1 May 2024

PARKINSON'S UK
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Research Roundup

We would like to say thank you for your continued support and interest in Parkinson's research, and a warm welcome if you are new to the Research Support Network.

This month we discuss research exploring a diabetes drug for Parkinson's and look at how gut bacteria may play a role in the condition. Read more for the latest research news, events, and opportunities to get involved.

Research news

£600,000 awarded to support the next leaders of Parkinson's Research

Parkinson's UK has funded two future leaders in Parkinson's research who are pushing forward our understanding of the early stages and causes of Parkinson's.

New funding has been awarded to two researchers through our Fellowships programme: Dr Sophie Farrow at the University of Oxford and Dr Eduardo de Pablo-Fernandez at Queen Mary, University of London. The Fellowships will allow these researchers to devote their time to Parkinson's research, work towards establishing their own independent research groups and help nurture them as the next generation of leaders in Parkinson's research.

What are Sophie and Eduardo aiming to do?

Both researchers aim to add to our understanding of Parkinson's by looking at the causes of the condition and ways to detect the condition earlier.

Dr Sophie Farrow has been awarded £300,000 to explore how and why some changes in certain genes can increase a person's risk of Parkinson's. She will look at different types of brain cells and use existing samples from people with Parkinson's, such as blood samples and fluid from around someone's spinal cord, to try and build a better picture of how these genes are contributing to what goes wrong in Parkinson's.

Dr Sophie Farrow shares her aspirations for her research:

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“My long-term goal is to use genetic approaches to provide insight into the origins of Parkinson’s, to enable the development of preventative or curative treatments, as opposed to treating symptoms. I will integrate multiple genomic approaches to identify and prioritise potential drug targets, with the vision to accelerate early-stage drug target selection and repurposing for people with Parkinson’s.

“I am also eager to understand the considerable variability that exists between people with Parkinson’s. My research will have the potential to help us better understand how to use genetics to stratify people with Parkinson’s. This in turn will facilitate the development of targeted therapies tailored to unique genetic profiles of different individuals.”

Dr Eduardo de Pablo-Fernandez has been awarded £299,237 to help find a way to detect Parkinson’s earlier. He will do this by looking at people who experience symptoms related to sudden drops in blood pressure (pure autonomic failure) which can be an early sign of Parkinson’s. He will follow a group of 100 people over 2 years to look at their symptoms and blood tests to see how many individuals go on to develop Parkinson’s.

Dr Eduardo de Pablo-Fernandez shares his aspirations for his research:

“In addition to leading an exciting study on a neglected area of Parkinson’s research, this fellowship represents an important step to become an established independent researcher. Results from this study will lay the foundation to create the first study in the UK to follow people with pure autonomic failure.

“Symptoms of pure autonomic failure can be the early signs of Parkinson’s. By understanding what symptoms and blood tests predict the development of Parkinson’s we will be able to detect the condition at the earliest stages, even years before typical motor symptoms develop. My focus on the early detection of Parkinson’s and testing new treatments in clinical trials will hopefully move us closer to a cure.”

Gut bacteria transplant may improve Parkinson’s movement symptoms

Early research shows transplanting gut bacteria from healthy individuals to people with Parkinson’s, called a faecal microbiota transplant, is safe and may ease motor symptoms.

The human gut contains billions of microorganisms, including bacteria, which are collectively known as the gut microbiome. The bacteria in our gut are very important for healthy digestion, helping us break down food, make vitamins and fight infection.

These bacteria vary over time, depending on our diet and environment. Some evidence suggests that gut bacteria can vary in different health conditions. Previous research has shown that the gut bacteria in people with Parkinson's is different to that of people without the condition. This could mean that changes in the gut microbiome may play a role in the development, or even the progression of Parkinson's.

What did the researchers do?

The research team, based in Belgium, looked at whether replacing the gut bacteria in people with Parkinson's with gut bacteria from healthy donors could improve symptoms of the condition.

46 people with Parkinson's with mild to moderate symptoms were included in the study. Everyone received a faecal microbiota transplant (FMT), a procedure where bacteria and other microorganisms from a donor are transferred to the recipient's gut through a tube which passes through the nose to the small intestine. Participants either received a sample from a healthy donor's stool, or a sample from their own stool as a placebo.

All participants were monitored for a year after the treatment. The researchers looked at motor symptoms and non-motor symptoms of Parkinson's in both groups, including constipation, a symptom commonly experienced by people with Parkinson's.

What were the results?

Results from the study showed that after 12 months, people with Parkinson's who had received a FMT from a healthy donor saw significant improvements in their movement symptoms, compared to the placebo group. Those who received gut bacteria from healthy donors also tended to have less severe constipation.

There was no clear difference in any other non-motor symptoms between the groups, except that those who received gut bacteria from healthy donors reported that they were more tired at the end of the study.

These findings may suggest that FMTs may have long-lasting benefits on motor symptoms of Parkinson's in people with mild to moderate symptoms. More research is required to confirm these benefits, and to look in more detail at the changes in gut bacteria of people with Parkinson's before and after receiving a FMT from a healthy donor.

Emma Rodgers, Research Communications Officer at Parkinson's UK, comments:

"Exploring the possible link between Parkinson's and the gut is a very active area of research. This study shows that FMTs are well tolerated and deemed safe for people with Parkinson's. This may encourage further studies to take place.

"Whilst encouraging, it's important to note that before the 12 month mark, no significant differences in motor symptoms were seen between the group receiving a FMT from healthy donors and the placebo group. This means that the placebo group also saw a large and long-lasting improvement in their symptoms up to 6 months after receiving a FMT from their own stool, suggesting that there was a strong placebo effect.

"We hope to see future studies to better understand the potential benefits of FMTs for Parkinson's, as well as increase our knowledge of how the gut microbiome may be linked to the condition."

Diabetes drug shows potential to slow progression of movement symptoms

Lixisenatide, a diabetes drug being investigated for Parkinson's, shows potential to slow the progression of movement symptoms.

Clinical trial results show that movement symptoms in people with Parkinson's receiving lixisenatide treatment did not deteriorate over a 12 month period, compared to those receiving a placebo where there was a slight worsening.

The results are from a study (LixiPark) of 156 people with Parkinson's who were less than 3 years into their diagnosis. 75 people received daily injections of lixisenatide, and 75 people an inactive (placebo) injection, over 12 months. This was conducted at multiple research sites across France and was supported by Cure Parkinson's and the Van Andel Institute through the International Linked Clinical Trials programme.

What is lixisenatide?

Lixisenatide is currently used in the treatment of type 2 diabetes. It works by targeting glucagon-like peptide-1 (GLP-1) receptors in the pancreas, which causes the release of a hormone called insulin and results in increased uptake of glucose (a form of sugar) by cells.

It is being investigated for Parkinson's because GLP-1 receptors are also found in the brain, and lab-based experiments have suggested that activating them can boost the function of dopamine connections, have anti-inflammatory properties, improve energy production, and switch on cell survival signals. Lixisenatide is the second diabetes drug to go through clinical trials for Parkinson's. The other one being exenatide.

What do these results mean for people with Parkinson's?

Clinical trial results from both drugs show their potential to slow motor symptom progression. But, similarly to the results from the most recent exenatide trial, people taking lixisenatide didn't report any changes to their quality of life, or measurements of non-motor symptoms. This leaves unanswered questions about the potential of these drugs for people with Parkinson's. A phase 3 study of exenatide is underway to help answer some of these questions.

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

"The most significant part of these results are the lack of deterioration seen in the clinical measurement of motor symptoms in those receiving lixisenatide over the 12 months. This is promising, but from this study it's hard to say whether the drug is slowing the progression of the condition. A longer trial could be able to show this and could be a logical next step.

"It will be interesting to see the results from a similar drug called exenatide. Previous clinical trial results suggest it could be more beneficial than lixisenatide. The Parkinson's community urgently needs new treatments so they, and we, eagerly await the results from this ongoing phase 3 trial, expected later this year."

TOP HAT trial closes early - an update

The TOP HAT trial is closing early and we have an important update on next steps.

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What is the TOP HAT trial?

This major trial funded through Parkinson's UK's Virtual Biotech programme set out to test a drug called ondansetron in people with Parkinson's or Lewy body dementia (LBD) who experience visual hallucinations.

Ondansetron is a drug that is already approved and in use in the UK, mainly to help reduce nausea in people undergoing cancer treatment. The drug first showed potential for treating visual hallucinations in Parkinson's in the early 1990s.

A nationwide study to test ondansetron for safety and effectiveness

Chief Investigator, Professor Suzanne Reeves from University College London, explains the aims of the TOP HAT trial:

"Up to 75% of people with Parkinson's may experience hallucinations at some point but current treatment options can cause side effects and increase mortality (risk of death).

"We desperately need better treatments to help people who experience hallucinations as part of their Parkinson's and small studies have suggested that ondansetron could have potential.

"That's why we were keen to put it to the test in a large-scale study. More than 40 hospitals and clinics across the UK joined in the effort to achieve our goal of enrolling several hundred participants.

"We wanted to investigate whether ondansetron is better than a placebo at reducing the frequency and severity of visual hallucinations.

"Secondly, we wanted to understand whether ondansetron would be safe and well-tolerated in people with Parkinson's - this is always a vital question for any potential new treatment."

Why is the study closing early?

As in all clinical trials, an independent team, called the Data Monitoring and Ethics Committee (DMEC), was set up to monitor the trial.

For TOP HAT they carefully monitored a wide range of things. These included known side effects of ondansetron on things such as heart rate and rhythm, constipation and headache. It also included other events such as falls, attendance at A&E, hospital admissions and deaths.

After the first 100 participants had taken part in the study a preliminary analysis was carried out to look at how well the study drug was tolerated and address any safety concerns as promptly as possible.

After looking at this data, the DMEC recommended that recruitment to the TOP HAT trial should stop as there were more safety issues in those who received ondansetron than the placebo.

It is disappointing that the TOP HAT trial is stopping earlier than planned but any sign that a drug may be causing harm means the study must stop.

Next steps for the trial

All current participants have been asked to stop taking their study drugs (ondansetron or placebo) but will continue to be monitored to record any further safety issues as well as to assess their hallucinations.

In the coming months the TOP HAT team will finish collecting all the data from remaining participants in the study.

They will then be able to conduct the final analysis. This will include looking in more detail at all the safety issues reported throughout the study as well as to see whether ondansetron had a beneficial effect on hallucinations. This will then inform whether ondansetron is still a viable option to be explored further for people with Parkinson's.

Arthur Roach, Director of the Parkinson's Virtual Biotech at Parkinson's UK, comments:

"We are very grateful to every person who has taken part in this pioneering study. The results will give us vital information about the safety and effectiveness of ondansetron for people with Parkinson's. We will work with the TOP HAT team to share the full findings from this important study as soon as we can.

"If you or a loved one has participated in the study and you have further questions please contact the hospital team where you participated in the trial in the first instance."

Upcoming events

You’re invited: ‘Medications for Parkinson’s: Current, new and in development’

The South East Research Interest Group (SERIG) is hosting 4 guest speakers for their online Spring Research Conference. Join to hear from Helen Groves, Shelley Jones, Dr Kevin McFarthing and Professor Camille Carroll as they discuss why we need dopamine, the evolution and future of drug treatments for Parkinson’s, and the potential of drug repurposing to find new treatments.

When: Saturday 11 May 2024
Time: 10.30 am - 1.30 pm
Where: Online via Zoom

If you have any questions, please contact Liz Nash at Parkinson's UK on **lnash@parkinsons.org.uk** or **020 7963 9398**.
Register for the event: **tinyurl.com/PUKserig**

Take part in research

The development of new Parkinson’s treatments is only possible if everyone is part of the research process. We need your help to push promising research forward.

Future planning: What is important to people with Parkinson’s?

A PhD researcher at Oxford Brookes University aims to explore how people with Parkinson’s and their health care professionals think about future planning. Future planning is a process where individuals who are at risk of being affected by memory or communication problems in the future discuss future priorities with their loved ones and health professionals.

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Who do the researchers need?

- 150 people with Parkinson's

What is involved?

- Completing a 15 minute survey. This can be completed online, or by post. Request a postal version of the survey by contacting the researcher.
- For more information, please contact the researchers to be sent a copy of the participant information sheet

Interested in taking part?

Please contact Rachel Lee by email at 17028653@brookes.ac.uk or by calling 07891 655 100.

The deadline for taking part in this research is **1 August 2024**.

Research results: thanks to you

Many people with Parkinson's experience low mood as a symptom of their condition. It can feel overwhelming, but can often be well managed with the right help and support.

In July last year, we shared an opportunity to take part in a study to understand whether a self-guided nature-based mental health programme could reduce low mood in people with Parkinson's. Participants of the study took part in the 4-week programme which involved increasing levels of activity, going on outings into nature spaces, and practising mental therapy techniques such as mindfulness. Mood, quality of life, and overall feelings about the programme were measured throughout the study using questionnaires and interviews.

Thanks to you, the target number of participants was reached for the study. The results showed that everyone who took part was satisfied with the programme. Most participants also reported an improvement to their mood, wellbeing or quality of life at the end of the programme. The team now hope to see further research investigating nature-based programmes for people with Parkinson's who experience low mood.