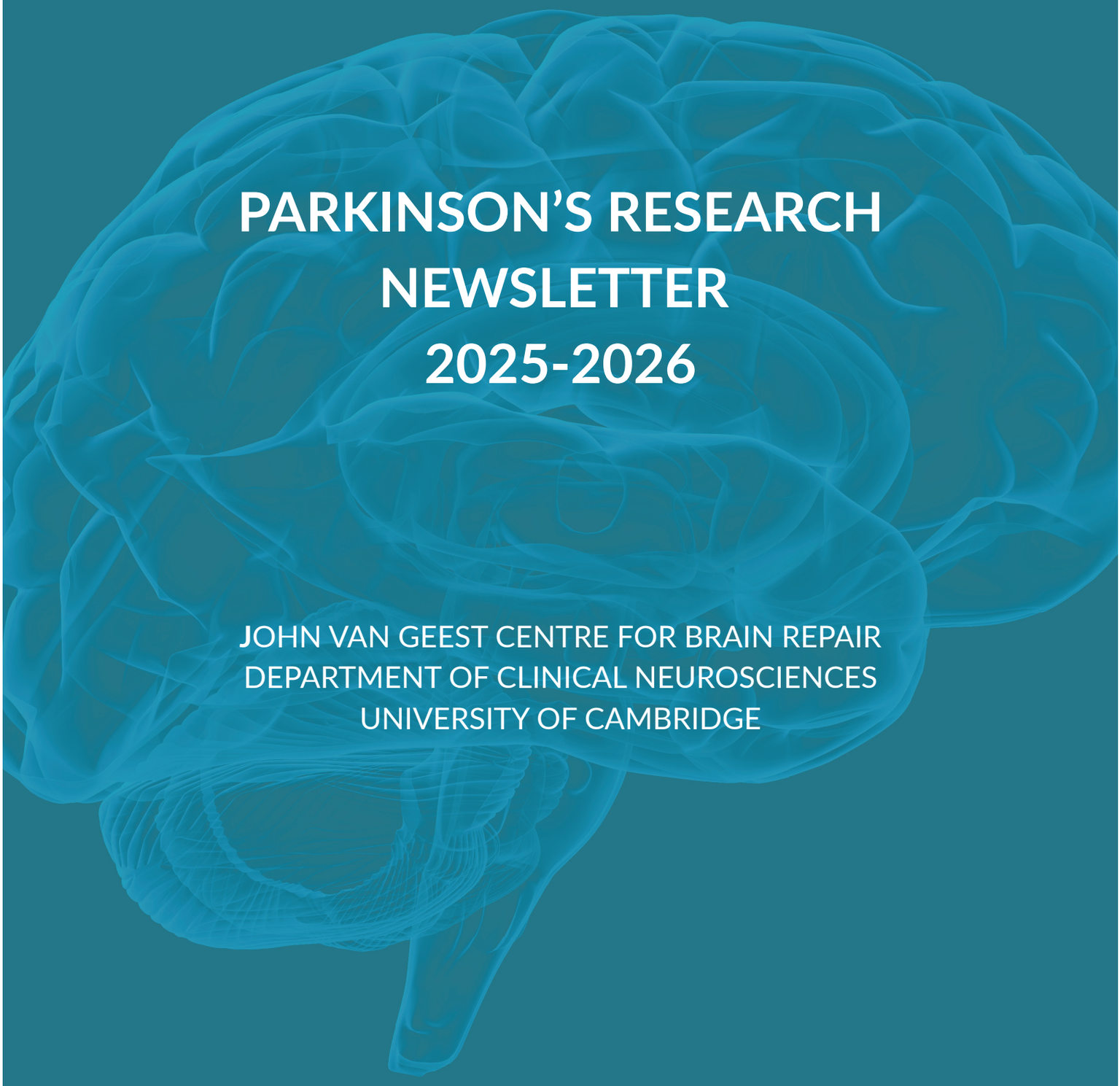


PARKINSON'S RESEARCH NEWSLETTER 2025-2026

JOHN VAN GEEST CENTRE FOR BRAIN REPAIR
DEPARTMENT OF CLINICAL NEUROSCIENCES
UNIVERSITY OF CAMBRIDGE

IN THIS ISSUE

Welcome to the 2025-2026 Parkinson's Newsletter!

We hope you will enjoy this annual update from the research teams led by Roger Barker and Caroline Williams-Gray at the University of Cambridge's Centre for Brain Repair.

Our research ranges from experiments on cells in the lab, through to studies measuring changes in biosamples and brain scans in people with Parkinson's, studies tracking how clinical symptoms vary in different groups, and clinical trials testing new therapies for Parkinson's. We know that PD can affect people in very different ways, and one of our key goals is to develop new treatments which are targeted to different subgroups.

We are making good progress towards this goal, through studies testing several new types of treatments. These new approaches include transplanting stem cells into the brain to repair dopamine networks, using immunosuppressant medicines to reduce brain inflammation, and targeting gut function with the aim of improving associated changes in the brain. We hope you enjoy reading more about all this in the following pages.

Thank you so much to all of you who have participated in our research this year. We are incredibly grateful for your support and could not do this without you! Please do get in touch with any comments and feedback about our work. We are always keen to hear from you.

The John van Geest Centre for Brain Repair

Meet the Team

Prof Roger Barker
Professor and Honorary Consultant Neurologist

Dr Caroline Williams-Gray
Principal Research Associate and Honorary Consultant Neurologist

Dr Marta Camacho
Postdoctoral Research Associate

Dr Annelies Quaegebeur
Cambridge Brain Bank Research Director and Consultant Neuropathologist

Dr Alexander Peattie
Postdoctoral Research Associate

Dr Imran Waggan
Postdoctoral Research Associate

Dr Bina Patel
Clinical Research Associate

Dr Julia Greenland
Clinical Research Associate

Dr Saeed Kayhanian
Clinical Research Associate

Emma Cutting
Senior Trial Coordinator

Katie Andresen
Research Manager

Dr Shaline Fazal
Research Manager

Meet the Team

Clotilde Tournerie
PhD student

Alex Friend
PhD student

Kerry Dresser
Clinical Trials Coordinator

Meisha Davies
Clinical Trials Project Coordinator

Molly O'Reilly
Clinic Administrator

Miriam Schaepers
Clinical Research Assistant

Amy Evans
Clinical Trials Assistant

The Parkinson's Research Clinic

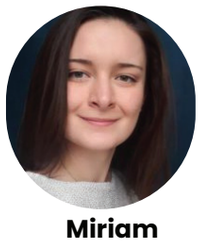
Our Parkinson's Research Clinic takes place every Thursday at the John Van Geest Centre for Brain Repair. We see people with PD as well as individuals who have a condition called REM Sleep Behaviour Disorder (RBD) which increases their risk of developing PD. Companions without the condition are also invited to take part as 'control' participants. Our aim is to collect detailed information about symptoms and problems associated with the disease, and measure progression over time.

Clinic visits include questionnaires, physical and neurological assessments, memory and thinking tests, and the collection of blood and other biological samples. Together, these measures help us understand differences in rates of disease development and progression between individuals.

Caroline Williams-Gray

Bina Patel

Julia Greenland



Miriam Schaepers

Marta Camacho

Molly O'Reilly

Imran Waggan

As well as recruiting new participants to the clinic, we are continuing long-term follow-up of participants in our established cohort studies – CamPaIGN, PICNICS, and ICICLE-PD, which now provide over two decades of valuable information about long-term outcomes in PD and factors that influence them.

A new development in the clinic is that we are now inviting people with Rapid Eye Movement Sleep Behaviour Disorder (RBD) to take part. RBD is a condition in which individuals act out their dreams during sleep because the usual muscle relaxation during REM sleep is lost. RBD can be an early marker of changes in the brain that precede Parkinson's disease by several years. By studying people with RBD, we hope to better understand the earliest biological changes associated with Parkinson's.

People seen in the research clinic may be eligible for a range of further PD-related research studies or clinical trials. In addition to trials led by our own team, we are also a site for large UK multicentre Parkinson's trials such as ASPro-PD (testing a medicine called ambroxol) and EJS-ACT-PD (a new multi-arm multi-stage trial testing several different therapies at the same time). We will continue to keep participants informed of new opportunities to take part in trials as they arise.

The Parkinson's Research Clinic and all of our clinical research studies are supported by the National Institute of Health Research Cambridge Biomedical Research Centre.

TransEuro

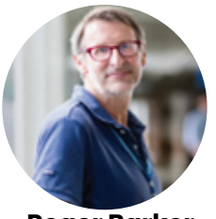
TransEuro is a large multicentre European study which includes a cell transplantation trial and an observational component. The main goal of the study was to advance the development of safe cell-based treatments for PD, particularly for patients whose symptoms are not well controlled with standard medications.

The observational study has been ongoing for nearly 15 years. It involves 6-monthly assessments looking at movement, memory, thinking and mood. The aim is to gather detailed information on how Parkinson's disease behaves and progresses over time and to provide a comparison group for the transplant study. 153 participants have been involved in this component of the study, and 22 continue to be followed up (12 in Cambridge and 10 in Lund, Sweden).

The transplant study involved surgical injection of dopamine producing cells into the striatum, a part of the brain which is known to be affected by PD. There were 11 patients recruited in the UK and Lund, Sweden. The study was completed in December 2022, and the results were published in the journal Nature Biotechnology January 2025. You can read the full results online:
Barker, R.A., Lao-Kaim, N.P., Guzman, N.V. et al. The TransEuro open-label trial of human fetal ventral mesencephalic transplantation in patients with moderate Parkinson's disease. Nat Biotechnol (2025). https://doi.org/10.1038/s41587-025-02567-2

This was a challenging study due to very limited availability of tissue for transplantation and difficulty standardising the transplantation approach across different centres. The results showed that transplantation did not have a significant benefit on the main outcome measure (a measure of movement problems) but there were some positive findings including a reduction in the amount of dopaminergic medication needed following transplantation and a reduction in 'off' time. PET scans showed that there was some increase in dopamine levels in the brain following the transplants, but this varied between centres which used different surgical devices for injecting the cells.

Overall, TransEuro has provided important insights into the factors that need to be taken into account in new stem cell-based dopamine cell replacement trials in PD. It has been an important stepping stone for shaping our new stem cell transplant study, STEM-PD.



Roger Barker

Amy Evans

This study was funded by Funded by an EU FP7 grant and the Cure Parkinson's Trust

STEM-PD

Stem-PD is a study that is taking place between ourselves here in Cambridge and our longstanding collaborators in Lund, Sweden. The whole project is led by Malin Parmar in Lund, with the transplant trial itself being led by Roger Barker. This transplant trial involves grafting human stem cell derived dopamine cells into 8 patients with moderately advanced Parkinson's. This study builds on many years of work in the lab which has sought to work out how we can take human stem cells and turn them into the dopamine cells of the type lost in Parkinson's. Once this was done, the work then had to be repeated using similar approaches with reagents and cells that were of the grade needed for human trials. This work took many years and was very expensive but eventually we got permission to start the trial which began in 2023 and finished in terms of grafting in the autumn of 2024. We have now reached the primary end point of the study which is safety and tolerability at 12 months following transplants in the last patients.

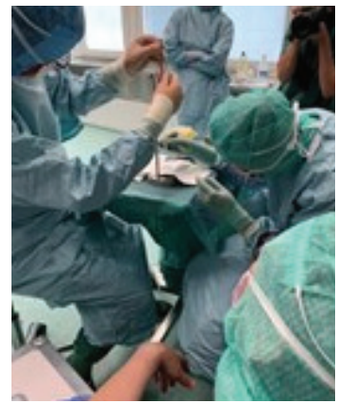
The patients chosen for this study came from the TransEuro observational study (see page 6) and involved both Swedish and UK patients but with all the surgery being done in Lund in Sweden. The reason for this was that the device we elected to use for delivering the cells was made in Lund and could only be used there. The first four patients in this trial received one dose of the cell therapy and the second four received a higher dose. So far, we have seen no major problems relating to the surgery or the cells themselves.

This work was supported by a grant with Novo Nordisk with the hope that we would then collaborate with them further on a new trial in larger numbers of patients - the so called TRANSCEND 1 and 2 studies. Having got ethical and regulatory permission for all this, Novo Nordisk sadly decided to pull out of the cell therapy field altogether late last year for business reasons, and this included our work with them. However, we are confident that the work will continue and that another company will pick up this therapeutic approach from Novo Nordisk, and then work with us on developing it further - with the hope that it will significantly improve dopamine responsive symptoms and thus become a therapy for many people with Parkinson's in the future.

Roger Barker

Saeed Kayhanian

Amy Evans



The STEM-PD cells being drawn up into the surgical implantation device during an operation.

The STEM-PD trial is funded by a research grant from Novo Nordisk

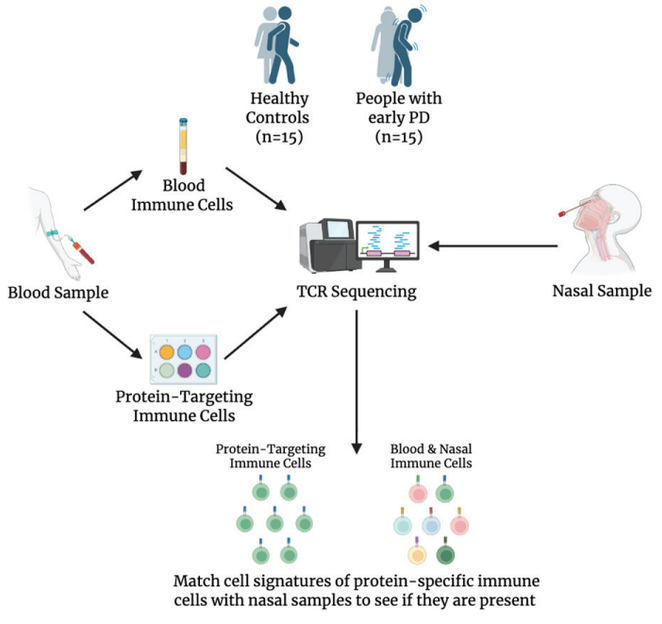
Are immune cell responses in the nose linked to Parkinson's disease?

In Parkinson's disease, we know that there is a build-up of abnormal clumps of protein in brain cells. These clumps are mostly made up of alpha-synuclein. Immune cells (called T cells), which specifically respond to alpha-synuclein or other relevant proteins, have been found at higher levels in the blood in people living with PD during the early stages of disease. When activated, these T cells can cause inflammation which might contribute to brain cell damage and drive disease progression.

The alpha-synuclein build-up is thought to start in the nose before spreading to the brain. This aligns with one of the earliest onset symptoms in PD: loss of smell. Our current research is exploring whether there are immune cells present in the nose that are attacking these abnormal clumps of protein, and whether this could be driving the progression of PD. Such cells could offer a potential target for nasally-delivered treatments or could be useful as an early marker of PD before the onset of movement symptoms.

T cells which respond specifically to alpha-synuclein are challenging to find as they are only present in small numbers in the blood. They are likely to be even harder to find in nasal swab samples, as these samples are smaller and contain many different types of cells - it is a bit like looking for a needle in a haystack! To try and identify these cells, we are taking blood and nasal swab samples from people living with PD as well as people without PD ('controls'). Through stimulating immune cells ('PBMCs') from the blood with alpha-synuclein, we can expand the number of protein-specific immune cells in the blood and use a technique called T-cell receptor (TCR) sequencing to detect their cell 'signature'. We will then scan the nasal sample to see whether it contains a matching cell signature. This will enable us to search the entire haystack and determine if these cells are present within the nose in people living with PD.

Alex Friend



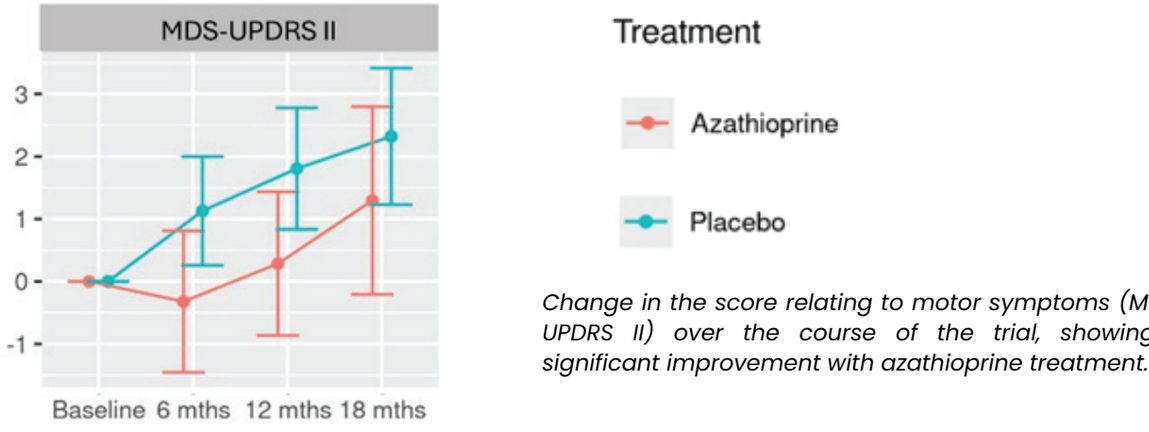
This work has recieved funding from the NIHR Cambridge Biomedical Research Centre Neurodegeneration and Dementia theme.

The AZA-PD Trial

The AZA-PD trial was a proof-of-concept trial investigating immunosuppression as a new treatment approach for Parkinson's disease. We completed the trial in 2024, and presented the results at the international AD/PD conference in Vienna in April 2025. We have also recently published the results in the journal 'Lancet Neurology' - you can read the full results online:
Greenland JC, Dresser K, Cutting E, et al. Azathioprine for the treatment of early Parkinson's disease (AZA-PD): a randomised, double-blind, placebo-controlled, proof-of-concept, phase 2 trial. Lancet Neurol. 2026 Jan;25(1):39-49. https://www.doi.org/10.1016/s1474-4422(25)00386-2

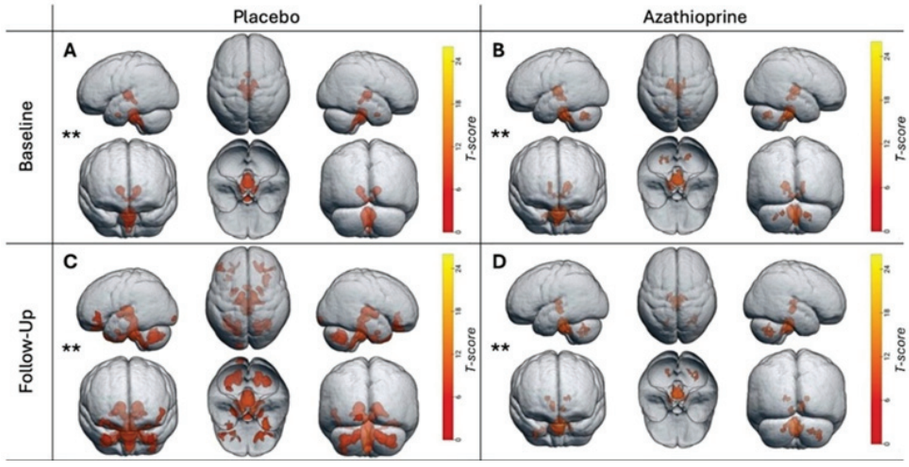
66 participants were treated with either an immunosuppressant drug called azathioprine or placebo tablets for one year. Azathioprine is currently used to treat inflammatory conditions such as rheumatoid arthritis and inflammatory bowel disease but this type of drug had never been used before in PD. The trial was aiming to test whether treatment with azathioprine could improve clinical progression in Parkinson's.

We did not find a beneficial effect on our pre-specified "primary outcome", which was a score assessing posture, balance and walking. However, participants who took azathioprine scored significantly better over the course of the trial on a questionnaire which assessed symptoms relating to problems with movement. Female participants had more widespread benefits from treatment, with improvement in non-motor symptoms and quality of life as well as motor symptoms. This is not yet enough evidence to support the use of azathioprine as a treatment for PD - but the findings are promising and suggest that we should continue to pursue research into immune-targeting therapies for Parkinson's.



Change in the score relating to motor symptoms (MDS-UPDRS II) over the course of the trial, showing a significant improvement with azathioprine treatment.

As well as assessing changes on clinical measures during the trial, we collected blood samples, cerebrospinal fluid samples (via lumbar punctures) and performed PET brain scans to measure inflammation. Our results have shown that azathioprine reduced immune cells in the blood and spinal fluid which have been associated with Parkinson's, and reduced the spread of brain inflammation. Together, these findings provide evidence that immunosuppressive treatment can reduce immune activation and inflammation in PD.



PET brain imaging was done both before and after 12 months treatment, using a marker which measures brain inflammation ([11C]PK11195). There was a spread of brain inflammation over time in the placebo group (left column), but in contrast, inflammation did not spread in the group who received azathioprine (right column).

The trial has contributed to our understanding of the role of the immune system in Parkinson's disease, and our next steps are to understand why some people responded better to treatment than others. This will help us to design future studies aiming to slow down Parkinson's by targeting the immune system.

Julia Greenland received a Junior Faculty Award for her work on the trial at the ADPD conference in Vienna in April 2025

Julia Greenland

Caroline Williams-Gray

This work was funded by the Cambridge Centre for Parkinson-Plus and Cure Parkinson's

The DAPA-PD Trial

Our research over the past few years has shown that an overactive immune response is linked to faster progression of Parkinson's disease. A key player in this is the NLRP3 inflammasome, a sensor within immune cells that detects threats and triggers inflammation. In Parkinson's, abnormal proteins can overstimulate this sensor, leading to long-lasting inflammation and contributing to the loss of nerve cells in the brain.

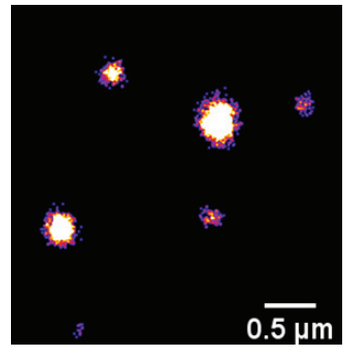
Dapansutrile is a new drug developed by Olatec Therapeutics that blocks the NLRP3 inflammasome. We are testing whether this drug can help reduce inflammation in people with Parkinson's disease in a new clinical trial called DAPA-PD. The trial is opening in early 2026 and will involve 36 people with Parkinson's who will take either dapansutrile or placebo for a period 6 months, following which all participants will receive dapansutrile for a further 6 months. Monitoring will be done to assess safety, to measure changes in inflammation, and to explore changes in clinical symptoms.

In order to help us determine the best way to measure changes in inflammation induced by dapansurile, we are also doing experiments with immune cells (monocytes) in the lab. We are extracting monocytes from blood samples from people with Parkinson's and exposing these cells to bacterial toxins to activate the NLRP3 inflammasome. Working with our colleagues in the department of Chemistry (Professor Sir David Klenerman and Dr Evgenia Lobanova), we are measuring protein clumps called 'ASC specks' which are released by the monocytes when the inflammasome is activated. These ASC specks can be seen using special staining techniques and super high resolution microscopes. The next step is to treat the activated monocytes with dapansutrile to see whether this reduces the level of ASC specks. If this work is successful, we will be able to use a similar technique to measure ASC specks in blood samples in the DAPA-PD trial - providing a useful 'read out' of reduction in inflammation in people taking dapansutrile.

Bina Patel

Caroline Williams-Gray

Evgenia Lobanova



Super high resolution microscopes can be used to visualise ASC specks (inflammatory proteins) in the blood in people with Parkinson's

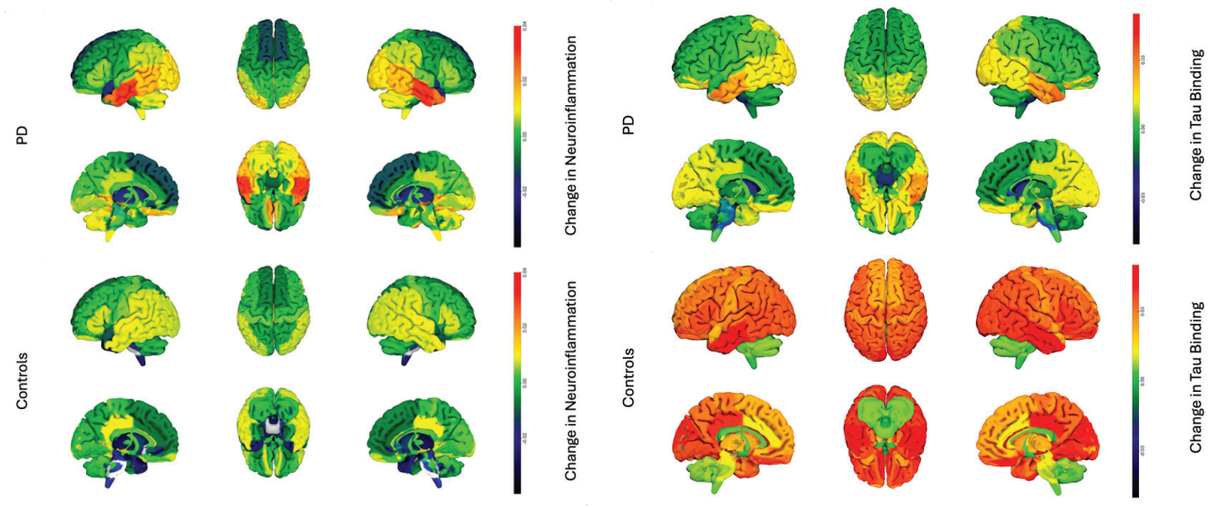
This work is funded by Cure Parkinson's and the Van Andel Institute

Using PET scanning to investigate memory problems in PD

The NEuroinflammation and Tau Accumulation in Parkinson's Disease Dementia (NET-PDD) study has used Positron Emission Tomography (PET) scanning to investigate brain changes over time in Parkinson's. 40 people with PD and 40 'controls' have taken part and have had brain scans on 2 occasions 3 years apart. We are now following-up these participants to assess how the changes that we have seen on the scans are related to the development of memory and thinking problems later on.

The PET technique uses a radioactive tracer that is injected into the bloodstream and and travels to the brain where it binds to a specific protein or marker of interest. A PET/MR scanner allows us to detect where the tracer binds and so allows us to visualise the location of the protein. Therefore, we can use this technique to track biological changes happening within the brain.

In the NET-PDD study, we have been using 2 types of PET tracer to track both brain inflammation and tau protein accumulation. Both of these processes are thought to adversely affect brain function by causing brain cell damage. We have found that early inflammation on PET scans is a better predictor of the development of memory and thinking problems in PD than accumulation of tau. Over time, inflammation increased in specific brain regions in PD, but the PET scans indicated no signficant increase in the amount of tau. In contrast, in people without PD (but of a similar age), tau accumulation in the brain did increase over time, but there was much less change in inflammation. We are still collecting clinical follow-up data and blood samples from participants in the study and will continue to do so for up to 10 years. This will allow us to better understand how these brain changes we have observed during the early stages of the disease are linked to long-term outcomes - and ultimately help us to find better ways to combat memory and thinking problems in PD.



The images show change in inflammation and tau accumulation across different brain regions over a 3-year period in people with PD and controls. The colour represents the degree of change with red being the highest, and blue being the lowest.

This study has received funding from the Evelyn Trust and the Medical Research Council

Alexander Peattie

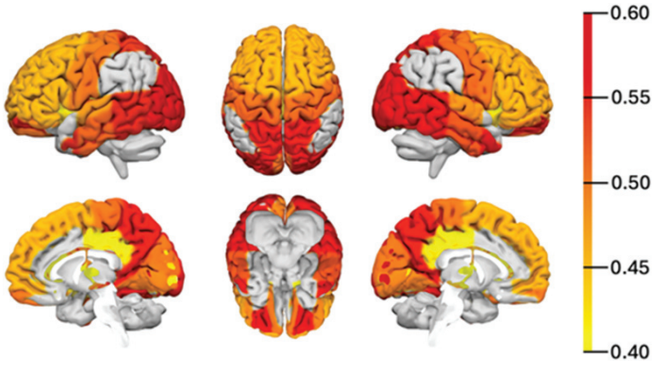
Constipation is linked to brain inflammation in PD

Our previous research has tracked the course of Parkinson's symptoms and problems over time in large groups of people with PD, and has shown that those who suffer with constipation early in the disease course are at increased risk of progression to dementia. The reason for this connection was unknown, but one theory is that inflammation might be a key factor. We already know from our previous work that brain inflammation is linked to dementia risk in Parkinson's, and there is increasing evidence to suggest that constipation might be linked to inflammation in the gut - which might in turn influence inflammation in the brain via the 'gut-brain axis'.

To investigate whether constipation was associated with brain inflammation, we looked at PET brain scans of 27 people with early-stage PD. These scans used a tracer which is injected into the blood and travels to the brain where it binds to inflammatory cells. The research participants had also completed the Gastrointestinal Dysfunction Scale for Parkinson's disease (GIDS-PD), a questionnaire which we developed in our research group to measure the severity of PD-related gut symptoms, including constipation. In addition, we collected samples of blood and cerebrospinal fluid (CSF, the fluid surrounding the brain and spinal cord).

Our results point to a strong link between more severe constipation and brain inflammation. Higher constipation scores were associated with increased inflammation across multiple parts of the brain, including the frontal, parietal, temporal, and occipital lobes, which are involved in controlling various functions like movement and memory. Constipation scores were also linked to markers of immune activation in the body - specifically higher numbers of immune cells (lymphocytes) in the CSF, and elevated levels of specific types of T cells in the blood.

This discovery suggests a possible mechanism that could explain why constipation is a risk factor for faster PD progression. It highlights the importance of the gut-brain axis (the communication pathway between the digestive system and the brain) in Parkinson's disease. The study was published in the journal Movement Disorders in 2025. (*Camacho M, Greenland JC, Peattie ARD et al. Constipation Is Linked to Neuroinflammation in Early Parkinson's Disease. Mov Disord. 2025. https://doi.org/10.1002/mds.70102*)



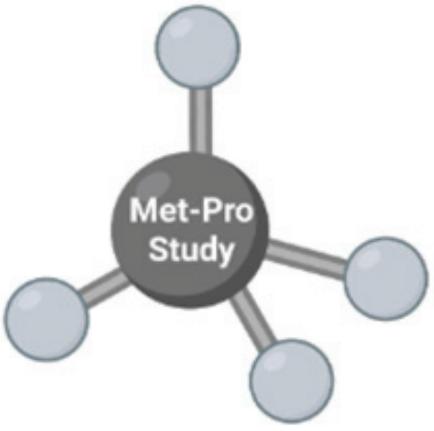
Regions in the brain where the level of inflammation was associated with higher constipation scores. The hotter colours (orange and red) indicate a stronger association.

Marta Camacho

Julia Greenland

The Met-Pro Study

Much attention has recently been dedicated to the role of gut bacteria in Parkinson's. However, other less known gut microorganisms, such as methane-producing archaea, might also be relevant. Our previous research has shown that higher breath methane levels are common in people with PD and have been linked to constipation and worse movement problems. We also know that constipation is a risk factor for dementia development in Parkinson's, but links between methane and memory and thinking problems in PD have not previously been investigated.



The Met-Pro study, led by Marta Camacho, started in June 2025 and is using breath tests to investigate whether overproduction of methane is linked with cognitive problems and other Parkinson's symptoms. The study is also assessing how breath methane levels are linked with the number of archaea organisms in stool samples and with gut function. Participants include people with Parkinson's, people at high risk of developing Parkinson's, people with memory problems, and controls. A subgroup of people with PD have been invited to take a daily probiotic supplement to test whether this can reduce breath methane levels and improve gut symptoms. If the results of this pilot study with probiotic supplementation are encouraging, this may support a larger clinical trial in the future.

This image, generated using an electron microscope, shows archaea, single-celled organisms that resemble bacteria in shape and produce methane in the human gut.

Marta Camacho

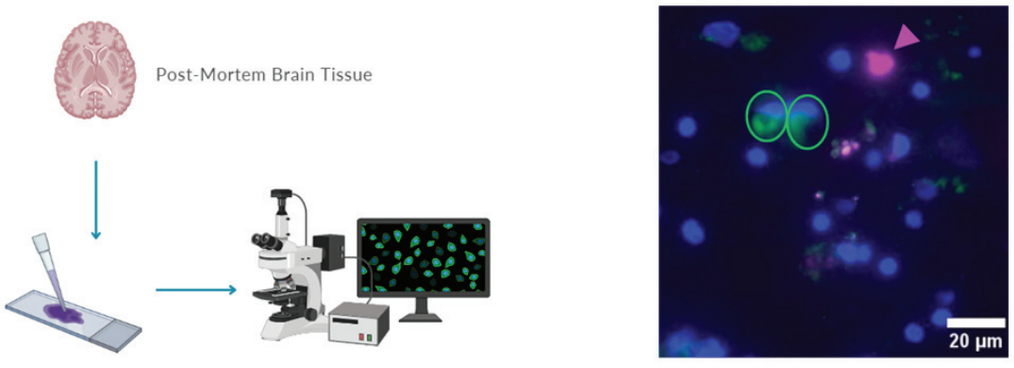
This work is funded by Parkinson's UK

Visualising immune cell infiltration into the brain in Parkinson's disease

The immune system is intended to help repair damage in the body and to protect us from unwanted infections, but in some people with Parkinson's, it may be causing excess inflammation which contributes to brain cell damage. Clotilde Tournerie (PhD student) is specifically studying a part of the immune system called the innate immune system, which provides a non-specific response to injury and infection, to investigate its role in Parkinson's. The key cell types involved in the innate immune response are natural killer (NK) cells, monocytes and neutrophils. These cells circulate within the bloodstream but we would not expect these cells to travel into the healthy brain. Clotilde is looking for evidence of infiltration of these cells into the brain in Parkinson's.

In order to do this, she has been staining post-mortem brain tissue with fluorescent markers which specifically label these cells, and visualising them using a fluorescent microscope. So far, in regions of the brain where most damage occurs in Parkinson's, she has been able to see that NK cells are present in larger numbers in the brains of people with PD compared to people without PD, and that these NK cells are found in close proximity to abnormal clumps of a protein alpha-synuclein, which are known to play a key role in PD.

Moving forwards, she will be carrying out similar work to look at neutrophils and monocytes, with the goal of providing evidence that these cell types are a promising target for therapies to decrease harmful brain inflammation in people with PD.



The image on the left shows the method of staining post-mortem brain tissue with markers of innate immune cells which are then visualised under a fluorescent microscope, and on the right is a representative image of NK cells in PD brain (green circle) in close proximity to alpha-synuclein (pink arrow).

Clotilde Tournerie

Clotilde's work is supported by the MRC-DTP PhD programme

The role of ‘jumping genes’ in driving brain inflammation in Parkinson’s

This is a team project which involves the labs of Roger Barker, Jo Jones and Annelies Quaegebeur in Cambridge, and Johan Jakobsson in Lund, Sweden. The project focuses on so-called “jumping genes” (transposons) in the brain. Transposons play a role in many different living organisms. In corn, these genes cause the beautiful multicoloured cobs you see in farm shops, however in humans there is evidence that they may be linked to conditions such as Parkinson’s disease. These jumping genes are often remnants of ancient viral infections that afflicted our ancestors thousands of years ago and have since become part of our genetic make-up. We are investigating whether these genes get activated/jump in people developing PD and if so, how this might drive the disease process.

In particular, we are interested in the theory that these genes are activated in the brain in PD, leading to production of proteins which the body mistakenly thinks is due to a viral infection. This could then lead to inflammation and brain cell damage.

We have now completed an initial study looking at tissue from a large number of post-mortem brains from people with PD. We found that the jumping genes are activated in certain brain areas and that this is associated with inflammation in those regions (especially the dopamine pathway linking the substantia nigra to the putamen). We are now looking at how this might happen using different types of human cell models in the lab. In addition, we are studying post-mortem brains from people without PD, but with a possible precursor to it, called Incidental Lewy Body Disease. This is to explore whether jumping gene activation and inflammation may be happening very early on in the development of PD. This work could open up an entirely new theory as to what goes wrong in PD - which could in turn lead to new treatment approaches.

James Shonhard

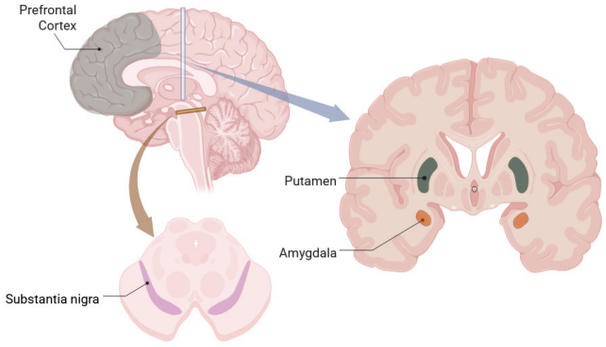
Annabel Curle

Shaline Faizal

Roger Barker

Annelies Quaegebeur

Jo Jones



We are comparing the genetic signature and activation of transposons (jumping genes) in different regions of the brain at different PD stages. The regions we are focusing on include those strongly affected in Parkinson’s such as the substantia nigra and the putamen, as well as regions that are less affected in early disease, including the prefrontal cortex and amygdala.

This study is funded by Aligning Sciences Across Parkinson’s (ASAP)

Brain Donation

You are probably familiar with organ donations of the heart, kidneys or eyes to sustain the health or even the life of people in need. Tissue donation can also be valuable for research.

Brain donation for research is a precious and unique gift. Scientists can learn and understand more about brain diseases such as Parkinson's when they are able to work on donated tissue. Ultimately, we hope that scientific work of this kind will lead to better and more effective treatments and that future generations will benefit from the help of brain donors.

Registering to donate the brain and other parts of the nervous system is a big decision and needs to be discussed with family and friends. Advice is available from the Cambridge Brain Bank team, who would be very happy to discuss any concerns or questions you or your family may have. Email add-tr.cambridgebrainbank@nhs.net, telephone 01223 245151, for further information, or visit https://www.cuh.nhs.uk/patient-information/the-donation-of-brain-pituitary-tissue-and-cerebrospinal-fluid-after-death/

Ann Mary Alias
Specialist Brain Bank Research Nurse

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Facebook: The Barker / Williams-Gray Lab

Donations

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