parkinsons.org.uk



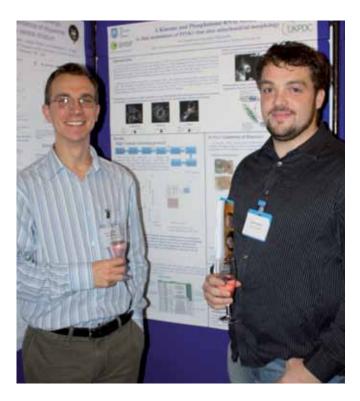
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RESEARCH: our impact in 2010

Last year was an exciting year for Parkinson's UK research. Our researchers made a massive international impact — publishing 95 articles in prestigious scientific journals, sharing their ideas at our biennial research conference in York, and making the headlines in the news. Here are a few of the highlights...

Our conference brings researchers together

In November, we welcomed more than two hundred scientists and clinicians to our second Parkinson's UK research conference in York.



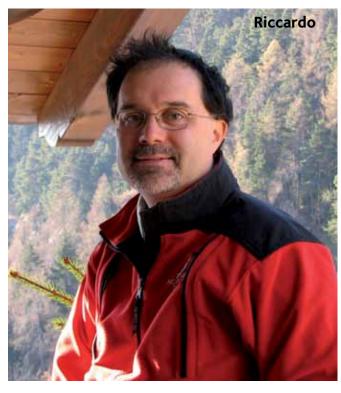
We covered every area of Parkinson's research, sharing discoveries and discussing challenges. Topics ranged from understanding the complex causes of Parkinson's, through to the latest breakthroughs in cell and gene therapies. Discussions between researchers led to new ideas and partnerships forming. With people asking about our 2012 event already, the enthusiasm around the conference shows the dedication of Parkinson's researchers working in the UK and the key role that Parkinson's UK plays in supporting this research.

Parkinson's UK-funded researchers hit the headlines

We work hard to make sure our researchers' achievements get noticed. In 2010, we helped their discoveries make a media splash in the national papers, radio and on TV. Here are just a couple of examples.

Putting a stop to dyskinesia

In November, Professor Riccardo Brambilla published the results of research co-funded by Parkinson's UK. His research has moved us closer to stopping distressing side effects of current Parkinson's drugs, such as dyskinesia. We made sure Riccardo's exciting research hit the headlines. Articles appeared in the Mail Online, WalesOnline, The Sun, the Daily Telegraph and a spot on the Good Morning Wales BBC radio show.



ROGRESS

Stem cells from people with Parkinson's

In July, Dr Richard Wade-Martins spoke at the UK National Stem Cell Network annual conference about exciting new research exploring how we can make and use stem cells from people with Parkinson's.



This groundbreaking work made the headlines – including Richard discussing his research on the BBC Radio 4 *Today* programme. Our Director of Research and Development, Dr Kieran Breen, also appeared on BBC *Breakfast* to explain the importance of this research. He also had the opportunity to emphasise the important role the charity plays in supporting Parkinson's research.

Our support led to exciting new projects

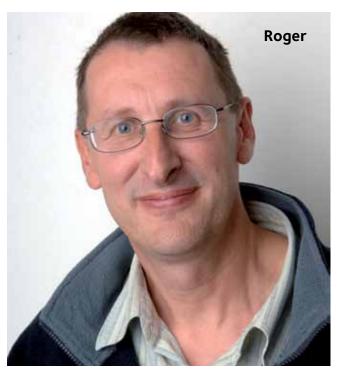
In 2010, our funding and support helped researchers to develop major research trials and set up a new centre dedicated to Parkinson's research.

EU funding for new cell transplant trial for Parkinson's

Following a series of crucial meetings funded by Parkinson's UK, the European Commission awarded a grant of €12million for one of the largest ever trials of cell transplantation for people with Parkinson's.

The trial is being co-ordinated by Parkinson's UKfunded researcher Dr Roger Barker:

"We hope that our new trial will prove that cell transplants can work consistently for people with Parkinson's – potentially paving the way towards future treatments that use stem cells to repair the Parkinson's brain. The support of Parkinson's UK was crucial for establishing the research group that obtained the EU funding."



Please visit parkinsons.org.uk/researchimpact to learn about how we made an impact in other important areas of Parkinson's research.

RESEARCH FORUM

We're delighted to announce the launch of our new research forum on the Parkinson's UK website.

The forum is a great place for people who are interested in research to exchange opinions, information and experiences on all aspects of Parkinson's research throughout the world.

Find out what research topics people are talking about by visiting: parkinsons.org.uk/researchforum

If you have any questions about the research forum, please email **forum@parkinsons.org.uk**

NEW RESEARCH We reveal five new projects we're funding. These studies

We reveal five new projects we're funding. These studies focus on finding out more about how Parkinson's develops and whether we can improve the treatments that are currently available.

Using skin cells to tell us more about Parkinson's

The causes of most cases of Parkinson's are unknown, but research has shown that changes in genes can play a key role. Changes (mutations) in a gene called LRRK2 have been shown to be particularly important for Parkinson's. One particular mutation in this gene is the single most common cause of the inherited form of the condition. But not everybody with this genetic change will get Parkinson's. So, studying it in detail may give us further clues to what other factors contribute to the death of nerve cells.

Dr Oliver Bandmann at Sheffield Institute for Translational Neuroscience (SiTRaN) will be using his three-year grant of £226,181 to investigate how LRRK2 mutations may lead to Parkinson's. His research will focus on the mitochondria, which are like the batteries or 'power houses' of cells, generating the energy to allow them to work properly.



Oliver and his team have already carried out pilot experiments using skin cells (fibroblasts) taken from people with Parkinson's (see page 6). In this new study, they want to find out why only some people with the altered form of LRRK2 will develop Parkinson's. They'll use a number of approaches. Firstly, they will 'turn off' LRRK2 to see what effect this has. This may have a similar effect to cells having a mutant form of the gene, and will therefore prevent them from generating enough energy to work properly.

They then want to see whether they can rescue the cells and actually prevent them from dying. Because skin cells are easy to grow in the lab, they can be manipulated in various ways – changing their genes, or adding drugs – to see whether these possible treatments could protect the cells. They will also examine cells from people with the altered form of LRRK2, but who don't have Parkinson's. This will help us to better understand why some people develop the condition.

"Our research will hopefully help us to understand why the mitochondria don't work in people who develop Parkinson's because of a mutation in the LRRK2 gene," says Oliver. "This particular gene change can contribute towards the development of Parkinson's in up to 30% of all people who have the condition. But even if you have the mutation, that doesn't mean that you'll get Parkinson's, just that you're at greater risk. We hope to get a better understanding of the underlying mechanisms leading to Parkinson's and possibly find new ways that we might be able to treat the condition in the future."

Read about Oliver's other Parkinson's UK-funded projects on page 5.

ROGRESS

The development of Parkinson's in the brain

We know that people only develop the movement problems associated with Parkinson's when more than 70% of the nerve cells in a specific part of the brain have died. But there is also data to suggest that nerve cells in other parts of body may be affected. These include cells in the gut and those that connect the gut with the brain.

Post-mortem examinations of the brains of people with Parkinson's show the presence of Lewy bodies within nerve cells that are in the process of dying. Lewy bodies are clumps of protein that are generated as nerve cells die. They are a key component of the changes that occurs in the brains of people with Parkinson's. But previous studies have also reported that Lewy bodies can also be found in cells outside the brain. The presence of Lewy bodies may be one of the earliest features of Parkinson's. They may contribute towards some of the early non-motor symptoms, including constipation and the loss of a sense of smell.

We've awarded a three year project grant of £247,868 to Dr Roger Barker and Professor Maria Grazia Spillantini (pictured below) at the

Cambridge Centre for Brain Repair. They will investigate how Parkinson's develops and spreads to affect different parts of the body.

"We will first use mouse models of the condition to learn whether Lewy bodies can spread from the qut to the brain," says Roger.

"Then we can work out how the disease could spread within the brain. This will involve transplanting pieces of brain tissue from people with Parkinson's who have died into mouse brains, to see whether the Lewy bodies that are present in the transplanted tissue will transmit into the mouse brain. Previous research looking at the brains of people who had received foetal brain tissue transplants suggested that Lewy bodies could spread from one part of the brain to the other.

"This work will help us better understand how Parkinson's may progress. It could open up new ways to develop therapies to slow down or stop the progression of the condition."

You can learn about Roger's other projects on pages 8 and 14.

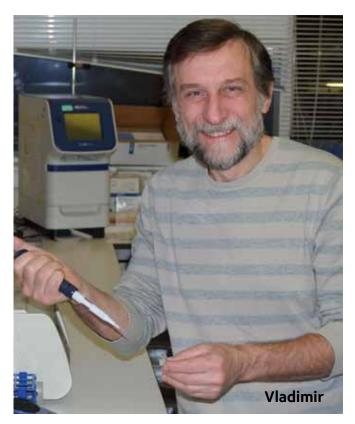


What does alpha-synuclein do in nerve cells?

Alpha-synuclein is a protein associated with Parkinson's. It is a key part of the Lewy bodies found in the nerve cells that die in Parkinson's.

A small number of people have the inherited form of Parkinson's due to changes in the alphasynuclein gene. We know that the development of Parkinson's and the formation of Lewy bodies goes hand-in-hand with certain changes in alphasynuclein within nerve cells. And researchers have shown that the development of Lewy bodies leads to a decrease in the amount of the normal form of the protein inside the cell. We know that a build-up of alpha-synuclein can be harmful. But we also need to find out what the effect of decreased amounts of normal alpha-synuclein will be on a cell.

Professor Vladimir Buchman at Cardiff University has been awarded a three-year research grant of £184,778 to create a new animal model that should help us to understand more about the causes and development of Parkinson's.



"My group and I are asking whether the decrease in the levels of the normal alphasynuclein protein may cause nerve cells to work less efficiently," says Vladimir. "We will generate mice models that have normal amounts of the protein in their nerve cells

while they are growing up, and we will suddenly turn it off when they get older. This will be similar to what happens when the alpha-synuclein in the cell clumps together to form Lewy bodies. But this study will allow us to find out what the effects of the decrease in the alpha-synuclein are without the toxic Lewy bodies being formed.

"If we can better understand what happens to nerve cells when their alpha-synuclein levels drop due to age, we may be able to develop better therapeutic targets for the new generation of drugs to treat the Parkinson's rather than the symptoms. This may bring us even closer to a cure."

Read on to find out more about other projects involving alpha-synuclein and Lewy bodies.

Targeting brain rhythms to find better treatments for Parkinson's

The brain needs to use certain electrical impulses, or rhythms, to co-ordinate movement. Different rhythms have different roles. The rhythm that allows us to maintain our posture and control our movement – called 'beta' rhythm – is different to the one that allows us to perform active tasks, such as reaching out for a mug of tea. This is known as 'gamma' rhythm.

Dr Ian Stanford at Aston University talks to *Progress* about his preliminary research in this area.

"We have shown that the levels of beta rhythms are increased in people with Parkinson's. We've also shown that people with Parkinson's have problems switching between beta and gamma rhythms. This could help to explain why people with Parkinson's have problems with movement. These difficulties can be improved by taking levodopa, but this therapy becomes less effective over time.

"We have shown that low doses of zolpidem, a drug commonly used to treat insomnia, can reduce these abnormal rhythms. People with Parkinson's who have trialled this drug have shown improvement in their movement without experiencing side effects. Because zolpidem only affects the abnormal rhythms, it could be used to make an early diagnosis.

"All of our studies so far have been carried out using people with Parkinson's who are already on medication. My three-year Parkinson's UK grant of £177,578 will allow me to study people who have recently been diagnosed with Parkinson's and who have not yet started any drug treatment. We will give them a low dose of zolpidem and then see if there is any link between changes in their brain rhythms and symptom relief. We also want to look at whether prescribing zolpidem alongside levodopa may have additional benefits.

"Our ultimate aim is to develop a better treatment for Parkinson's, improve early diagnosis and reduce or delay the need for treatment with drugs such as levodopa. As levodopa treatment can have numerous side effects, a reduction or delay in the dose has potentially huge value for people with Parkinson's.

"This project is based on the results from an innovation grant awarded by Parkinson's UK. It's great that we can get initial funding for a piece of research to test a new theory and then use it to bring the possibility of better treatments in the clinic closer."

Should we treat Parkinson's earlier?

More than 70% of dopamine-producing nerve cells have died by the time the movement symptoms of Parkinson's appear. This means that the brain has done a remarkable job of hiding symptoms until a critical point is reached and it can't compensate any longer.

This compensation is managed by a process in the brain called 'brain plasticity'. It's a bit like turning off heating in rooms that are not used in winter, so that fuel is just used to keep essential rooms warm. Some recent trials of Parkinson's drug treatments have suggested that people who started drug treatment soon after being diagnosed seem to respond better than those who delay the start of their treatment. This may be related to brain plasticity. It's possible that the drugs focus on the circuits that are still working and make the most of them, rather than the brain signals being a bit more haphazard in people who are not taking medication.

In a three year study costing £109,794, Professor Kailash Bhatia at the Institute of Neurology, London, will be testing this hypothesis.

Kailash and his team will involve 30 people who are newly diagnosed with Parkinson's. Of these, 15 will have decided to delay treatment, while the other 15 will start on drug treatment straight away.



The team will use a specialised test to measure the electrical signals within the brain (called transcranial magnetic stimulation or TMS). This test will indicate the amount of plasticity in a specific part of the brain.

"Our plan is to compare people who start on treatment right away with those who decided to delay treatment," says Kailash. "We will see whether there is a difference in brain plasticity after a year. The question is, once a person is diagnosed and the symptoms are apparent, should they start treatment straight away, or should it be delayed? Because treatments can have side effects, it may be better to delay treatment while the symptoms are still manageable. But if treatment is delayed, can this lead to symptoms becoming worse more rapidly in the future? This study will help to point us towards the answer."

INNOVATION GRANTS

Here, we report on four new high-risk, high-reward projects. These last for up to 12 months and provide researchers with a chance to test out new and innovative ideas.

Projects that focus on alpha-synuclein

A classic hallmark feature of Parkinson's is the presence of clumps of proteins or Lewy bodies inside the nerve cells that die in Parkinson's. These cells are mainly made up of the protein alpha-synuclein. We have awarded funding to two new innovation research projects to study this protein. You can also read about other projects studying alpha-synuclein and Lewy bodies on pages 10 and 11.

Developing tools to study alpha-synuclein in Parkinson's

Most proteins such as alpha-synuclein exist in many different forms. In order to study these, we need to be able to identify them individually. Specific tools called antibodies can be used to identify different forms of a specific protein. But at the moment we cannot use antibodies in this way with alphasynuclein. So we've given a grant for £34,697 to Dr Rina Bandopadhyay at the Institute of Neurology, London, to develop these antibodies.

Rina

"Antibodies that will recognise individual forms of alpha-synuclein will be made using tissue from the Parkinson's UK Brain Bank," says Rina. "These will help us to understand more about how Parkinson's develops, and they may be used as a marker for diagnosis of the condition. The antibodies will be available for any researchers who want to use them as part of their research."

This is a great example of how Parkinson's researchers are working together to bring us closer to developing a cure for the condition.

Tracking the spread of Parkinson's pathology

Lewy bodies are tiny protein deposits that are found inside the nerve cells that have died in the brains of people with Parkinson's. Researchers have suggested that Lewy bodies can slowly spread from one brain cell into other neighbouring cells (see page 10). Using a grant of £34,253, Dr Michel Goedert at the Medical Research Council laboratory in Cambridge is looking at this in more detail.

"Not all Lewy bodies are exactly the same, and we will test the idea that different types may be responsible for some of the variation in symptoms in Parkinson's," says Michel. "We will also compare them with two related conditions called dementia with Lewy bodies and multiple system atrophy, which also involve Lewy bodies.

"We hope that our findings will lead to a better understanding of how Parkinson's develops. It will also help us to design animal models that can be used for testing drugs in clinical trials. And this is one of the key components of the Parkinson's UK research strategy."

Are proteins on the cell surface involved in selective nerve cell death in Parkinson's?

Specific dopamine-producing nerve cells die in Parkinson's, although we're not sure why they are targeted. To explore this in detail, we have awarded an innovation grant of £34,795 to Dr Roger Barker at the University of Cambridge.

Roger and his colleague Dr Simon Stott, who is also involved in the project, believe that there must be something specific about the particular nerve cells that are more likely to die in Parkinson's. Intriguingly, many of these nerve cells have a protein on their outer surface called CD24.

"Because this protein is only on the nerve cells that die in Parkinson's, it may play a role in the selective death of the cells," says Roger. "So far, most experiments involving CD24 have been completed in mice, so now we wish to investigate the protein in the human brain. This will involve analysis of post-mortem brains from the Parkinson's UK Brain Bank.

"Using mice, we will also look at the consequences of not having CD24 on nerve cells. If the death of nerve cells is reduced in a mouse with no CD24, this would suggest that it may be involved in the death of these cells in Parkinson's. We hope that this research will point towards CD24 as a novel target for future research and therapeutic approaches in Parkinson's."

Why do some people with Parkinson's have abnormal posture?

Many people with Parkinson's experience changes in their posture. This can result in them stooping forward (also known as camptocormia; see opposite page) or leaning to one side (also known as Pisa syndrome). We have awarded Dr Karen Doherty at the Institute of Neurology, London, an innovation grant of £28,175 to look at why this may happen.

Changes in posture can make it harder to walk, and curvature of the spine can make it more difficult to look straight ahead. This can cause breathing difficulties, and pain that most commonly affect the arms, legs, joints and back.

Karen's study aims to answer some basic questions related to postural changes, including how common they are in people with Parkinson's, and what impact they have on people's lives.

"We will examine around 80 to 100 people with Parkinson's to find out whether they have experienced any changes in posture," says Karen. "Participants who have the most clinically obvious symptoms will then be invited to take part in a more intensive interview. This will include an examination and imaging, using X-rays and CT scanning, which allows pictures of the bones to be taken. We will also collect information about people's Parkinson's history, any pain they've experienced and how well they can carry out everyday tasks. From this we will try to work out what kinds of posture problems need the most urgent attention.

"Understanding the causes of postural problems and a person's level of flexibility will help us choose the appropriate treatments for them. These will include physiotherapy or injections of botulinum toxin, a treatment that can temporarily relax muscles. We can also identify who is a good candidate for spinal bracing and who may need spinal surgery.







Images of an individual with Parkinson's who has camptocormia

"At present, we don't know how common these postural problems are in Parkinson's, or who is at most risk of developing them. We also need to investigate the impact they can have on peoples' mobility and quality of life, in order to provide more appropriate treatments. This study will be a building block to providing better management of these problems."

Find out more

If you are interested in finding out more information about the study visit our website parkinsons.org.uk/researchstudies

For more information on other research projects we are currently funding, visit parkinsons.org.uk/research





ONGOING AND COMPLETED RESEARCH



Venomous lizard helps people with Parkinson's

An exciting new clinical trial at University College London Hospital will test the drug Exenatide as a treatment for people with mild to moderate Parkinson's. Exenatide (or EX-4), which is already used to help control diabetes, originates from the saliva of the venomous lizard the 'Gila monster' (pictured above).



The new trial builds on several important studies exploring the benefit of EX-4. This includes a three-year project led by Dr Peter Whitton at the School of Pharmacy in London, which was funded based on the results from an innovation grant funded by Parkinson's UK.

The results of this project suggested that EX-4 may protect the remaining dopamine-producing nerve cells in the brain in a model of Parkinson's, as well as stimulate the re-growth of new ones. So, EX-4 may be able to stop the progression of Parkinson's.

The project results also suggested that EX-4 enhances the effects of levodopa. This could mean that EX-4 could be effective in helping to treat the symptoms of Parkinson's, but at lower doses. So giving EX-4 with levodopa could result in a reduction of unwanted side effects including dyskinesia.

Peter tells us more:

"Most studies of new drugs with 'promise' in Parkinson's use doses that are well above what could be safely tolerated. However, the doses of EX-4 that we have used are very similar to those used for people with diabetes.

"Overall our findings are highly encouraging. Not only are we carrying out studies to better understand what EX-4 does, but the drug is now being tested in a clinical trial. And all this is based on the initial results from the Parkinson's UK innovation grant."

About the new trial

The research team, led by researcher and consultant neurologist Dr Tom Foltynie, has recruited 40 people with mild to moderate Parkinson's from the London area to take part in the 12-month trial. Half of the participants will receive the EX-4 drug and the rest will act as a comparison group.

By carefully monitoring symptoms in both groups, the researchers hope to show that EX-4 can slow the development of the symptoms of Parkinson's – something no current treatments can do.

Clinical trial for potential new treatment is underway

An exciting new clinical trial at Imperial College London will test whether the drug deferiprone can be used to treat people with Parkinson's.

Deferiprone is a drug used by people who have a blood disorder called thalassaemia major that causes iron to gather in organs such as the heart and liver. Deferiprone works by combining with the iron to form a complex that the body can remove.

This new clinical trial stems from several key studies, including two funded by Parkinson's UK which were carried out by Dr David Dexter and Professor Peter Jenner in London.



Previous research has shown that dopamine-producing nerve cells, which are the ones that die in Parkinson's, contain too much iron. The latest study by Dr Dexter and Professor Jenner showed that an increased level of iron in the brain may play a key role in the development of Parkinson's. While iron plays an important role in helping the brain to work normally, too much can actually damage the nerve cells. But we don't know yet what causes it to build up.

When deferiprone was used in rat models, the drug removed the excess iron from the brain and also protected dopamine-producing nerve cells from dying.

So what the researchers plan to do next is to test whether it works in people with Parkinson's.

About the new study

The research team, led by Dr Dexter and Professor Paola Piccini, will recruit 45 people with Parkinson's to take part in the six-month pilot trial. These will be people who are currently not taking any drugs for their Parkinson's and who live in the greater London area.

30 participants will be randomly assigned to receive one of two different doses of deferiprone and the other 15 participants will act as a comparison group. The researchers hope to show that the drug can successfully remove excess iron from the brain using MRI brain scans. The team will also assess whether deferiprone may help to overcome some of the symptoms of Parkinson's.

The research team will be funded by the National Institute for Health Research. If this pilot trial is successful, they will then carry out a larger clinical study in a number of different clinics. They will investigate whether deferiprone can not only treat some of the symptoms of Parkinson's but could actually slow the progression of the condition. The use of deferiprone will be the first study of its kind in newly diagnosed people with Parkinson's.

"If effective, deferiprone may prove a vital drug for slowing the progression of Parkinson's," suggests David. "Before we started the clinical trial, we first tested the drug using human brain tissue from the Parkinson's UK Brain Bank. It's great to see the vital role the brain bank is playing in developing new treatments for Parkinson's."

Find out more

If you are interested in finding out more information about the study contact Dr David Dexter by calling **0207 594 6665** or emailing **d.dexter@imperial.ac.uk**

How does deep brain stimulation work?

Deep brain stimulation is a type of surgery that can be used to treat up to 4% of people with Parkinson's. This surgery has been around for nearly 20 years, but there are still question marks around how exactly it works. As a result it has been difficult to improve it as a treatment.



To look at deep brain stimulation in more detail, we awarded Professor Peter Brown at the Institute of Neurology, London a one-year grant worth £56,000 in 2009. The team believe that they now have a better understanding of how deep brain stimulation works and how the surgery may be improved.

This surgery is generally only used to treat people under 70 who have had Parkinson's for some time and whose symptoms are not being well controlled by medication. This can include people who are experiencing severe involuntary movements (dyskinesia) due to their drugs.

Deep brain stimulation involves the implantation of a thin wire, termed an electrode, into a specific part of the brain. The wire is then connected to a small battery – like a pacemaker – that is implanted under the skin, usually in the chest.

The battery generates electrical signals to stimulate specific nerve cells in the brain that can stop or reduce the Parkinson's symptoms.

"In Parkinson's, we think that the nerves in a specific part of the brain are not generating the correct electrical signals," explains Peter. "And by giving a small electric current from the battery, the nerve cells will be 'shocked' into working normally – in the same way that a pacemaker that helps the heart to beat regularly.

"To explore this theory, we recorded the electrical signals from the brains of 16 people with Parkinson's who had previously undergone the surgery. This was done using a specially-designed device which would allow the brain's tiny signals to be detected while the nerve cells were being stimulated. Using this method, we showed that abnormal brain electrical waves in Parkinson's are suppressed during deep brain stimulation. But symptoms only improve once the battery stimulates the nerve cells.

"This suggests that abnormal brain electrical waves may cause some of the symptoms of Parkinson's. Using this information, it may be possible to design specific pacemakers that will stimulate the nerve cells only when abnormal brain waves are present. This should improve the efficiency and limit the side-effects of deep brain stimulation. It would also help to prolong the battery life as the nerve cells will only be stimulated when they need it, rather than all the time.

"We have now secured a grant of over £1.7million from the Medical Research Council to extend the study. The next stage involves checking to see whether we can continually record electrical signals within the brain over longer periods of time and whether the signals remain stable over months or even years."

Peter is also supervising Dr Ashwani Jha during his three-year career development award. Ashwani is exploring whether it is possible to develop treatments that are targeted to each individual's symptoms. To read about the progress made so far on this project see page 24 of the winter 2010 issue of *Progress*.

PROGRESS

NEWS FROM THE BRAIN BANK — supporting researchers

Registering to donate your brain to the Parkinson's UK Brain Bank is one of the most valuable contributions you can make to Parkinson's research. We have already learned about how brain tissue has been vital in the development of new treatments for Parkinson's (see page 17). The Parkinson's UK Brain Bank provides brain tissue to researchers from around the world who are working to better understand and ultimately develop a cure for Parkinson's.

Donated brain tissue was recently used in the largest and most comprehensive study to date of the role that genetic factors play in Parkinson's.

Professor Nick Wood led a team of international researchers at from the Institute of Neurology in London, who have discovered five new genes involved in Parkinson's. This shows that genetic factors play a greater role in Parkinson's than previously believed.



Dr Una Sheerin, who worked as part of the team, explains:

"We know that genetic factors play an important role in determining a person's susceptibility to developing Parkinson's. Recent studies have reported small changes in many genes in Parkinson's. We think that these genetic changes then combine with other factors such as aging, environmental factors and lifestyle to determine whether or not a person is at greater risk of developing the condition.

"We combined all of the data from a number of separate studies and looked for differences in the genetic information from 12,000 people with Parkinson's and more than 21,000 people without. While we confirmed the role of the six genes that had previously been reported, we also identified a further five new genes that play a role in the development of the condition.

"Discovering five new genes is an exciting step forward and will help us understand more about why and how nerve cells die."

Join the Parkinson's Brain Donor Register

If you want further information on the Brain Bank and how to register, contact the Brain Bank directly: 020 7594 9732 pdbank@imperial.ac.uk

parkinsons.org.uk/brainbank

JOIN OUR RESEARCH SUPPORT NET WORK – and help search for a cure

Our Research Support Network brings together Parkinson's UK members, local groups, supporters, staff and researchers, all driven by the urgent need to find a cure and better treatments for Parkinson's.

And, everyone can get involved in research that will improve treatments and turn the vision of a cure into a reality.

We're passionate about beating Parkinson's. So, if you have a keen interest in research and would like to support our groundbreaking work, please join us.

Become a research supporter

By signing up to the network, we'll keep you up to date with the latest news, events and volunteering opportunities by email.

There are a variety of ways to get involved and you can decide how small or big a part you want to play. It depends on your interests, skills and availability.

All of our opportunities are optional, and range from activities you can do at home to those that you can do in your community. For example, you could:

- come to a talk to find out more about our research
- chat about research on our online discussion forum
- raise funds so we can continue our vital work
- take part in a survey or research study (see pages 25 – 27)

George Hardman talks to Progress about his inspiration to join the network.

George Hardman, 76, was a chartered surveyor, before becoming a Methodist Minister. His wife Jean was diagnosed with Parkinson's in 2003 at the age of 66. Jean and George celebrated their 54th wedding anniversary in March 2011.

What inspired you to become a member of the Research Support Network?

"It was really Jean's idea. She noticed an advert in *The Parkinson* asking for people to join the network. I wasn't certain of what I had to offer because I don't have a scientific or medical background. But Jean was very persuasive and I was interested to learn more about Parkinson's. I also wanted to be able to support her in any way I could."

What sort of things have you worked on?

"I've been involved in a number of different projects. I've worked as a lay grant reviewer, so I've given my opinion on which research projects I think are really worth pursuing and, therefore, should be funded. I've also worked on the Brain Bank assessment panel. This involved discussing the potential benefits of having a joint Brain Bank with the Multiple Sclerosis Society."





"I have also enjoyed being on the Monument Discovery Award assessment panel where I could have a say on which of the shortlisted research teams should be awarded this prestigious grant. This is one of the charity's most expensive projects, costing £5million over five years. But if it leads us closer to a potential cure for Parkinson's, then it has certainly been a worthwhile project. I feel privileged to have had an input."

What area of research are you interested in?

"It is difficult to pinpoint one area, but because I've been on the Brain Bank review panel I have developed an interest in its valuable work. I am surprised that so many cases of Parkinson's are still misdiagnosed and it is only after a person has died that you can definitively tell that they had Parkinson's. So there is an urgent need to find more specific ways to diagnose Parkinson's accurately. I believe that this is one of the charity's priorities.

"I am also interested in learning more about how genes such as LRRK2 and parkin are linked to the development of Parkinson's.

"Ultimately, I hope that research will one day identify a cure for Parkinson's. But I am particularly interested in research that not only identifies the causes of the condition and understands what leads to nerve cell death, but also focuses on helping people cope with Parkinson's on a day-to-day basis."

What do you get out of being a member?

"I have enjoyed meeting some really remarkable people – people who are never scared of Parkinson's. I have had the opportunity to meet researchers involved in Parkinson's, as well as meeting members of staff at Parkinson's UK. To feel I have made a contribution makes me feel richer as a person!"

What advice would you offer any one who wishes to join the Research Support Network?

"I would say don't hesitate. Don't be put off by not having a scientific background because everybody will have something to offer. My experience has been very rewarding and I feel humbled to be part of the network. I have met people of all walks of life who face similar challenges, whether it is someone who has Parkinson's or a carer. It is a great way to share experiences and I would feel a lot poorer for not being part of the network."

JOIN US

Our network is free to join and open to anyone interested in Parkinson's research. To find out more or to sign up, contact Emily Hughes, Research Support Network Manager, on **020 7963 9376** or **rsn@parkinsons.org.uk**

ROGRESS

PARKINSON'S AWARENESS WEEK

arkinson's Awareness Week (11–17 April 2011) highlighted research as one of the key priorities of Parkinson's UK. The theme of 'Join us' focused on getting as many people as possible involved in all aspects of our research work. We spread the word at events across the UK, through national and local media coverage, and online via our website, Facebook, Twitter and YouTube.

At the start of the week, we launched Dr Alastair Noyce's project 'Can we predict Parkinson's?' The Predict PD study aims to identify people who may be at risk of developing Parkinson's. By June this year, we had recruited 120 of the target 1,000 healthy, internet-users without Parkinson's aged 60 to 80 needed to take part in the study. If you would like find out more visit parkinsons.org.uk/predictpd. For further information, see the winter 2010 issue of *Progress*.

A series of research events took place in London, Cambridge and Sheffield to showcase the cuttingedge research supported by Parkinson's UK.

London

We welcomed around forty-five Parkinson's UK members to our national office in Victoria, to hear about our plans for developing a cure for Parkinson's. Dr Patrick Lewis, a Parkinson's UK-funded Research Fellow based at the Institute of Neurology, London, spoke about his work on LRRK2 – the most common gene associated with Parkinson's. His current research looks at what the normal LRRK2 gene does in order to understand how it can go wrong. The results may help to develop new therapies that could correct the problems associated with the faulty gene. You can find more information on this study on page 13 of the winter 2010 issue of *Progress*.

Professor Ray Chaudhuri from King's College Hospital spoke about his work on the non-motor symptoms of Parkinson's such as depression and sleep and memory problems. He spoke about the importance of developing questionnaires that healthcare professionals can use to identify non-motor symptoms.

The event was also attended by a young Parkinson's UK fundraiser, Jess Ridge (pictured below). Ten-year-old Jess presented our Director of Research and Development, Dr Kieran Breen, with a cheque for £6,090 that she had raised to support our work.



All of the feedback from those who attended was very positive. Members enjoyed having the opportunity to ask researchers questions about their groundbreaking work that is being funded by Parkinson's UK.

Cambridge

For the second year in succession, Parkinson's Awareness Week was marked in Cambridge by the Gretschen Amphlet memorial research lecture. Generously supported by the Amphlet family, this extremely popular event brought together people with Parkinson's, healthcare professionals and Parkinson's UK supporters to learn about the progress being made in Parkinson's research.

This year's lecture was given by local neurologist and University Reader in Clinical Neuroscience, Dr Roger Barker from the University of Cambridge, whose latest research projects feature on pages 10 and 14.

A packed auditorium at Fitzwilliam College in Cambridge was captivated by Roger's inspiring lecture entitled, 'Solving the Clues to Parkinson's'. He addressed four key questions:

What do we know about the causes of Parkinson's?

Roger mentioned the key milestones that have increased our understanding of the condition. Starting with the condition's original description by Dr James Parkinson in 1817, Roger took us through to the most recent studies around the genetics and molecular causes of Parkinson's.

How we can better study Parkinson's?

This included plotting the journey from the early studies around dopamine replacement therapy that started with levodopa in the 1960s, to our increasing ability to create stem cells in the laboratory that have the potential to become nerve cells and therefore replace those lost in Parkinson's.

How does Parkinson's progress once it has started?

This revealed a fascinating emerging hypothesis that Parkinson's may be considered as a 'prion' disorder. This essentially means that the condition could be caused by the generation of an abnormal form of a specific protein called alpha-synuclein. This could then set off a domino-like effect with the abnormal or prion form of the protein being transmitted to other parts of the body. It has been proposed that the process may actually begin outside the brain (such as in the gut) but that it would eventually be spread by nerves which connect the gut with the brain. Read page 10 to learn about Roger's Parkinson's UK-funded study that is looking at tracking the spread of Parkinson's.

How can we improve the treatment of the condition?

He referred to the CamPalGN study that recruited people with Parkinson's in Cambridge between 2000 and 2002. These have now been followed up and clinical data has been collected from around 240 people with either Parkinson's or other parkinsonian conditions, such as multiple system atrophy, that are also associated with the death of nerve cells in specific areas of the brain.

From the results, he concluded that better treatment depends on us recognising that there are different types of conditions that exist within the umbrella term 'Parkinson's' and that we need to match specific therapies to each sub-category of the condition.

We are extremely grateful to the Amphlet family for making the lecture possible and enabling us to highlight the contribution that research in Cambridge funded by Parkinson's UK, is funding are making to the search for a cure.

Sheffield

Dr Oliver Bandmann hosted a research open day at the newly opened Sheffield Institute for Translational Neuroscience (SiTRaN). The event was opened by the Duke of Devonshire and was attended by around one hundred people, including around thirty people from Parkinson's UK local groups.

Stacey Storey, Research Co-ordinator at Parkinson's UK, reports back on the day:

"The talk that stood out was one given by Graham Wood, who is a member of the Research Support Network [find out more about the network on pages 20–21]. He spoke about the value of involving people living with Parkinson's in our research. I also enjoyed learning about Dr Oliver Bandmann's work on the zebrafish [learn more about Oliver's work on pages 5 and 9]."



find a cure.

ynda Hemming, a mother of two from Blackpool, was diagnosed with Parkinson's just under seven years ago, at the age of 36.

Since her diagnosis, Lynda has tried a range of medications, including levodopa, but like some people with Parkinson's, found that the tablets

didn't always work. "They had terrible side effects and there were times when the medication didn't work and I couldn't walk," she says.

Lynda had heard about deep brain stimulation and in May last year she went to her specialist to discuss it as a treatment option. They agreed it would be worth trying. Lynda reflects: "When you've got a family, you want to try whatever you can."

It was several months later – on 19 January this year – that Lynda had her deep brain stimulation operation. But the operation didn't just give her hope for the future, it also spurred on a very successful fundraising event to raise money for Parkinson's UK.

"I was mortified at having to have my head shaved for the operation. So my husband Adrian said he would get his head shaved too, and then friends also offered to get involved and be sponsored to get their heads shaved." That led to organising a Party for Parkinson's on the Friday before her operation in their local pub, the Sandpiper in Cleaveleys. With the help of family and friends, they raised an astonishing £2,412. They held a raffle, with prizes donated from local shops. Lynda's 10-year-old daughter Alisha manned a table for a 'guess the name of the teddy' competition and

her 17-year-old son, Ryan, ran the tombola. Their friends also managed to get hold of auction prizes, including two signed football shirts, which raised £250 each

Lynda's advice to anyone thinking about hosting a Party for Parkinson's is to, "get as many people involved as possible. I couldn't have done it on my own."

If it wasn't for people raising which raised £250 each.

money, you'd never get anywhere to to get hold of auction prizincluding two signed footly which raised £250 each.

Lynda's advice to anyone about hosting a Party for

Her message about raising funds for Parkinson's is clear: "If it wasn't for people raising money, you'd never get anywhere to find a cure."

It can take up to 12 months for the full effects of deep brain stimulation to be felt, but Lynda is optimistic following her operation. "It means there's a light at the end of the tunnel," she says.

If you would like to host a Party for Parkinson's, you can request a pack by contacting the Events team on 020 7963 9319 or emailing party@parkinsons.org.uk

To learn about Parkinson's UK studies involving deep brain stimulation, see page 18.

TAKE PART IN PARKINSON'S RESEARCH

In this section is a selection of current Parkinson's research projects from around the UK which may be recruiting participants. The list is provided for information only, and should not be treated as advice or a recommendation to join in any of the studies.

If you're considering taking part in a research study, we would advise that you consult your specialist or Parkinson's nurse before contacting the healthcare professionals managing the study. To find out more about getting involved in a particular study, visit parkinsons.org.uk/researchstudies or contact the researchers directly.

LOCATION	TITLE AND RESEARCH SUMMARY	CONTACT PERSON	WEBSITE ADDRESS
Web-based studies	23andme Parkinson's genetics study This web-based study, supported by Google cofounder Sergey Brin, aims to uncover vital changes in genes that affect the risk of developing Parkinson's. Participants fill in an internet survey about their symptoms and lifestyle and provide a sample of saliva containing their DNA.	pd-help@23andme.com	www.23andme.com/pd
South England	Monument Discovery Award: Understanding the early pathological pathways in Parkinson's This study, part of the £5million Parkinson's UK-funded Monument Discovery Award, aims to find new ways to spot Parkinson's earlier. The researchers will look for subtle differences in DNA, brain imaging, samples of blood and cerebral- spinal fluid from people in the early stages of Parkinson's. It will recruit people from the Thames Valley region.	Miss Kathryn Lucas Thames Valley Clinical Research Network (DeNDRoN) Room 4401D Level 4 John Radcliffe Main Hospital Headley Way Headington Oxford OX3 9DU 01865 234310 k.lucas@nhs.net	http://public.ukcrn.org. uk/Search/StudyDetail. aspx?StudyID=9101

LOCATION	TITLE AND RESEARCH SUMMARY	CONTACT PERSON	WEBSITE ADDRESS
North-east and east England	Identifying predictors of dementia in Parkinson's This Parkinson's UK-funded project that aims to find ways of identifying people with Parkinson's who are at greater risk of developing dementia. This will help us diagnose dementia earlier on, enabling better treatment and improving quality of life. This study is open to all people with Parkinson's diagnosed since 1 June 2009 and who meet study criteria.	Recruitment centres are located in Newcastle and Cambridge. Dr Alison Yarnall, Dr Gordon Duncan or Dr Tien Khoo Clinical Ageing Research Unit Newcastle University Newcastle upon Tyne Tyne and Wear NE4 5PL 0191 248 1295 alison.yarnall@ncl.ac.uk gordon.duncan@ncl.ac.uk	http://public.ukcrn.org. uk/Search/StudyDetail. aspx?StudyID=5643
North-east England	Can studying walking help to predict thinking and memory problems in Parkinson's? This Parkinson's UK-funded project will use detailed gait analysis to attempt to identify people with Parkinson's who are at higher risk of developing thinking and memory problems. Identifying these people early would allow earlier treatment.	Dr Sue Lord Newcastle University CARU Campus for Ageing and Vitality Newcastle upon Tyne NE4 5PL sue.lord@ncl.ac.uk	http://public.ukcrn.org. uk/Search/StudyDetail. aspx?StudyID=8470
London	How changes in genes lead to Parkinson's This project will use cells from people who have genetic changes that are known to be involved in Parkinson's. Studying how gene changes affect how the cells work will lead to a better understanding of how Parkinson's develops in the brain.	Prof Anthony Schapira Royal Free Hospital Pond Street London NW3 2QG anthony.schapira@ royalfree.nhs.uk	http://public.ukcrn.org. uk/Search/StudyDetail. aspx?StudyID=8886

North-west England	Why do people with Parkinson's have trouble swallowing? This Parkinson's UK-funded study will investigate how and why swallowing problems develop in people with Parkinson's. The researchers want to know how Parkinson's medication affects the areas of the brain and muscles that control swallowing.	Dr Emilia Michou A111 Clinical Sciences Building Salford Royal NHS Foundation Trust Stott Lane Salford M6 8HD 0161 206 1510 emilia.michou@ manchester.ac.uk aimilia-emilia.michou@ srft.nhs.uk	http://public.ukcrn.org. uk/Search/StudyDetail. aspx?StudyID=9882
East England	Psychiatric aspects of Parkinson's Many people with Parkinson's experience emotional or other psychiatric symptoms related to the condition. This project is investigating what may trigger these symptoms, using a combination of interviews and brain imaging techniques.	Dr Graham Murray University of Cambridge Addenbrookes Hospital Hills Road Cambridge CB2 OQQ 01223 764678 gm285@cam.ac.uk	http://public.ukcrn.org. uk/Search/StudyDetail. aspx?StudyID=8364

This is not a complete list. You can find more studies by visiting parkinsons.org.uk/researchstudies

Progress is produced by the Parkinson's UK Research and Development team in collaboration with the Information Resources and Communications teams

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