



# **UNDERSTANDING THE CAUSES TO FIND TREATMENT FOR PEOPLE LIVING WITH PSP & CBD**



**PSPA Helpline:  
0300 0110 122**

**FOR RESEARCH INFORMATION**  
[research@pspassociation.org.uk](mailto:research@pspassociation.org.uk)

**“For people affected by PSP & CBD, hope for better treatments, and even one day a cure, depends on the research we can encourage and fund right now. As a neurologist caring for people with these conditions, their willingness to take part in and support research is inspirational. I have no doubt that this powerful partnership between clinicians, scientists and people affected by PSP & CBD will deliver better care and new treatments, and prospects for progress have never been brighter.”**

*Professor Nigel Leigh, Consultant Neurologist  
Chair of the PSPA Research Committee*

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*The research information included in this issue are updated to October 2022*

**PSPA is the only UK charity offering support and information to people living with PSP & CBD. We do this by providing support and information to people living with PSP & CBD, while funding and promoting life-changing research.**

Progressive Supranuclear Palsy (PSP) is a neurological condition caused by the premature loss of nerve cells in certain parts of the brain. A protein called TAU builds up in certain areas of the brain and forms into clumps (neurofibrillary tangles), which are believed to damage the nerve cells.

Corticobasal Degeneration (CBD) is also a degenerative brain disease that affects people from the age of 40 onwards. Although there are similarities to PSP, with similar nerve cell damage and the build-up of a protein called TAU in certain parts of the brain, the classical clinical picture is quite distinct.

People diagnosed with CBD may go on to develop features of PSP and vice versa. The overlap between the two conditions is now well recognised.

PSPA funds research to better understand the cause of PSP & CBD, improve diagnosis, and discover effective treatments.

This leaflet will provide you with information regarding completed and ongoing research studies sponsored by PSPA thanks to our supporters and donors.

For more information about living with PSP & CBD and support offered by PSPA, please contact us on:

Helpline: 0300 0110 122

Email: [helpline@pspassociation.org.uk](mailto:helpline@pspassociation.org.uk)

[www.pspassociation.org.uk/information-and-support](http://www.pspassociation.org.uk/information-and-support)



**“Providing people with a better quality of life is underpinned by developing a greater understanding of the causes and development of PSP & CBD and building a network of interest in research both nationally and internationally.**

**Funding research is a central part of the work of PSPA, and we are committed to growing our investment in the future.”**

*Rebecca Packwood, PSPA Chief Executive*

## RESEARCH ON PSP & CBD CAUSES AND TREATMENT

It is estimated that PSP & CBD affect 5,000 adults in the UK, but this number could be more than 10,000 as many are misdiagnosed with other conditions.

**“One of the most important discoveries so far for PSP & CBD has been the identification of the TAU protein. When the TAU protein becomes sticky it clogs up the nerve cells. This knowledge of the disease mechanism provides new targets for drug therapies. This includes the TAU antibody approach that is currently being explored by pharmaceutical companies.”**

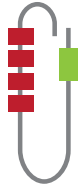
*Professor Huw Morris, Consultant Neurologist*

Professor Morris also acknowledges that research support offered by PSPA has made a big difference to the understanding of the diseases and the drive to develop new treatments.

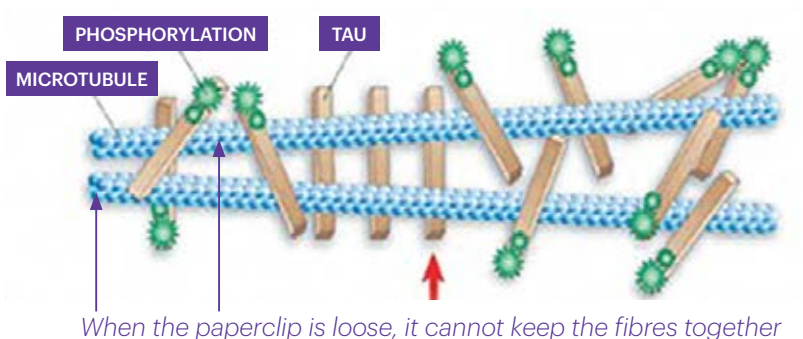
**“PSPA’s funding has paved the way for new drug trials in the UK and its initial funding has allowed us to successfully apply for other grants, so the charity’s money has gone a long way.”**

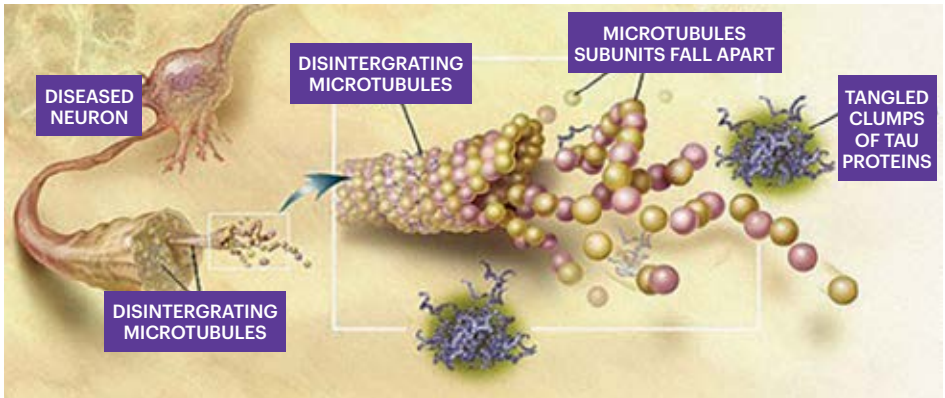
## WHAT WE KNOW ABOUT TAU

One of the most important advances so far for PSP & CBD research has been the discovery that nerve cell deterioration is associated with the build-up of a protein called TAU in certain parts of the brain (TAU abbreviated from Tubulin Associated Unit). TAU is present in healthy brain cells, where it stabilises the long, hollow tubes known as microtubules that support the cell's structure. It is hypothesised that TAU has a 'paperclip' conformation where one side is entangled within the tubule structure to make the tubule stronger. The clip keeps the fibres together (see red arrow in the figure below, from wikipedia).



In PSP, CBD and some other neurodegenerative diseases, TAU molecules become misshapen because a process called phosphorylation alters the paperclip structure. These changes result in TAU disconnecting from the tubules, causing instability and TAU forms into clumps known as neurofibrillary tangles. The accumulation of these clumps is associated with the deterioration and eventual death of nerve cells (neurotoxic effect). Recent research has revealed that the structure and shape of the TAU fibres forming the clumps differs in PSP & CBD.





*Schematic from ADEAR: Alzheimer's disease education and referral center*

In addition, the area of the cell where TAU clumps form is linked to the disease specific presentation as they accumulate in the centre of cells in PSP and more peripherally in CBD.

Other alterations of TAU have been detected in affected brains and may also contribute to neurotoxicity. The altered TAU also seems to spread from one cell to the next, meaning that the area of the brain affected by the disease gradually increases as the disease progresses. Symptoms are influenced by which areas of the brain are involved.

TAU abnormalities have a common pathological role across several different neurodegenerative diseases. Indeed, TAU is associated with other conditions such as Alzheimer's and Parkinson's, therefore it is of great interest as a potential target for treatment.

Much of the current focus is on blocking the development or enhancing the removal of neurofibrillary tangles, whether by stopping the spread of altered TAU through the brain or by

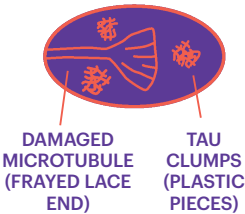
preventing TAU from changing in the first place. Creating a model of TAU alterations in laboratory or animal experiments is one of the multiple ways that researchers are using to find a cure for neurodegenerative conditions such as PSP & CBD.

Pharmaceutical companies are currently developing and testing drugs to target the abnormal TAU protein. Results of these studies are promising but they have not yet shown a definitive solution for the different ways TAU impairs brain cells.

One of these studies is looking into using a monoclonal antibody, a laboratory-produced molecules engineered to recognise a specific protein. The antibody should link abnormal TAU in PSP patients and avoid defective TAU propagation. Only one site in the UK is open to recruitment with strict criteria for eligibility. The results of the study will be available in 2024.



IF THE TAU BREAKS AWAY



*The fraying end of a shoe's lace represents the progressive nature of PSP & CBD and aims to open up conversations about the rare conditions.*



## RESEARCH FUNDED BY PSPA AND PARTNERS

### PSPA has funded projects aiming to



Understand causes



Improve diagnosis



Make progress towards treatments



Encourage new researchers and clinicians to focus on PSP & CBD



Establish a UK-wide Research Network working on PSP & CBD

## **PSPA is supporting one of the largest studies on PSP & CBD to better understand how these conditions progress.**

The **PROSPECT-M-UK** study programme is an ongoing multicentre, multi-stage study led by Professor Huw Morris based at the National Hospital for Neurology & Neuroscience at UCL, London. This study has recruited over 1,000 people with PSP & CBD and control participants across 29 study sites within the UK, making it one of the largest studies of PSP globally.

The study title means **PRO**gressive **Su**Pranucl**E**ar Palsy **Co**rTico-Basal Syndrome **M**ultiple System Atrophy Longitudinal Study **UK**.

Significant outputs of the study have been the creation of an international research network and the PROSPECT bio bank of data, samples and brain images. The data collected has enabled researchers to better understand underlying disease biology, potential therapeutic targets, genetic determinants, and clinical varieties of atypical parkinsonian disorders as PSP & CBD.

With the data collected, the PROSPECT study has so far shown:

- PSP affects people in different ways and that some forms of PSP are similar in the early stages of Parkinson's.
- PSP is twice as common as was previously thought and may affect around 8,000 people in the UK.
- Genetic factors may determine the different clinical presentations and the progression of PSP & CBD, and these findings will be used to define new treatments.

- Data analysis on 1,001 people demonstrated an influential finding on the association between a specific gene mutation and survival in PSP which was published in a leading neurology journal.
- Early onset PSP, defined by motor symptom onset at 55 years old, is often clinically similar to Parkinson's disease and that genetic analysis can help differentiate between the two disorders.
- Genetic mutations and spinal fluid markers have been identified for CBD and they could help early diagnosis.
- The study teams collaborated to improve the current diagnostic criteria of CBD so the condition can be diagnosed more accurately in life.
- The imaging component of the study used magnetic resonance techniques to show that in PSP brain atrophy progresses in a particular way, providing an important insight into the mechanisms of disease progression.
- Researchers identified areas of the brain specifically affected by CBD and that can help diagnosis using imaging.

## **RESEARCH PARTNERSHIP**

As part of our research commitment to our members, a joint-funded study by the Scottish Government and PSPA focusing on diagnosis and care in PSP & CBD is also running. Dr Diane Swallow based at the University of Aberdeen established a rich set of data involving 92 PSP & CBD patients, 82 carers, and

83 Parkinson's disease patients as controls. Data shows that individuals with PSP & CBD take approximately four times longer to reach key diagnostic milestones. This is due to a tendency within primary care to misattribute identified relevant symptoms to alternative diagnoses resulting in a wide secondary care referral pattern to non-movement disorder specialties.

**“Improving this area is of huge importance to patients and their families and will enable them to plan ahead and best manage the condition, access vital support and benefits and avoid the stress of incorrect diagnosis... we are also seeking to evaluate tools which might assist that process.”**

*Dr Swallow*

### **SMALL RESEARCH GRANT**

Last year the PSPA research appeal generated a Small Research Grant that has been allocated to a project exploring how people with PSP & CBD can achieve the best possible quality of life. The project will evaluate the impact of clinics involving multidisciplinary teams (organising and coordinating health and care services to meet the needs of individuals with complex care).

Dr Boyd Gosh, the recipient of one of the PSPA Small Grants, will compare the quality of life and health resources utilisation (e.g., mental health support requests and number of specialty visits) in patients in different areas of Dorset and Wiltshire with different availability of services. This will potentially pave the way to a model of multidisciplinary structure for neurology clinics across the UK.

## PARTICIPATION IN RESEARCH

Participation in research studies is of extreme importance for rare disease patients and their carers. Benefits have been shown beyond the additional information the participant will receive about the condition and option for treatment. People who have taken part in research felt they have been contributing to the wellbeing of society, and the advancement of medical research as well as giving hope for future generations.

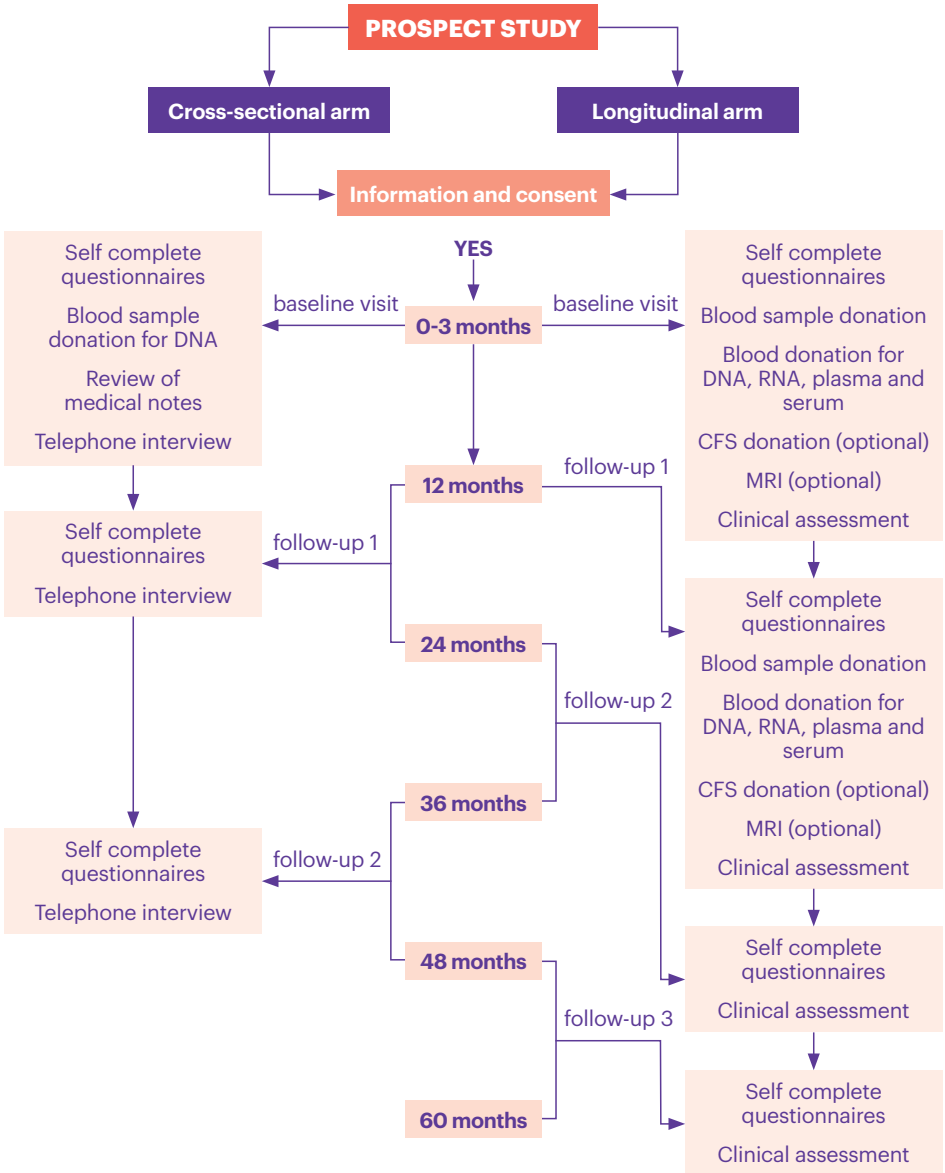
Participation in research studies is completely voluntary and consent to participate can be withdrawn at any time the volunteer is no longer comfortable with continuing, or no longer able to participate.

### Current recruiting studies are:

- PROSPECT-M-UK Study (see details in page 10 and 14), multi-site in the UK, running till the end of 2024 and recruiting PSP & CBD patients.

*The image in the next page shows the 'journey' of a patient recruited into the PROSPECT-M-UK study.*

- OxQUIP – **O**xford study in **Q**uantification **I**n **P**arkinsonism, with the aim of identifying measures that can detect disease progression over much shorter time periods than is possible at present, is recruiting patients with Parkinson's disease and PSP.
- Invicro (name of an imaging facility) study looking into the mechanisms of PSP, evaluating TAU protein density in the brain of patients with PSP using specific imaging techniques. It is based at University of Exeter.



The 'journey' of a patient recruited into the PROSPECT-M-UK study

- PiPPIN (**P**ick's disease and **P**rogressive Supranuclear Palsy, **P**revalence and **I**ncidence), collecting data on how many Frontotemporal Dementia (Pick's disease), PSP & CBD affected patients are in the catchment area, their demographics details, and condition specific tests, including patients and healthy control in Cambridgeshire or Norfolk.
- NORAPS: a Cambridge based study on **NOR**adrenaline treatment of **AP**athy and impulsivity in participants with Progressive **S**upranuclear Palsy syndromes.

If you would like to express your consent to be contacted for research activities, please find the **Register of Interest in Research** form on our website using the link below or contact us via the helpline to receive a paper copy:

[www.pspassociation.org.uk/research/patient-carer-voices-in-research/register-your-interest-with-us](http://www.pspassociation.org.uk/research/patient-carer-voices-in-research/register-your-interest-with-us)

Helpline: 0300 0110 122

### **What will happen to your details?**

Your details will be sent to institutions conducting studies and the study coordinators who will then contact you to explain what is involved in taking part in the study. They will then be able to tell you whether you are eligible to join the study.

## CURRENT PSPA RESEARCH ACTIVITIES

### **Rising stars in clinical neurology having access to research training**

Our 2020-2025 research strategy includes the goal of supporting emerging research talents via small grants and fellowships. We have teamed up with the Association of British Neurologists (ABN) to offer a two-to-three-year neurology clinical fellowship for a neurology trainee to complete a higher research degree in any area of Clinical Neuroscience of clear benefit to those with primary neurological diseases, including PSP & CBD. PSPA will also provide the opportunity to get some patient involvement in their work via our PRIM group (see page 18).

### **Research information days**

We are in the process of organising a second, information-packed research information day for early 2023 in order to provide patients, carers and their families with the most recent information on research progress in identifying causes, establishing best practice in care, and finding a cure for PSP & CBD. More information will be shared via PSPA Matters and on our website.

You can watch videos from previous events, here [www.pspassociation.org.uk/research-information-day-and-strategy-launch](http://www.pspassociation.org.uk/research-information-day-and-strategy-launch)



## **Research symposium 2024**

We have partnered again with our North American counterpart, CurePSP, for the second PSP & CBD International Research Symposium. Scientists from academia and pharma will present their latest research results in the field of PSP, CBD, and related diseases. More information will be shared via PSPA Matters and on our website.

You can watch videos from the first symposium here [www.pspassociation.org.uk/research/symposium](http://www.pspassociation.org.uk/research/symposium)

## INVOLVING YOU IN RESEARCH ACTIVITIES

Members of the public can have their voices heard via involvement in research, where members of the public (patients, carers, family members, supporters) are actively involved in research projects and act as a 'critical friend' for drug companies and researchers. This is different from participation.

Examples of public involvement are:

- involvement in identifying research priorities
- commenting and developing patient information leaflets or other research materials
- improving the relevance, clarity and feasibility of research design, tools and outcome measures
- suggesting the translation of the research outputs by using language and messages that are more easily understood by a public audience.

The existing PRIM (PSPA Research Involvement Members) group meets once a month virtually, if you would like more information, please email [research@pspassociation.org.uk](mailto:research@pspassociation.org.uk)



## OUR COMMITMENT

Best-practice care is the top priority for people affected by PSP & CBD and best practice is often achieved after evidence is produced from high good quality research.

Research has always been a key priority for us at PSPA. In the strategy for 2022-2026, PSPA reiterates the importance of research as the mean to create a better future for everyone affected by PSP & CBD.

We are committed to continue to play an active role in the research community and contribute towards the global search for future effective treatments, and, one day, ultimately a cure.

We are only able to fund this research thanks to members of the PSP & CBD community who have seen first-hand the devastation caused by these diseases. Thanks to them our funding is not only part of the global fight to find a cure but is also helping lead researchers and neurologists to unlock other sources of funding to progress towards finding a cure.

**“I see a better future for people with PSP & CBD, with progress on causes, care, and a cure. This is urgently needed for patients but can only succeed with patients, in partnership with research teams across the UK. That partnership begins with an early accurate diagnosis.”**

*Professor James Rowe, Consultant Neurologist, PSPA Trustee*

**PSP/**

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