

PROGRESS

The research magazine of Parkinson's UK |
Autumn 2019

A clinical trial of CBD

We talk to the
experts about
how a chemical
in cannabis
may help with
Parkinson's
psychosis

MITOCHONDRIA AND PARKINSON'S

Could these cell batteries
hold the key to new
treatments?

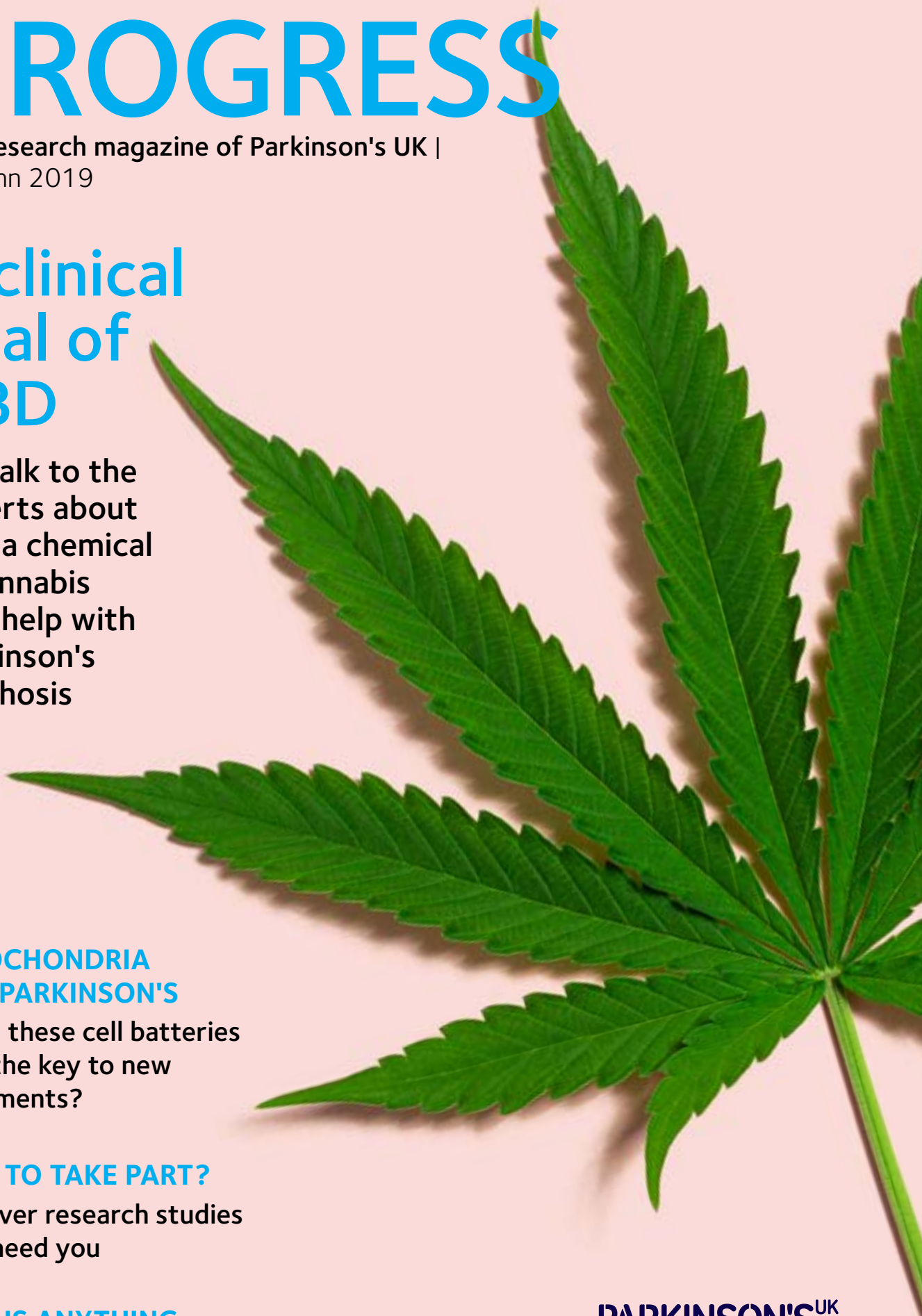
TIME TO TAKE PART?

Discover research studies
that need you

ASK US ANYTHING

Our new feature
answering your questions

PARKINSON'S^{UK}
CHANGE ATTITUDES.
FIND A CURE.
JOIN US.



Dave Wilson from Glasgow has lived with Parkinson's for the past six years. He is a volunteer with Parkinson's UK. As well as being a member of the Scotland Development team, Dave has recently joined the *Progress* Magazine Review Board.



I'll never forget the words: "I think you have Parkinson's." It was like being smacked in the face with a cricket bat. That immediate initial reaction was soon replaced by a thirst for knowledge. What is Parkinson's? What causes it? How will it affect me and my future? A million and one questions.

Where to start? The internet of course! I was like a dried-up sponge, soaking up information. But I needed to be sure that I could trust the information I was reading. It was no accident that before long I was searching the Parkinson's UK website. I was lucky – my neurology consultant had recommended it at my first appointment. I soon joined Parkinson's UK, and with membership came a heap of printed resources, including the research magazine *Progress*.

By now, my mind was becoming focused less on symptoms and treatment – I was now more keen than ever to learn about current research. What research is being funded? When will we see a cure? And what can we do until then to improve quality of life for everyone living with Parkinson's?

To be honest, I didn't quite appreciate what a gem *Progress* magazine was or the range of research topics it covered. I'd normally flick through it, just reading the articles that caught my eye. It was only when I was asked to participate in a focus group that I found myself reading several back issues cover to cover. What a wealth of information!

From in-depth reports like the one on Parkinson's psychosis on

page 11, to brief updates like the news roundup on page 4, there's something in every issue to pique your interest. You'll also find in this issue a new feature called 'Question time', allowing you to become even more engaged with *Progress*. This was a suggestion from one of our focus groups and I'm delighted to see it feature in *Progress* so quickly.

So, if you have just picked up the latest edition of *Progress* and started to flick through it, reading bits and pieces, I would encourage you to keep going – read it all and stay informed about Parkinson's research news and what's on the horizon. ■

Dave

Progress is our free, twice-yearly magazine on the latest research into Parkinson's.

ON THE COVER

Our main story focuses on what Parkinson's psychosis is and how researchers are using cannabidiol (CBD) to target this distressing symptom.

■ 11

Psychosis in Parkinson's – ask the expert



NEWS

■ 4

News roundup

Catch up on some of the latest research stories making the headlines over the past few months.

■ 16

New research

From exercise to genetics, we take a look at some of our newest research projects.

■ 30

Research results

Our research projects have identified existing drugs with potential for treating Parkinson's, investigated the role of rare genetic changes, and helped us understand the effect of deep brain stimulation on brain cells.



FEATURES

■ 6

Coast to coast

We're funding research across the UK to find a cure for Parkinson's.

■ 20

Trials to treatments: mitochondria

How targeting the cell batteries is leading towards new treatments

TAKING PART IN RESEARCH

■ 27

Take a look at some of the latest opportunities to get involved in research.

QUESTION TIME

■ 34

We find out about diabetes and protein-rich foods.



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For more information on *Progress*, contact our Research team directly.

Email the Research team on research@parkinsons.org.uk or phone on **020 7963 3964**.

NEWS

ROUNDUP

Prostate drug shows promise in Parkinson's

A drug used to treat enlarged prostates may have exciting potential for slowing down Parkinson's, according to new research.

In a mouse model of Parkinson's, treatment with the prostate drug, terazosin, was able to increase dopamine levels and improved movement symptoms. Researchers believe that the drug can protect nerves from damage by boosting the levels of energy in the brain cells.

The study also looked at people already taking the drug. By comparing data from 150,000 people treated for an enlarged prostate – where half were on drugs such as terazosin and half were on alternative medication – they found that those on terazosin were less likely to develop Parkinson's.

And looking at people with Parkinson's who have been treated for an enlarged prostate, those treated with terazosin seemed to have less severe symptoms and slower progression of their Parkinson's.

The prostate drug now needs to be tested in clinical trials to see if it alters the progression of Parkinson's – clinical trials are currently being planned in the US.

Professor David Dexter, Deputy Director of Research at Parkinson's UK, says:

"These exciting results show that terazosin may have hidden potential for slowing the progression of Parkinson's, something that is desperately needed to help people live well for longer."

New research puts serotonin at the heart of Parkinson's

Researchers from King's College London have used brain scans to uncover early changes in the brain that may happen years before the symptoms of Parkinson's appear.

Serotonin is a chemical produced by nerve cells to send messages across the brain, often called the "happy hormone". Researchers looked at the brains of people with extremely rare genetic mutations that meant they had a very high risk of developing Parkinson's in the future.

They showed that changes in serotonin signalling may happen in the earliest stages of Parkinson's – before significant loss of dopamine-producing cells. The changes could also be found ahead of dopamine cell loss in other areas of the brain, as the condition progressed.

Research has previously shown associations between Parkinson's and serotonin, but this is the first study to show that changes in serotonin signalling may be an early consequence of Parkinson's, challenging the traditional view of what causes the condition.

Dr Beckie Port, Research Communications Manager at Parkinson's UK, says:

"Detecting changes that are happening in the brain in the early stages of Parkinson's is a crucial gap in research at the moment. Picking up on the condition earlier and being able to monitor its progression would aid the discovery of new and better treatments that could slow the loss of brain cells in Parkinson's."

Research shows home exercise improves movement symptoms

A study has found that people taking part in a home-based exercise programme experienced improvements in their motor symptoms

The results, published in the journal *The Lancet Neurology*, highlight the potential of an indoor cycling programme to improve symptoms in those with early-stage Parkinson's. 130 people with Parkinson's took part in the study, either using an exercise bike or taking part in gentle stretching.

The results showed that motor symptoms improved more in those doing the aerobic exercise programme than the control group. However, no difference was seen in non-motor symptoms such as sleep and memory.

Dr Katherine Fletcher, Research Communications Officer at Parkinson's UK, said:

"There is still much to be learnt about what types of exercise and physical activity improve different types of Parkinson's symptoms, and how exercise may be having a long term effect on our brain.

"What we do know is that exercise is good for all of us, and for those with Parkinson's it can be as important as medication for managing symptoms."

READ OUR BLOG

Find out the latest research news, and go behind the headlines, by visiting our research blog at parkinsons.org.uk/blog ■

Coast to coast

From Glasgow to Plymouth, our researchers are tackling Parkinson's across the UK. We're supporting the most promising scientists to unlock the ideas that will lead to new treatments and, one day, a cure. You can read a full list of our research projects at parkinsons.org.uk/projects

GLASGOW

The ambitious Tracking Parkinson's study examines how and why people differ in their symptoms and progress over time. Understanding these differences will help us develop better and more targeted treatments.


CARDIFF

Can transplanting dopamine-producing cells into the brains of rats help with the symptoms of Parkinson's? Researchers in Cardiff are using stem cell technology to answer this question.

PLYMOUTH

Researchers in Plymouth want to understand more about how Parkinson's affects turning, which can lead to falls. It's hoped that this information will lead to ways to reduce turning problems in everyday life. Turn to page 17 for more information.





Parkinson's UK is the largest charitable funder of Parkinson's research in Europe. Over the past 50 years, we've invested more than £96 million into groundbreaking research, with nearly £60 million awarded in the last 10 years.

We fund more than 50 teams of scientists across the UK with their research. We're also spearheading pioneering projects including our Virtual Biotech and the Critical Path for Parkinson's, so we can find a cure for everyone with Parkinson's, together.

SHEFFIELD

Can existing drugs treat Parkinson's? Researchers in Sheffield are looking to see if licensed drugs can protect nerve cells and therefore slow or stop Parkinson's progression.

OXFORD

The Oxford Parkinson's Disease Centre is a unique, collaborative initiative that brings together the best scientific minds to speed up the search for better treatments and a cure.

LONDON

The Parkinson's UK Brain Bank is the world's only tissue bank dedicated to Parkinson's research. The brain and spinal cord tissues are supplied free of charge to researchers studying Parkinson's all over the world.

FEATURE

A two-pronged approach

We fund research to advance our understanding of Parkinson's, what causes it, and how we can cure it in the future. But Parkinson's is happening now – so we also fund research that aims to improve treatments and therapies to make life easier for people living with the condition.

Towards a cure

It's only by truly understanding the complex causes of Parkinson's, and how it progresses, that we'll be able to come up with strategies that can stop, reverse or even prevent the condition.

Since 2009, we've invested over £30 million into understanding the causes of Parkinson's, investigating a broad range of areas including misfolded proteins, genetics and mitochondria. We're even moving outside the brain to look at whether the gut plays a role.

And this increased understanding is being used to help us search for a cure. By looking at existing

drugs and developing new ones we are moving forward towards stopping Parkinson's.

Making a difference now

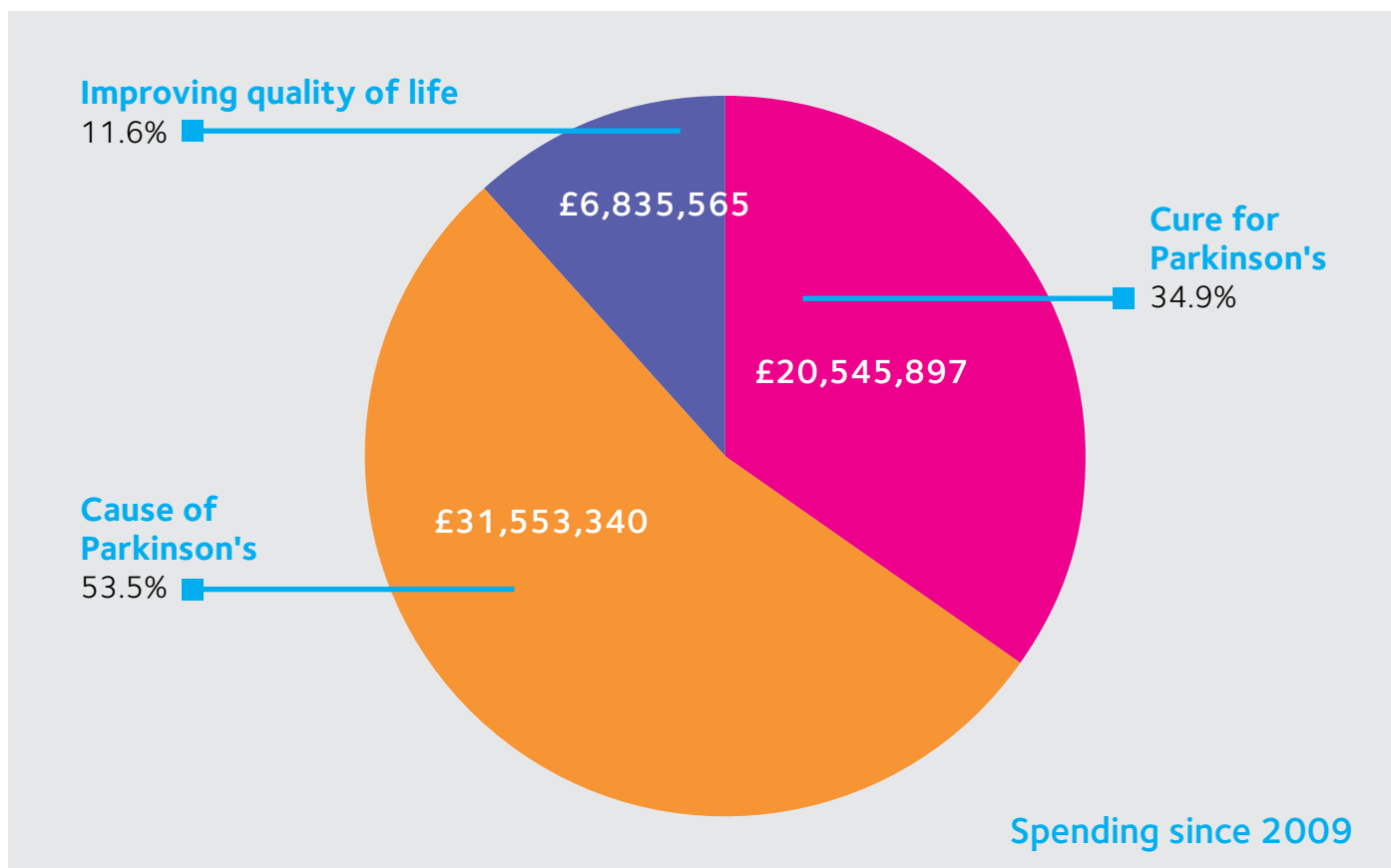
We know that finding a cure will take time – so we also fund research to improve the quality of life for people with Parkinson's and their families.

From finding treatments that can improve memory problems, to optimising therapies to help manage feelings of anxiety, we're doing all we can to help people living with Parkinson's now.

Making the right decision

All medical research is expensive – a lab-based research project can easily cost hundreds of thousands of pounds. This means at Parkinson's UK, we have a big responsibility to invest money wisely – ensuring the research we fund has the highest possibility of success.

Every year, we invite researchers from across the UK to apply to us for funding of their work. The



applications are then evaluated by Parkinson's research experts. They assess the quality of the proposed research and its potential for moving our understanding of Parkinson's forward, before making recommendations for funding.

We also have up approximately 100 lay grant reviewers, who are personally affected by

Parkinson's. Feedback from lay grant reviewers allows us to incorporate the unique and valuable perspective of people affected by Parkinson's into how we decide which projects to fund.

Find out more at parkinsons.org.uk/researchvolunteer



Speeding up the hunt for a cure

Despite decades of research and major breakthroughs in our understanding of Parkinson's, a cure always seems to be five, 10 or even 20 years away. We know that people cannot wait this long. That's why Parkinson's UK is leading on innovative programmes to bring forward better treatments in years, not decades.

Our Virtual Biotech fast tracks the most promising scientific discoveries to rapidly develop and test promising Parkinson's treatments and push them forward into clinical trials (see page 25). But we know that's not enough to ensure people get the new treatments they've been waiting for. Clinical trials are the most costly and lengthy part of the whole research process. And in recent years, several promising new treatments for Parkinson's have failed to show a benefit in clinical trials. So we've also co-created the Critical Path for Parkinson's – an international collaboration to increase the efficiency and speed of clinical trials.

Ultimately we want to make trials smarter, faster and more likely to succeed. The Critical Path for Parkinson's will do this by using data from previous trials and studies to develop new tools and strategies to improve clinical trials for Parkinson's. And we're already seeing progress with new tools being approved to help select the right people to take part in research studies.

Together, our Virtual Biotech and Critical Path for Parkinson's are shaking up the way research is done and lighting the way for promising research to be turned into life-changing treatments.

'It gives me a sense of purpose'

Mark Hoar is a lay grant reviewer for Parkinson's UK. He talked to us about his role in helping to progress Parkinson's research.

"I was diagnosed with Parkinson's when I was 40. I was working as a policeman before my condition forced me to take early retirement 10 years later. It was difficult to cope with – like I'd lost my feeling of self-worth."

A vital role

"I got more and more involved with Parkinson's UK, initially being recruited as a volunteer fundraiser, where I gave talks to the community about my condition and the work of the charity.

"I soon realised I needed to know more about the research side of things. Having last studied biology in 1979, the questions I was being asked were slightly above me!

"So I signed up to be a member of the Patient and Public Involvement Steering Group. I now have the opportunity to learn all I can about my condition, and make sure the voice of the common man is represented in Parkinson's research.

"I also review the plain English summaries from the application forms submitted for research funding. I provide feedback on how accessible the research is and, more importantly, if I think the work will make a difference to the lives of people living with Parkinson's.

"For me, having people living with Parkinson's help shape the direction of research is vital. You can learn a lot about Parkinson's in a textbook, but until you live with it, it's impossible to understand how complex, varied and difficult this condition is. And it's this perspective that's essential if we're going to drive research forward."

Not a tick-box exercise

"The researchers are very respectful of our opinions. You're absolutely listened to. And you can tell when researchers have taken the advice of people with Parkinson's – the applications are often much improved.

"It's not just a tick-box exercise. It's an essential part of making sure the research idea is the best it can possibly be before funding.

"Happily, I get so much out of it as well. It gives me purpose – a way to give back. I'm not a scientist but I can make a real difference." ■





PSYCHOSIS IN PARKINSON'S – ASK THE EXPERT

Some people with Parkinson's may experience hallucinations or delusions – this can also be known as Parkinson's psychosis. But what exactly is Parkinson's psychosis, and could a chemical in cannabis be the answer to tackling this troublesome symptom?

ON THE COVER

There are many different symptoms of Parkinson's and not everyone will experience the same ones.

Evidence indicates up to 60% of people with Parkinson's go on to develop symptoms of Parkinson's psychosis as their condition progresses. And this risk increases in people with Parkinson's dementia.

These symptoms can be extremely distressing for both the person with Parkinson's and their families.

We're joined by experts in neurological conditions and psychosis from King's College London: Dr Sagnik Bhattacharyya, Dr Latha Velayudhan and Dr Dominic Ffytche. They answer some of the key questions on this topic.

Q What is Parkinson's psychosis?

Dominic:

Parkinson's psychosis is a specific term used to describe psychosis symptoms in Parkinson's. It's separate to psychosis found in other conditions.

Everyone is unique and not everyone who has Parkinson's will develop these symptoms.

Parkinson's psychosis usually starts with perceptual disturbances where things are misinterpreted, for example:

- seeing a branch of a tree as a cat
- seeing movements or figures in the corner of your eye
- having a feeling that someone is close or nearby, or feeling a presence.

As Parkinson's progresses, psychosis symptoms may evolve into more formed hallucinations, for instance, seeing people or animals that are not there. At this stage, people are usually aware when something is a hallucination and can appreciate that it's not real.

But this can change, and as Parkinson's progresses it may be that people can't separate reality from hallucinations or delusions.

Delusions are strange beliefs, such as a belief that:

- things have been stolen
- their spouse is being unfaithful
- someone is out to hurt or harm them.

This stage of Parkinson's psychosis has more similarities with psychosis found in other conditions, such as schizophrenia.

Q Why can psychosis occur in Parkinson's?

Dominic:

Dopamine-replacement medication such as levodopa has been around for more than 50 years and it was always assumed that Parkinson's psychosis was a side effect of these medications.

Especially as sometimes people report psychotic symptoms after increasing their dose or changing their medication.

But this is not always the case, and the fact that not everyone experiences psychosis suggests it must be more than a side effect of the medication.

Now we believe that changes in parts of the brain, including the parts that control movement and vision, may play a role in the causes of Parkinson's psychosis.

Sagnik:

But overall, we do not fully understand what causes the psychotic symptoms in Parkinson's.

Latha:

This symptom can be further complicated if someone develops an infection, such as a urinary tract infection, making them more prone to hallucinations. This is more common in older people.

Q What should someone do if they are experiencing psychosis? Are there currently any treatments?

Latha:

In the early stages of Parkinson's psychosis, when someone is aware that they are experiencing hallucinations or delusions, reassurance and management strategies such as changing the lighting can help reduce the impact of this symptom.

Once the awareness is lost, this might be when people are prescribed medications. One such drug is an antipsychotic medication called clozapine and although it reduces hallucinations, it has significant side effects and requires regular blood tests and monitoring of cardiac side effects.

Another drug called rivastigmine has been shown to reduce visual hallucinations, but this has only been shown in people with Parkinson's dementia. There is a promising anti-psychotic drug called pimavanserin that is approved in the US but currently not licensed here. However, this medication too has cardiac side effects.

So in summary, none of these treatments are ideal.

Dominic:

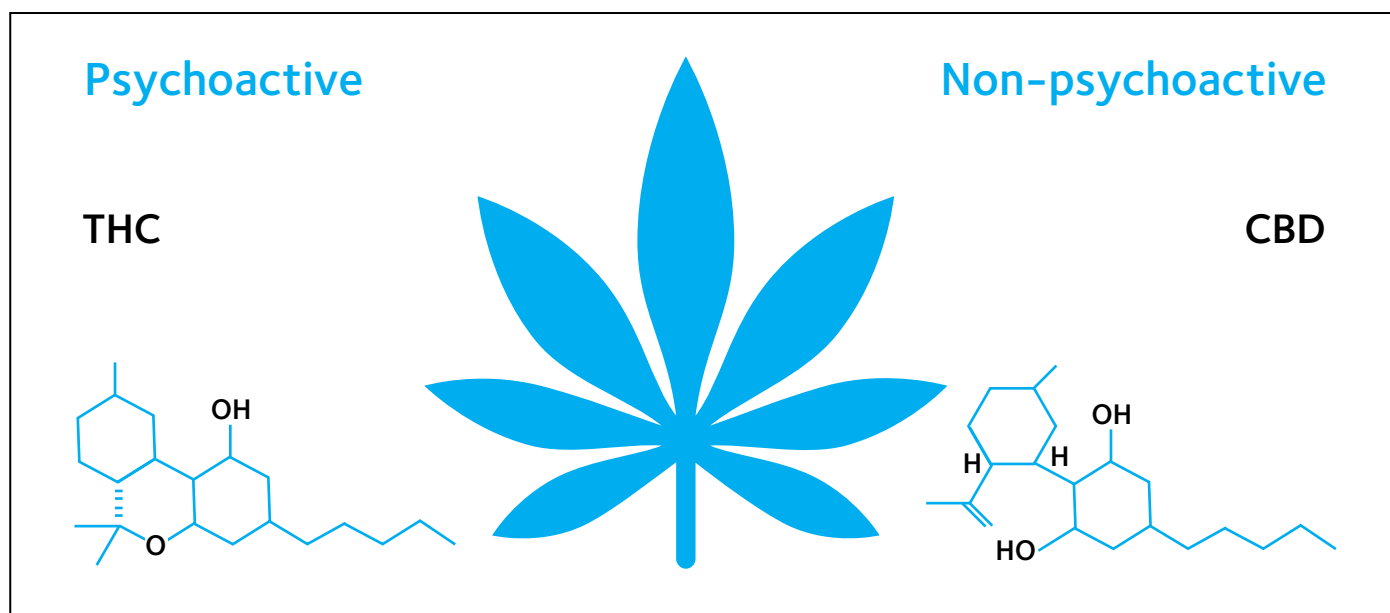
We also need to think about treatments in a wider sense because carers are often impacted more than the person with this symptom. Parkinson's psychosis can be distressing and troubling for the carers and can cause arguments and upset. This is why we are really keen to find a treatment for this symptom.


Q What research is being done?

Sagnik:

As Latha and Dominic have mentioned, existing treatments for psychosis in Parkinson's are not very effective or ideal for a long-term treatment. We need a treatment that can be simply administered and on a regular basis.

Cannabis has been shown in several studies to increase the risk of developing psychosis. But actually, the cannabis plant is made up of many different substances. Two of the most commonly studied are THC (tetrahydrocannabinol), the compound responsible for the psychoactive properties of the plant, and CBD (cannabidiol), which is not psychoactive [see below].





“ In our survey of 1,200 people with Parkinson’s, 59% hadn’t used cannabis-derived products before but would consider using them to control their symptoms. ”

From the Parkinson’s UK 2019 cannabis survey. Read more at parkinsons.org.uk/cannabisresults

Research shows that CBD, when taken alone, may actually have the potential to reduce the symptoms of psychosis. There have also been previous studies that have shown that CBD is well tolerated when given as a treatment and seems to have few side effects. But what has not been done is investigating the impact of CBD on Parkinson's psychosis. We're partnering with Parkinson's UK, through the Parkinson's Virtual Biotech, to investigate just this.

At a cost of £1.2 million over three and a half years, we're recruiting for a clinical trial to test the safety and benefits of CBD on Parkinson's psychosis.

The first stage of the trial will recruit up to 24 people with Parkinson's psychosis to an initial six-week study.

The focus will be on understanding the safety of CBD in people with Parkinson's psychosis. Participants will be carefully monitored for any side effects or interactions between their current drugs and CBD. A range of doses will be tested to select the most appropriate one to use in the next stage.

In the second stage, we will aim to recruit 120 people with Parkinson's psychosis to take part in a 12-week study. Half the group will receive CBD and half will receive a placebo (a dummy drug). As well as continuing to monitor safety, we will carry out detailed assessments of psychotic symptoms. We will also be keeping an eye on other symptoms, in case CBD has an effect on them as well.

Finally, 40 participants from the second stage of the trial will be invited to undergo MRI brain scans. We also aim to recruit 20 people with Parkinson's who do not have psychosis and 20 people of a similar age without either condition to participate in this part of the study. This will enable us to compare patterns of brain activity in the trial participants with those of people who don't have Parkinson's psychosis or Parkinson's, as well as examine the changes in brain activity following treatment. We hope this will help us to understand more about how CBD works.

CBD – the story so far

The law around cannabis and CBD can be confusing. In November 2018, medicinal cannabis was legalised for certain conditions, but with strict criteria in place, only a handful of people have accessed it to date.

For CBD, as long as sellers don't make explicit health claims about the product, they don't need a license to sell it. While this means that CBD is widely available on the high street and online, it also means that there's little regulation as to what's actually in the product you buy.

For Ros, who has Parkinson's, trying CBD oil to manage her symptoms didn't work out so well: "It tasted awful and it only managed to dye my gum shield a funny colour! I'd say more research is needed."

As more and more clinical trials into CBD happen, we'll have a better idea of whether it can improve Parkinson's symptoms. And if it can, proper licensing would guarantee that what's in each batch of CBD oil is closely regulated.

This project is being supported through the Parkinson's Virtual Biotech, the drug discovery arm of Parkinson's UK. You can read about our other new projects on page 25.

You can help to fund more cutting-edge research, like Dr Bhattacharyya's CBD trial. Your gift will ensure that the results of groundbreaking studies like this one will be seen in life-changing breakthroughs for thousands of people affected by Parkinson's.

Donate at parkinsons.org.uk/cbd ■

NEW

We are currently funding over 45 research projects. Here we highlight some of our newest projects – including work to understand the early signs of Parkinson's and research into promoting exercise to help manage symptoms.

RESEARCH



NEW RESEARCH

❶ Delivering a collaborative exercise approach for people with Parkinson's

Who? Julie Jones

Where? Robert Gordon University

What? £240,258 over three years

Stage? Clinical trial

For many, exercise is an effective way to help manage their Parkinson's – some evidence suggests that regular exercise may limit the progression of the condition. Julie's team will explore a collaborative exercise intervention called PDConnect, which includes physiotherapy, community-based group exercise classes and supported self-management. They will test this approach to see if it is an effective way to support people with Parkinson's to engage in exercise.

"We do not currently know the best way of delivering exercise to people with Parkinson's in order to encourage them to adopt more active lifestyles. We do know that people are more motivated to take part in exercise when they see specialist professionals who understand Parkinson's. We hope this unique collaborative approach will prove to be a sustainable and effective means of supporting people to engage in exercise, thereby taking control of their future quality of life."

Julie Jones

❷ Does sensory information impact turning mobility in people with Parkinson's?

Who? Dr Terry Gorst

Where? University of Plymouth

What? £31,449 over one year

Stage? Clinical trial

People with Parkinson's often have difficulty turning, which can lead to problems with balance and falls. People affected by Parkinson's have identified this area as one of the top priorities for research. Research has shown that people with Parkinson's have difficulty using sensory information properly, which means they tend to look at their feet when walking – this is not always practical and is bad for posture.

This project will explore the potential of a band worn on the shin, which vibrates when the foot is in contact with the ground, to see if providing sensory information in this way can improve turning in people with Parkinson's.

"We will test if sensory information changes how steady, how quickly and how many steps people with Parkinson's take when turning. We hope we will show that adding sensory information from a simple, lightweight wearable device may be very helpful in reducing turning difficulties in everyday life."

Dr Terry Gorst

🕒 Investigating the role of RAB39B in Parkinson's

Who? Professor Flaviano Giorgini

Where? University of Leicester

What? £264,522 over three years

Stage? Scientific discovery in the lab

Recent studies show that the build up of toxic proteins inside cells contributes to Parkinson's.

The Rab family of proteins play a role in the movement of proteins and cellular components to ensure the cell can function properly.

Researchers have shown that when the protein RAB39B is not working properly in fly models of Parkinson's there's a buildup of toxic proteins causing Parkinson's-like symptoms.

In this study, Flaviano and the team will further investigate the role of RAB39B by enhancing its function to see if it has a beneficial role in Parkinson's.

"The causes leading to brain cell loss in Parkinson's are mostly unknown, complicating the discovery of new therapies. We have found that in fruit flies that lack the fly version of RAB39B we see a loss of dopamine-producing brain cells.

In this study we want to understand more about RAB39B and see if enhancing the protein could offer a potential therapy in models of Parkinson's.

We hope this may enable the discovery of novel mechanisms and strategies for therapeutic intervention."

Professor Flaviano Giorgini

④ Steps towards a new diagnostic test for Parkinson's

Who? Dr Laura Parkkinen

Where? University of Oxford

What? £129,038 over one-and-a-half years

Stage? Scientific discovery in the lab

In Parkinson's, "sticky" clumps of proteins are thought to contribute to the death of vital brain cells. Laura and her team have developed a promising new diagnostic test for Parkinson's, focusing on the detection of a sticky version of a protein called alpha-synuclein in the fluid around the spinal cord (cerebrospinal fluid, or CSF). They have found that sticky alpha-synuclein is detected in CSF samples from people with Parkinson's but not in samples from those that don't have the condition.

In this project, they want to see how early this troublesome protein can be detected by looking at samples from people who have a higher than average risk of developing Parkinson's – those that have REM Sleep Behaviour Disorder. They will collect CSF samples over regular intervals and monitor the levels of sticky alpha-synuclein whilst also monitoring to see if the person goes on to develop Parkinson's symptoms.

They will also investigate if their test can tell Parkinson's apart from other related conditions such as Dementia with Lewy Bodies and Multiple System Atrophy, hoping it could lead to more accurate diagnoses. ■

"We think that this test could potentially detect Parkinson's before symptoms appear. We want to examine more samples that we have collected worldwide to see when the sticky alpha-synuclein can be detected.

We propose to investigate if our test can tell Parkinson's apart from other related conditions, as it is difficult for doctors to separate them according to symptoms alone, but correct early diagnosis is important for people to be treated correctly. We believe our study has the potential to improve clinical trials."

Dr Laura Parkkinen

Research like this only happens because of the participants. To find research projects in your area, visit parkinsons.org.uk/takeparthub



TRIALS TO TREATMENTS:

Targeting mitochondria

We know that, in Parkinson's, the batteries that power our cells don't work as well as they should. It's now up to researchers to find drugs that target these dysfunctional batteries, known as mitochondria, and protect the nerve cells from energy failure and death.

A chance discovery

It takes a lot of power for our brains to work properly. Making up just 2% of our total body weight, they use 20% of all the body's energy reserves. So out of all the organs in the body, the brain is particularly reliant on the work of the tiny batteries found in every cell – the mitochondria.

It's perhaps not surprising then that many neurodegenerative conditions have been linked to mitochondria going wrong. And Parkinson's is no exception.

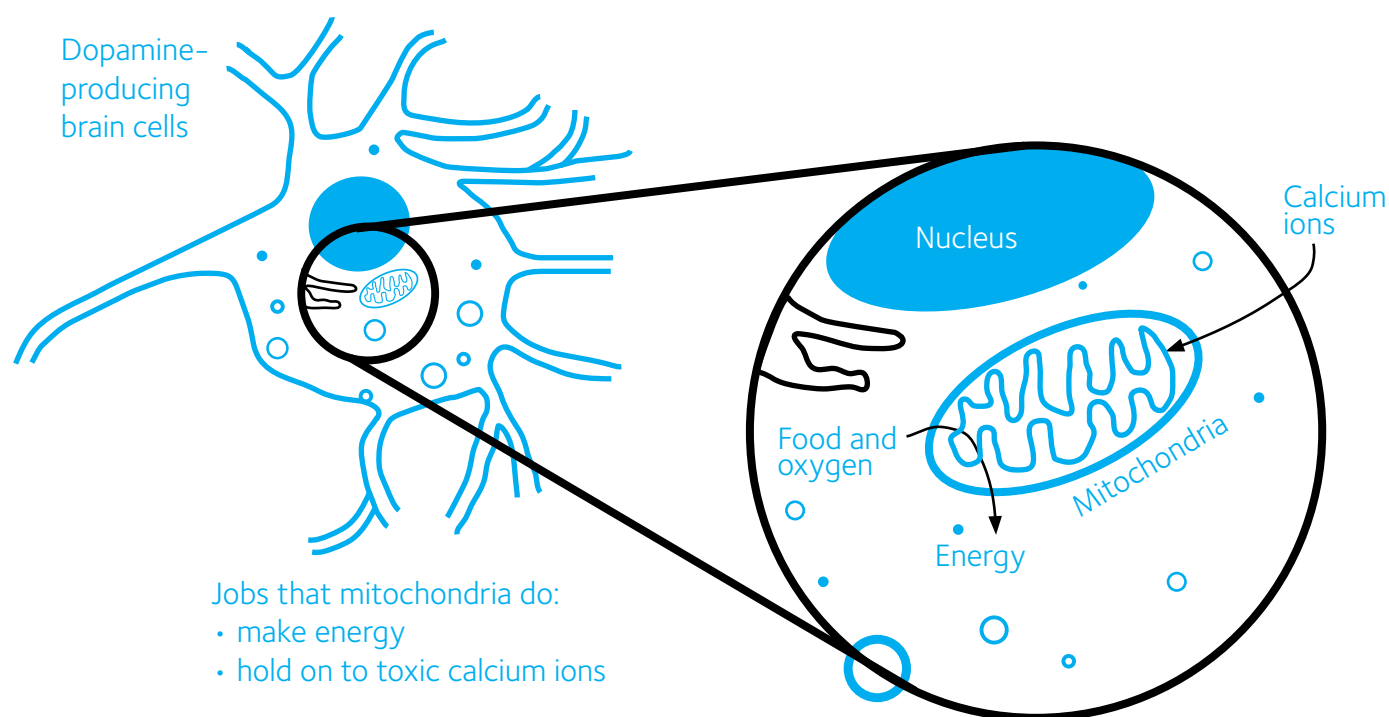
It was a freak incident in 1982 that gave the first clue that mitochondrial dysfunction may be linked to Parkinson's. People who had taken heroin suddenly lost the ability to speak or move,

appearing frozen. The symptoms were reversed by levodopa. It turned out it was a contaminated batch of heroin, containing the chemical MPTP. This man-made chemical was taken up by dopamine-producing brain cells and attacked the mitochondria, cutting off the cell's energy supply.

Since then, there has been lots of research showing that mitochondria play a role in both the onset and progression of Parkinson's. The race is now on to turn this knowledge into treatments that can stop Parkinson's.

The powerhouse of the cell

So new treatments targeting mitochondria could help treat Parkinson's – let's find out how these energy-producing batteries work.



The mitochondria are the powerhouse of the cell. They take nutrients from food and oxygen to produce a type of energy currency, a molecule called adenosine triphosphate, or ATP.

All parts of our cells require energy. To keep them working, mitochondria must constantly produce ATP while travelling the length of the cell – no mean feat in large and complex nerves.

This demanding lifestyle means that, just like regular batteries, mitochondria wear out and when they do, they need to be recycled and replaced with healthy mitochondria. As we'll see, this recycling process can go wrong in Parkinson's.

But it's not just energy production that mitochondria are responsible for. They also have an important role in helping brain cells communicate – and this involves managing calcium.

Calcium is essential for the body to work properly, and is particularly important for brain cells. As an electrical signal travels down a nerve, it triggers calcium to flood into the cell.

To reset the nerve cell so it can continue to send signals, the levels of calcium need to be reduced – this is where mitochondria come in. Mitochondria can temporarily store calcium until it can be removed.

But in times of stress, too much calcium might build up inside the mitochondria – this is bad news as researchers believe it could lead to the loss of brain cells.

Mitochondria and Parkinson's

Since the events in San Francisco in the 1980s, we've learnt a great deal about mitochondria and brain cell death in Parkinson's.

Dopamine-releasing nerves in the brain are relatively large, always active and have connections with many other nerves. It takes a lot of energy to run them, and they appear to be particularly sensitive to problems with mitochondria.

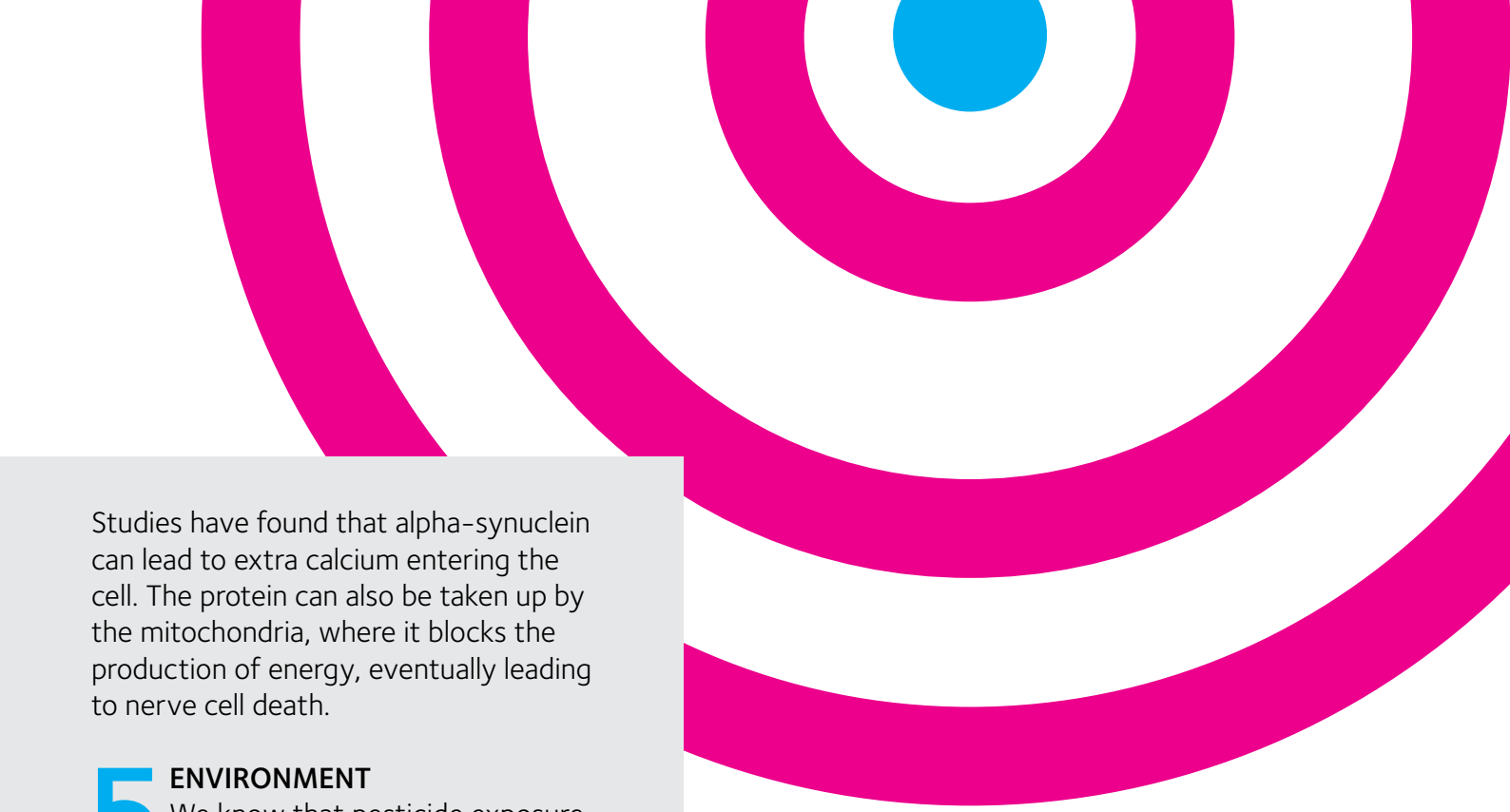
And we now know that in most people with Parkinson's, there are various problems with mitochondria:

1 GENETIC LINKS
The Parkinson's-associated genes PINK1 and Parkin help regulate the recycling of the old, worn-out mitochondria. Changes in these genes can mean that the recycling process doesn't work properly and the worn-out mitochondria end up hanging around in cells for too long. Old mitochondria are less efficient at producing energy and they also produce harmful waste chemicals that can damage the cell and lead to cell death.

2 CHANGES TO DNA IN THE MITOCHONDRIA
Mitochondria are unique in the cell – they have their own DNA which they use to make some of the proteins they need for energy production. This DNA is particularly susceptible to changes in its sequence during times of stress. A build-up of mutations seems to occur in the dopamine-producing brain cells in Parkinson's, affecting energy production and putting the cell at risk.

3 CALCIUM OVERLOAD
Dopamine-producing nerves use levels of calcium as a kind of pacemaker to enable consistent control of our movement. But this increased reliance on calcium levels likely puts further pressure on the mitochondria to manage calcium levels effectively.

4 ALPHA-SYNUCLEIN
We know that a protein called alpha-synuclein plays a pivotal role in Parkinson's – it can change shape and is found in clumps in all cells affected by the condition. And recent evidence suggests that it may be a partner in crime with mitochondria.



Studies have found that alpha-synuclein can lead to extra calcium entering the cell. The protein can also be taken up by the mitochondria, where it blocks the production of energy, eventually leading to nerve cell death.

5 ENVIRONMENT

We know that pesticide exposure increases the risk of developing Parkinson's. This may be to do with the effect pesticides have on mitochondria. For example, the pesticide rotenone is known to block ATP production in mitochondria, can induce Parkinson's-like symptoms in animal models, and has been linked to Parkinson's in the farming community.

Past treatments

Despite the wealth of evidence we now have that mitochondria play a central role in Parkinson's, no clinical trial of treatments targeting mitochondria has yet been found to slow or stop the condition.

The question is: why?



We spoke to Dr Heather Mortiboys, mitochondria expert and Parkinson's UK researcher at the University of Sheffield, for answers:

"I think one of the main reasons we haven't seen success is that tested drugs simply were not targeting the right parts of the mitochondria, or even targeting the mitochondria at all.

"Most of the compounds said to be mitochondrial protectors are actually antioxidants, which mop up the toxic waste mitochondria produce when they're not working properly. So while they are targeting one of the side effects of dysfunctional mitochondria, they aren't directly addressing the problem and restoring the function of the mitochondria.

"We now have more knowledge than ever before about what exactly goes wrong with mitochondria in Parkinson's. If we're going to have successful clinical trials, we need to be smart about how we use this information when developing drugs, making sure we're targeting the right areas of the mitochondria to make a difference."

Finding new targets

Parkinson's UK is currently investing over £2 million into six different projects designed to increase our understanding of how we can best target mitochondria to slow or stop Parkinson's progression. This includes looking at pores through which calcium ions get into the mitochondria, supporting mitochondria to make more energy, and finding ways to improve the recycling of damaged mitochondria from the cell.

Earlier this year, we invested in two new drug development projects that aim to target the energy-producing mitochondria that are affected by Parkinson's. By developing protective molecules that target problems with the mitochondria, the hope is to develop a safe and effective new treatment that will protect brain cells, slow the progression of Parkinson's, and extend quality of life. You can read about these two projects on the next pages.

The future of mitochondria and Parkinson's

Having healthy mitochondria is essential for most cells to function properly. If we can support the health of mitochondria in Parkinson's, we'd be on our way towards finding a treatment that stops or slows nerve cell death. But while targeting mitochondria holds definite potential for the treatment of Parkinson's, it may not be a cure-all for everybody.

Dr Mortiboys explains: "We can continue to identify drugs in the lab and make sure they're optimised to be as effective as they can be. But this needs to go hand in hand with early diagnosis and clinically defining the different groups of people with Parkinson's.

"For example, we know that problems with mitochondria are likely the cause of Parkinson's in people with changes in the PINK1 or Parkin genes, but for others, problems with the alpha-synuclein protein may come first, which then impact on the mitochondria. It's likely that the different groups will need different treatments or a combination of treatments."

Such personalised medicine is gaining momentum as the way forward for medical research, and in the case of mitochondria and Parkinson's, may well provide the cure.

Our new Parkinson's Virtual Biotech projects

We're investing over £1 million into two projects in our Virtual Biotech that will drive forward the development of drugs targeting mitochondria in Parkinson's.

① Developing molecules that close pores in the mitochondria

Who? NRG Therapeutics Ltd

Where? £997,000 over 12 months

Stage? Finding molecules

Parkinson's UK is partnering with NRG Therapeutics Ltd to discover and develop a new medicine that protects the brain cells affected by Parkinson's by closing pores that open when cells begin to struggle.

Project summary

In Parkinson's, brain cells that produce dopamine are slowly lost over time. These cells are very active and require an unusually high amount of energy. They must also handle large amounts of calcium ions that continually flow into the cell when it is active, and which can become toxic.

Mitochondria can help by holding on to the calcium ions, but there's a limit on how much they can hold. Recently, researchers have discovered that when mitochondria become overloaded with calcium, a pore in the mitochondria – known as the permeability transition pore (mPTP) – is opened. This starts the process that ultimately leads to the loss of dopamine-producing brain cells.

Using animal models of Parkinson's, researchers have found that preventing or delaying the opening of the pores can protect brain cells and may slow the progression of the condition.

Although molecules that stop the pores opening have been known about for many years, they come from natural products and cannot easily access the brain. More recent identification of small synthetic molecules that do the same job opens up the opportunity to develop novel therapies for Parkinson's.

The aim of this project is to develop potential drug molecules that stop the pores opening and that can also access the brain. The new drug-like molecules will then be tested to investigate if they can slow or stop the loss of cells in Parkinson's. If successful, this will pave the way for candidate molecules to be rapidly progressed into preclinical testing and, ultimately, clinical trials.

“We all know there is a tremendous need to find better treatments for Parkinson's that can slow down the progression of the condition. This pioneering research could be the first step towards identifying molecules that can protect mitochondria within dopamine-producing cells.”

Dr Arthur Roach, Director of Research at Parkinson's UK

② Optimising molecules that restore mitochondria

Who? Dr Heather Mortiboys

Where? £98,391 over 12 months

Stage? Finding molecules

Parkinson's UK is partnering with the University of Sheffield to design and develop a new medicine that protects the brain cells affected by Parkinson's.

Project summary

In previous work funded by Parkinson's UK, Dr Heather Mortiboys and her team identified compounds that have the potential to improve mitochondrial function in Parkinson's.

By turning skin cell samples taken from people with Parkinson's into dopamine-producing brain cells, the team was able to screen drug libraries in a relevant model, assessing which drugs could most effectively boost mitochondrial function.

They identified two compounds with excellent mitochondrial restoration properties with the potential to reduce nerve cell death. However, these compounds also have some less desirable side effects, including nausea and vomiting, making them unsuitable to progress towards clinical trials for people with Parkinson's.

The aim of this new project is to modify these compounds so to maximise their mitochondrial boosting effects, minimise side effects and increase their suitability for use in the clinic.

The project will bring together biology and chemistry experts to design and develop a superior group of compounds that have beneficial mitochondrial restoration properties with reduced side effects. The compounds will be tested in order to find the best compound to progress along the drug discovery pipeline and ultimately into clinical trials.

People with Parkinson's urgently need new treatments. But right now, there's a huge gap in drug development. At Parkinson's UK, we're stepping up to fund that gap.

We're investing £4 million every year in our Virtual Biotech. By partnering with institutions and pharmaceutical companies worldwide that already have the expertise, tools and infrastructure, we can fast-track the treatments with the greatest potential to transform life for people with Parkinson's. ■



TAKE PART IN RESEARCH



Interested in taking part in research?

Without volunteers, progress in Parkinson's research would be impossible. Research ranges from at-home questionnaires to trialling new treatments. Whatever you're ready for, you can make a difference by taking part.

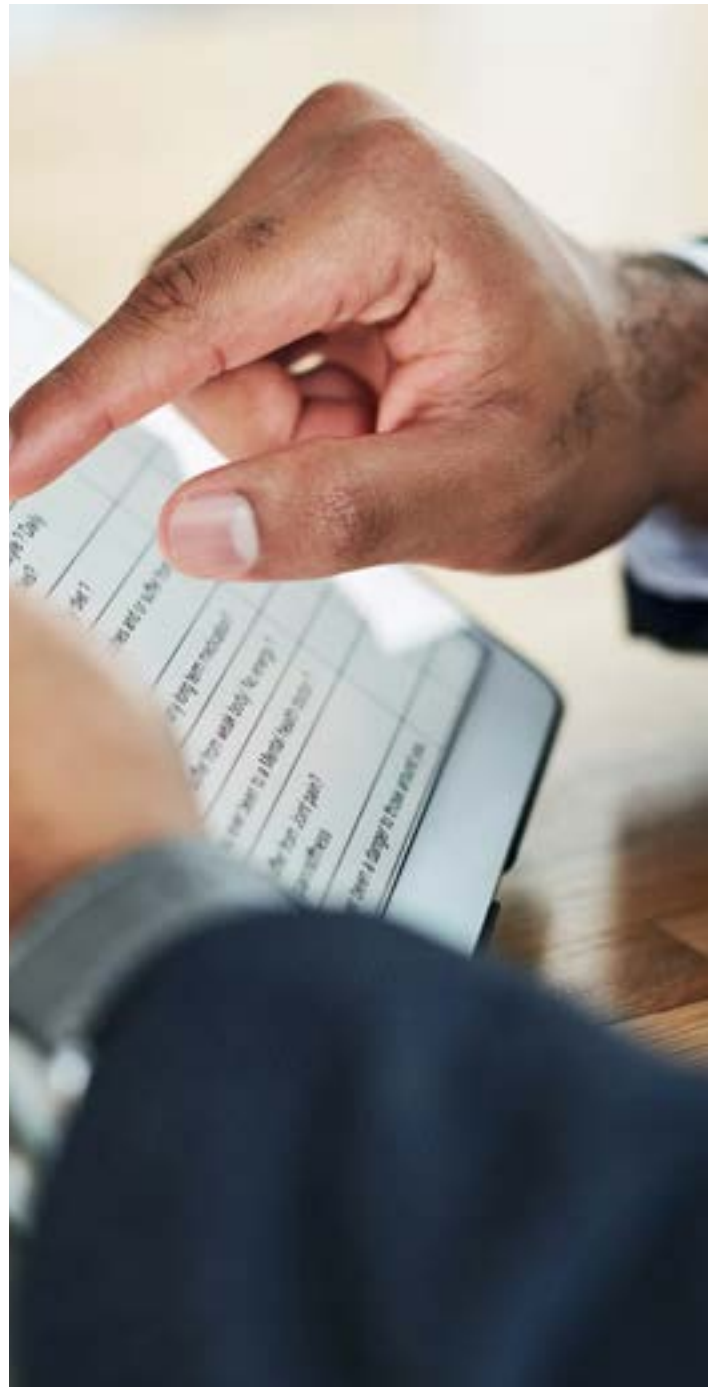
Find research near you

We heard from people with Parkinson's that they wanted more opportunities to take part in research. We listened and developed our Take Part Hub, which you can search using your postcode to find research happening in your area. And don't worry, all research opportunities on the hub have been ethically approved and fit in with our Research Support Policy.

Where can I go to find out more?

- Explore our Take Part Hub available at **parkinsons.org.uk/takepartresearch**
- Call our free, confidential helpline on **0808 800 0303**. Our advisers will be able to discuss what you're interested in and put you through to the Research team.
- Join our Research Support Network. As a member, you will receive regular emails telling you about any research you can take part in. Find out more at **parkinsons.org.uk/rsn**

We have a variety of opportunities to take part in Parkinson's research. Here are some projects looking for people available now ➡



FEATURE

DEVELOPING NEW TOOLS TO IMPROVE PARKINSON'S RESEARCH



Parkinson's has many different symptoms and everyone's experience is different. And this poses a challenge for measuring the outcomes of clinical trials. We need to improve clinical trials and how we measure whether they're successful or not. This is essential if we're to find better treatments, and ultimately a cure. One such study is looking into developing new questionnaires to see whether they can be used as a way to improve future research studies and trials.

Who do the researchers need?

⇒ People with and without Parkinson's.

300 people diagnosed with Parkinson's over the age of 18 who have access to a computer or similar. And 300 people who don't have Parkinson's, who are over the age of 18 and a carer of someone with Parkinson's.

What does it involve?

⇒ At home

You will be asked to complete a short online questionnaire three times over six months.

Interested?

For more information and to access the survey, visit our Take Part Hub at parkinsons.org.uk/newquestionnaires

PREDICTING AND UNDERSTANDING THE EARLY STAGES OF PARKINSON'S



We don't yet know exactly why people get Parkinson's, but researchers think it's due to a combination of genetic and environmental factors. Current evidence suggests that Parkinson's develops gradually, and for many it may be months

or even years before the symptoms become obvious enough for diagnosis. Researchers are interested in trying to understand more about the early stages of Parkinson's and who in the general population is at risk of Parkinson's. One ongoing study believes if we can predict who is going to get Parkinson's, we'll be closer to finding better treatments and a cure.

Who do the researchers need?

⇒ People without Parkinson's

Help us spread the word – the researchers need 10,000 people aged 60-80 years who do not have Parkinson's to help work out if we can predict Parkinson's.

What does it involve?

⇒ At home

Completing an online questionnaire, which should take approximately 30 minutes.

Interested?

For more information and to take part, visit our Take Part Hub at parkinsons.org.uk/predictpd

UNDERSTANDING THE SYMPTOMS OF PARKINSON'S



It's essential that we understand more about the different symptoms of Parkinson's and how the condition progresses. The more we understand, the more able we will be to develop better ways to manage the condition and improve quality of life. One example of such research is happening in Oxford and is looking at understanding how learning and memory may change in people with Parkinson's.

Who do the researchers need?

⇒ People with Parkinson's

30 people diagnosed within the last six years with Parkinson's aged between 50-70 years. You need to be taking regular medication for your Parkinson's.

What does it involve?

➡ Visiting a hospital in Oxford

You will be invited to attend a screening visit at the Warneford Hospital in Oxford which will take up to two hours. At the visit you will answer questions about your health and lifestyle. If you are eligible, you will need to be available to attend two more study visits.

Interested?

Find out more and visit our Take Part Hub at parkinsons.org.uk/learningandmemory

MANAGING THE SYMPTOMS OF PARKINSON'S



We know that current treatments for people with Parkinson's are not good enough. While work is underway to find a cure, we're supporting various projects testing new treatments for better management of symptoms. One example is a trial investigating a new device to help manage bladder control in people with Parkinson's.

Who do the researchers need?

➡ People with Parkinson's

200 people with Parkinson's who experience bladder symptoms (needing to go to the toilet frequently or urgently).

What does it involve?

➡ Visiting hospital and using a device at home

You will need to visit your nearest clinic to be shown how the device works, then use the device twice a week for six weeks. You will be called weekly by the research team to give you support, and you will complete questionnaires at the beginning of the trial and then 12 weeks after you start using the device.

Interested?

To find out where the research is happening and how to get involved, visit our Take Part Hub at parkinsons.org.uk/bladdercontrol

You can also read more about this project on page 8 of our lifestyle magazine, *The Parkinson*.

SLOWING OR STOPPING PARKINSON'S PROGRESSION



Research happening in Cambridge and London is looking for people with Parkinson's to trial an experimental gene therapy called OXB-102. This involves inserting genes into brain cells, enabling them to make dopamine. The hope is this therapy could halt or even reverse the progression of the condition. Researchers will be testing the safety and benefits of this experimental treatment.

Who do the researchers need?

➡ People with Parkinson's

16 people diagnosed with Parkinson's more than five years ago aged between 48-70. You will need to be considering or being considered for surgery to help your Parkinson's symptoms.

What does it involve?

➡ Visiting hospital and surgery

You will initially need to attend a sequence of screening visits at the centre in London or Cambridge, and if you are eligible you will undergo surgery to receive infusions of OXB-102 with further research visits continuing for up to 10 years.

INTERESTED?

Find out more and contact the researchers through our Take Part Hub at parkinsons.org.uk/oxb102

KEY



For people with Parkinson's



I can do at home



Visiting a study centre



For people without Parkinson's

RESEARCH RESULTS

At Parkinson's UK, we fund research with the best chance of making a difference for people with Parkinson's. From symptom management to finding a cure, these results are helping us move towards stopping Parkinson's for good.

Using existing drugs to help the brain protect itself against Parkinson's

We know that growth factors – proteins that stimulate cell growth and healing – have a key role in supporting the development, growth and survival of our bodies and brains. Fibroblast growth factor 20 (FGF20) has been shown to support dopamine-producing cells in the areas of the brain affected by Parkinson's. But growth factors are large proteins that can't naturally cross the blood-brain barrier – to date getting them into the areas of the brain where they are needed requires invasive and expensive surgery. What if there is another way?

In this project, Dr Susan Duty's team took existing drugs to see if they could encourage brain cells to make their own FGF20, without the need for invasive treatment. Using computer software, they were able to identify 16 suitable drugs from a list of over a thousand that could cross into the brain and potentially boost the natural levels of FGF20.

They were able to further identify four drugs to test in a rat model of Parkinson's. Of these four, the anti-asthmatic drug, salbutamol, and

an aspirin-like drug, triflusal, were both seen to increase FGF20 levels in the rat brain.

We are grateful for the donations that made the first steps of Dr Duty's research possible. Parkinson's UK are now funding the next stage of this study. Duty and her team will now test whether salbutamol and triflusal can protect or repair brain cells in rat models of Parkinson's.

.....
"Boosting production of the brain's own supply of FGF20 with a pill would offer a simpler, more accessible solution than relying on injecting a protein into the brain. In this follow-on project we will discover whether these FGF20-boosting medicines can protect against damage or repair already damaged cells in our rat model of Parkinson's.

"Because these medicines are known to be safe for clinical use, successful ones can progress relatively quickly into clinical trials. Our findings could provide better treatments for the next generation, and those already living with Parkinson's."

Dr Susan Duty
.....

Finding a way to stop the build-up of alpha-synuclein

When Parkinson's develops, the protein alpha-synuclein forms sticky clumps in the brain, which are associated with brain cell death and some of the symptoms of Parkinson's. Anle138b has previously been shown to reduce the clumping of proteins in neurodegenerative conditions, including Parkinson's. But in order to fully study the potential of anle138b for treating Parkinson's, the team first had to develop a better way to test it.

The researchers, led by Professor Maria Grazia Spillantini, created a new mouse model of Parkinson's that mimics the way alpha-synuclein gradually accumulates in areas of the brain affected by the condition.

In these mice, the levels of dopamine were reduced, with the mice developing symptoms that mimicked movement symptoms seen in people with Parkinson's.

The team found that by treating the mice with anle138b after nine months, the drug reduced alpha-synuclein clumps, restored dopamine levels in the brain, prevented nerve cell death and reversed some of the subtle motor symptoms.

These results suggest anle138b may be particularly effective at slowing, or even stopping, Parkinson's if given early enough – before the nerve cells are lost. More research is needed to investigate how anle138b is having these effects.

Understanding the PARK15 gene in Parkinson's

Over 20 years ago it was discovered that mutations in certain PARK genes are associated with an early-onset form of Parkinson's. Researchers at the University of Cambridge have experience studying a gene that we now know plays a fundamental role in brain cell health – PARK15. Research in animal models so far has been limited but is essential in helping understand the role of PARK15 in Parkinson's.

Dr Laman's team has now created a mouse model that lacks the PARK15 gene in the part of the brain primarily affected in Parkinson's. They found that deleting PARK15 in this specific region of the brain causes a decrease in dopamine levels, resulting in the mice having Parkinson's-like movement symptoms. The team showed that this was because, without PARK15, there's an exaggerated stress response that can result in cell death. This suggests that PARK15 is protective to brain cells and has a role in controlling responses to stress.

“Understanding how this gene protects brain cells could give rise to future therapies that can slow or reverse the progression of the condition. The mouse models are valuable tools for our continued research.”

Dr Heike Laman

‘Smelling’ Parkinson’s – understanding the powers of the super-smeller

There is currently no definitive diagnostic test for Parkinson’s and receiving a diagnosis often takes some time. It’s thought that if different chemicals are present on the skin in people with Parkinson’s, they could act as biomarkers – tiny changes in the body that can be measured to diagnose or monitor the condition.

The idea of being able to smell if someone has Parkinson’s was first raised by super smeller Joy Milne. She noticed that, to her, people with Parkinson’s had a distinct smell, which changed intensity as the condition progressed. The next step was to find out exactly what causes this unique smell.

A team from the University of Manchester developed a system to screen for molecules specifically found on the skin of people with Parkinson’s. A waxy fluid on the skin, known as sebum, was swabbed from 43 people with Parkinson’s, and 21 people without. The samples were then analysed using a technique called mass spectrometry.

The researchers found four molecules that were present at different levels in the sebum of people with Parkinson’s, compared with people without the condition. The odour produced by these chemicals was confirmed by Joy as having a Parkinson’s-like smell.

“Understanding the underlying differences at a molecular level, which cause a difference in odour, would provide potential targets for therapeutic intervention at a very early stage of Parkinson’s.”

Professor Perdita Barran

Understanding the effects of Deep Brain Stimulation (DBS) on brain cells

Deep Brain Stimulation (DBS) is a surgical treatment to manage symptoms of Parkinson’s. In DBS, very fine wires are inserted into the brain to electrically stimulate particular groups of brain cells involved in controlling movement. These wires are then connected to a battery pack, which is usually placed under the skin in the chest. The effect on symptoms is similar to taking levodopa, but the key advantage is that the effects of DBS are constant.

Despite the success of the treatment, it’s still not fully understood how this electrical stimulation works to improve movement. It’s particularly unclear how DBS works at a cellular level.

Researchers at Imperial College London examined the effects DBS has on the target brain cells using post-mortem brain tissue from the Parkinson’s UK Brain Bank. Specifically, they looked at the effects on the mitochondria – the batteries that power the brain cells.

10 brains were examined in total: three from people without Parkinson’s; four from people with the condition; and three from people with Parkinson’s who had been treated with DBS.

They found that, in the brains of people with Parkinson’s, the number and size of mitochondria were decreased compared with those without the condition. However, DBS was shown to increase the size of mitochondria back to healthy levels.

It’s known that mitochondria stop working properly in Parkinson’s, depriving the brain cells of the essential energy they need to function (see page 20 for more on these cell batteries). These new results suggest that DBS slows or stops the loss of mitochondria in Parkinson’s, boosting the energy levels in the brain cells. This, in turn, may help reduce problems with movement and tremors.

"This new study identifies another role for DBS to keep the brain functioning by reversing the loss of energy-producing mitochondria.

"The Parkinson's UK Brain Bank is the UK's largest dedicated to Parkinson's research and plays a vital role in the search for new and better treatments. It is currently supporting more than 100 projects using tissue from over 1,100 Parkinson's brain donations. We thank all the donors – past, present and future – for their contribution that continues to increase our understanding and drive us towards new and better treatments for Parkinson's."

**Professor David Dexter,
Deputy Director of Research,
Parkinson's UK**

FIND OUT MORE

Find out more about the Parkinson's UK Brain Bank at parkinsons.org.uk/brainbank ■



Question time

Got a question about research but not sure who to ask? In this new feature, our Research team answer your questions on Parkinson's research – no question is too weird or wonderful, so get in touch!

Q WHAT'S THE RELATIONSHIP WITH DIABETES?

Research suggests there may be a link between these two conditions. Indeed, one recent study showed that people with type 2 diabetes may be 32% more likely to develop Parkinson's than those without diabetes – although it is worth noting that the vast majority of people with diabetes will not go on to develop Parkinson's.

Understanding the link could be key to developing treatments that protect the brain cells affected by Parkinson's.

There is ongoing research into whether anti-diabetic drugs, such as exenatide, can slow the progression of Parkinson's. The ability to repurpose these drugs, which are already used to treat people with diabetes, could speed up the delivery of new and

better treatments to people with Parkinson's who urgently need them.

Read more at: parkinsons.org.uk/exenatideblog

Q CAN YOU TELL ME MORE ABOUT FAECAL TRANSPLANTS FOR PARKINSON'S?

Don't read about this over dinner, but the average person has up to 2kg of microbes living in their gut helping to digest their food, make vitamins, and fight bad bacteria and infection. Our gut bacteria interact with the rest of the body by releasing chemicals. Of particular interest is the fact that the microbiome can interact with the vagus nerve – the direct connection between the gut and the brain.

Gut problems are common in Parkinson's and researchers have recently discovered that early on



in Parkinson's, abnormal clumps of alpha-synuclein can be found in the gut and can travel up the vagus nerve to the brain. So some researchers believe that rebuilding a healthy community of bacteria in the gut, in theory, may help to protect against Parkinson's and help to combat symptoms.

One strategy to try and reintroduce good bacteria is to use a treatment called faecal transplantation. This involves collecting bacteria that live in the gut of a healthy donor from a stool sample, and preparing and transplanting them via a tube directly into the gut of the recipient. But while this may work for some conditions where the gut microbiota are abnormal, the process is difficult and still needs regulatory approval and safety checks before it can be made more widely available. So, researchers have been investigating other ways to get good bacteria back into the gut, including probiotics.

You can read more about this on our website:
parkinsons.org.uk/symprove

Q SHOULD I AVOID EATING PROTEIN-RICH FOOD IF I HAVE PARKINSON'S?

Protein helps our bodies to carry out key functions to stay healthy, including looking after our brains.

But some people with Parkinson's find that protein seems to interfere with how well the medication levodopa is absorbed by their body.

Recent research has found that following a low protein or a redistributed protein diet (only eating protein at a certain time of day) can be beneficial for people with Parkinson's, if they experience fluctuations in the effectiveness of their medication due to dietary protein.

However, there can be side effects to these diets, including increasing dyskinesia (uncontrolled movements) and weight loss, which need to be carefully monitored. We recommend that anyone concerned about their diet talks to their healthcare professional.

GETTING THE RIGHT ADVICE

Our research staff are not medically trained. If you have specific questions about your health, please talk to your healthcare professional.

FIND OUT MORE

Got a question about research you'd like answered in *Progress*? Email your question to research@parkinsons.org.uk and make sure to include the word "Progress" in the subject line. ■

Your mum, son or neighbour. Anyone can get Parkinson's, young or old. Every hour, two more people are diagnosed.

Parkinson's is what happens when the brain cells that make dopamine start to die. There are over 40 symptoms, from tremor and pain to anxiety. Some are treatable, but the drugs can have serious side effects. It gets worse over time and there's no cure. Yet.

But we know we're close to major breakthroughs. By funding the right research into the most promising treatments, we get closer to a cure every day.

Until then, we're here for everyone affected by Parkinson's. Fighting for fair treatment and better services. Making everyone see its real impact.

People with Parkinson's, scientists and supporters, fundraisers and families, carers and clinicians, all working side by side. Impatient for change, we're taking a stand, speaking out, chipping in, and playing our part.

**We are Parkinson's UK. Powered by people.
Funded by you. Together we'll find a cure.**

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Free confidential helpline **0808 800 0303**
Monday to Friday 9am–7pm, Saturday 10am–2pm
(interpreting available)

NGT Relay **18001 0808 800 0303**
(for textphone users only)

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