RESEARCH
SYMPOSIUM EDITION

PSPA MATTERS

WORLDWIDE RESEARCH UPDATES FROM NEURO 2023

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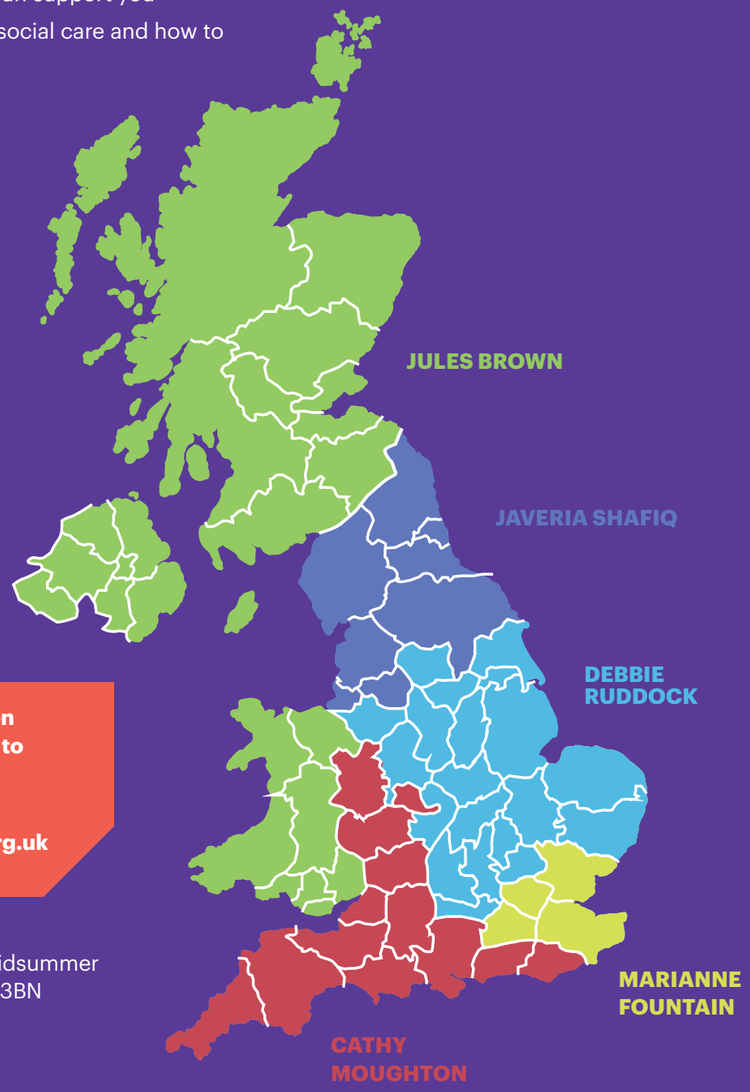
IN THIS ISSUE

PSPA
CREATING A BETTER FUTURE FOR PEOPLE LIVING WITH PSP & CBD

HERE FOR YOU

Our Helpline Care Navigators are here to support everyone affected by PSP & CBD. Each Helpline Care Navigator has a designated area (see map) where they provide proactive support, including:

- Information on all aspects of living with PSP & CBD, such as symptom management, benefits and entitlements and everyday living
- Emotional and practical support
- Contact details for local support, which may include Support Groups
- Information about how PSPA can support you
- Information about health and social care and how to access these services
- Signposting to other sources of information
- Referral for non-means tested benefits applications via Department of Work and Pensions (DWP) home visiting service
- Supporting evidence about PSP & CBD for Blue Badge applications and Continuing Healthcare applications
- Provide specific information written for health and social care professionals and access to Education Volunteers.



Our Helpline and information service is available Monday to Friday 9am to 9pm.

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WELCOME

Neuro 2023 was an inspiring event which bought hope for the future. With the world's leading scientific experts in Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) gathered in London for two days we were able to hear about the latest understanding of these rare conditions, and what might come next.

Over 250 people attended the event (either online or in person) and we covered a huge range of subjects. As a non-scientist at the event, some of the details of the research were beyond my understanding, and that was to be expected. This event was focused on scientists talking to scientists and it was right that the tone was about them learning from each other. Along with CurePSP, our American counterparts, we were aiming for the event to advance scientific knowledge and to pave the way for the next breakthroughs in research.

Not only did we hear from experienced scientists and clinicians from the UK, US, Canada, Singapore, India, and Germany (and many more countries) we were delighted to have over 30 poster submissions, many from junior researchers who we hope will create a career in researching PSP & CBD.

We were delighted to be joined by our Royal Patron the Duchess of Gloucester who has been a long-standing supporter of PSPA.

What struck me most about Neuro 2023 was that you could feel the enthusiasm and commitment at the event, the buzz as people made new connections that linked their work to something happening in another part of the world.

We aim to run the event in partnership with CurePSP every other year, I'm already looking forward to Neuro 2025!

Rebecca

Rebecca Packwood
PSPA CEO

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60 YEARS OF PSP & CBD – A HISTORICAL PERSPECTIVE

Next year, it will be 60 years since PSP was first discovered by researchers in the US. At the Neuro 2023 Symposium in London, leading movement disorders researcher Professor Anthony Lang from the University of Toronto, gave us a historical perspective of PSP and how we have got to where we are today.

PSP was first described by neurologists Dr John Steele, Dr Clifford Richardson and Dr Jerzy Olszewski in Toronto. In 1955, Dr Richardson began to treat a good friend who had symptoms of clumsiness, sight trouble and mild forgetfulness, but who also developed many symptoms over the following four years. Dr Richardson thought it was unusual, and after conversations with friends and colleagues he realised this wasn't an isolated case. More PSP patients were admitted to his neurology service, and there were more cases in Montreal.

VERY EARLY REPORTS OF PSP

In the 1960s, seven people diagnosed with postencephalitic parkinsonism had died. But Dr Olszewski disagreed with the diagnosis, with Dr Steele, he re-evaluated these cases.

In 1964, Dr Richardson, Dr Steele and Dr Olszewski published a paper in the journal Archives of Neurology describing a patient with a chronic, progressive brain disease, with defective eye movements as well as rigidity and stiffness. They called the condition 'progressive supranuclear palsy'.

In 1972, Dr John Steele reviewed the scientific literature and discovered the condition had been described before, as early as the 1930s. Others believe PSP existed even earlier - a passage from a Dickens novel could have described someone with PSP, while in 1888, a researcher called Charcot published a paper describing symptoms that might suggest PSP, and even PSP-CBD.

MAJOR RESEARCH MILESTONES

Dr Lang described several important historical landmarks in the last 60 years that underpin knowledge today.

The first landmark is diagnostic criteria – which have changed over the years. At first, doctors couldn't diagnose PSP without progressive supranuclear gaze palsy (where eyes cannot move together in a single direction) being present, but this has changed.

By studying post-mortem brain tissue, scientists realised how variable the disease was, that explained why patients had such different symptoms. Together, this made diagnosis difficult.

Researchers around the world reported patients with many symptoms, including pure akinesia (where people can't move on their own), inability to walk, difficulties with speech, rapid eye movements, and abnormally small handwriting. Researchers began to recognise early CBD and cognitive dysfunction. Researchers reported some of their patients also had frontotemporal dementia (FTD) - and indeed now, PSP & CBD are part of this group of syndromes.

We now know why there are so many clinical symptoms – and that's down to a protein called Tau. The amount of Tau and how it's distributed across the brain varies between patients.

2017 was a significant milestone – a paper was published describing criteria to help doctors diagnose movement disorders. This new criteria defines the characteristics while also highlighting variability. The PROSPECT-UK study is now helping to define these new diagnostic criteria. So far, the team have discovered more people were diagnosed with PSP using these criteria.

The other significant development was the clinical rating scale for PSP – which helps doctors monitor progression through various scales.

PATHOLOGY – A HISTORICAL LANDMARK

The second historical landmark is pathology – how scientists are beginning to understand what changes are happening to the brain that ultimately causes the symptoms people are living with.

In 1973, scientists discovered 'neurofibrillary tangles' in the brains of people with PSP, and shortly afterwards, scientists revealed they were tangles that were unique and different to those found in the brains of people with Alzheimer's disease. In 1989 scientists found different forms of Tau - forms called 3-repeat and 4-repeat (4R) were important in Alzhiemer's disease.

In 1990, scientists realised Tau and neurofibrillary tangles were also building up in other cells in the brain called glia and astrocytes. Later, scientists would discover this pattern is different in PSP compared to CBD.

LINKING TAU WITH PSP & CBD

The first-time Tau was linked with PSP came in the 1990s, when scientists discovered some patients with FTD and PSP had a fault in the Tau gene. For the first time, scientists linked 4R Tau to PSP & CBD– and in different locations to Alzhiemer's disease. PSP & CBD are now described as important '4R Tauopathies'.

In 2013, scientists discovered faulty Tau which may be linked to disease progression.

THE FUTURE IS BRIGHT – THE ERA OF CLINICAL TRIALS

Progress made over the last 60 years means we are now seeing large scale trials across the world we would never have dreamed of for a rare condition.

There are trials of drugs that work in several different ways, and potential drugs affecting Tau which are of interest to pharmaceutical companies. Biomarkers are on the horizon – molecules that we could use to diagnose and monitor disease. Potential biomarkers already exist for Alzheimer's disease and other neurodegenerative conditions, and Dr Lang believes we are on the verge of having the same for PSP.

THE FUTURE IS BRIGHT FOR PSP & CBD RESEARCH AND THE NEXT 60 YEARS COULD BRING REAL PROGRESS.

neuro 2023
The PSP and CBD International Research Symposium

WE KICKED OFF THE CONFERENCE WITH A TALK DESCRIBING HOW PSP WAS DISCOVERED 60 YEARS AGO AND HOW THINGS HAVE PROGRESSED OVER THE YEARS

neuro 2023

RESEARCH BRINGING HOPE AND OPTIMISM FOR THE FUTURE

Neuro 2023: the PSP & CBD International Research Symposium, organised by PSPA and CurePSP, saw 250 researchers from 20 countries around the world gather in London and online, to share their latest PSP & CBD research findings. PSPA's Chief Executive Rebecca Packwood opened the first symposium since 2018 alongside CurePSP's Executive Director and Chief Scientific Officer Dr Kristophe Diaz, and two jam packed days followed.

A HISTORICAL PERSPECTIVE

Professor Anthony Lang from the University of Toronto kicked off the conference with a talk describing how PSP was discovered 60 years ago and how things have progressed over the years, including greater hope in biomarkers and trials (read the full run down of the talk on page 4).

INFLAMMATION AND SYNAPSES – NEW TARGETS FOR TREATMENT

Dr Maura Malpetti from the University of Cambridge described how she believes neuroinflammation is a potential biomarker and might be a good target for new drugs. She uses a brain imaging technique called in vivo PET – where a 'tracer' solution containing a molecule that 'sticks' to particular brain cells is injected into the body and can be detected by the scan. Dr Malpetti discovered high levels of inflammation in PSP & CBD, suggesting doctors could use neuroinflammation to measure disease progression. She has discovered inflammation markers called cytokines are higher in people with PSP, correlating with scan results showing inflammation is higher in the frontal lobe and brain stem.

Professor James Rowe, also from Cambridge talked about synapses - the gaps between nerve cells that are crucial for them to communicate with each other. In disease, synapses help toxic Tau spread between cells, and are related to cognitive deficit - more than inflammation.

Professor Rowe believes synapses may be important in treating PSP. He described how stopping synaptic damage and inflammation – key points in the cascade of events leading to declining quality of life in PSP & CBD - could stop the catastrophic nature of the condition. Scientists discovered 20-30% of synapses have been lost by the time someone is diagnosed with PSP or CBD.

In PSP & CBD, patients lose more synapses in a year than people do in an adult lifetime, and this correlates with the clinical decline of a patient with particular effect on the brain's frontal lobe. Professor Rowe is now studying synaptic loss in post-mortem brain tissue.

Neuropathologist Dr Gabor Kovacs from the University of Toronto described novel approaches to tackle PSP. There are different types of PSP that affect people differently. He believes PSP frequency is higher in people over 80. He is looking at the molecular behaviour of Tau in PSP patients of varying severity. He described how Tau's properties help distinguish between different conditions – and 4R Tau is more prone to spreading within the brain.

STUDYING TAU IN DETAIL

Tau expert Professor Karen Duff described her work studying this protein in Alzheimer's disease, PSP and Pick's disease. Depending on the disease, Tau builds up in different places in the brain and can spread.

Professor Duff is studying whether faults in exon 10 of the Tau gene, which makes more 4R Tau, causes clinical effects, and how scientific outcomes such as nerve cell degeneration arise. Professor Duff will publish this shortly and also highlighted her new Lancet Neurology paper summarising neuroinflammation in PSP & CBD.

The audience heard how Tau type is specific to the type of disease, how scientists are using it to develop new diagnostic tests and the models they are using to study it.

FROM THE BENCH TO CLINICAL TRIALS

Dr David Vaughan from Queens Square Institute of Neurology in London is studying data from people with CBD taking part in the PROSPECT and CLEAR studies, and from the UK brain bank. Dr Vaughan described patterns of symptoms in different disease categories and will study how genes are involved.

Several talks were about drug discovery. Dr Amy Rommel from the Rainwater Foundation described how researchers need new biomarkers, a central biobank of tissues and samples, and a central place for cell, tissue and patient data. Dr Rommel encouraged scientists to enter data into an open access platform for all researchers to use, to progress drug discovery faster towards clinical trials.

Researchers in industry and academia described clinical trials for PSP & CBD (see article on page 10) and Motor Neurone disease (MND) researcher Professor Nigel Leigh shared his MND trial findings targeting neuroinflammation.

BRINGING LIVED EXPERIENCE TO THE FORE

Lived experience and care kicked off day two. Dr Stephanie Oscarson described CurePSP's work to understand patient journeys and showed moving films from patients and family members at various stages of disease. They shared their experiences and told the research community and industry why studying PSP & CBD is so important.

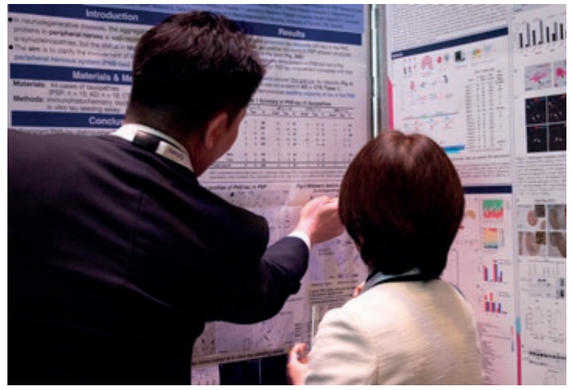
PSPA Trustee Paul Inness talked about PSPA's new research strategy, and how involvement of patients and their carers is embedded within it. PSPA's recent survey of people living with PSP & CBD revealed 60% of people were misdiagnosed initially, people want to take part in research but don't know how, how carers are crucial for people to take part, and how people want to hear results. He described the elements of wellbeing needed for people living with PSP & CBD and their carers to live the best life they can.

Riona Fumi talked about PROSPECT, about how they engage and inform patients. The study aims to speed up diagnosis, track disease progression, create a biobank of samples to use in research, and to create a 'clinical trial ready' group of people. Riona described how post-mortems can sometimes reveal patients have been misdiagnosed. Dr Gesine Respondek described her work mapping the clinical and emotional journey in PSP.

GENES, BIOMARKERS AND MEASURING PREVALENCE

Much of the morning of the second day was dedicated to research studies, including PROSPECT. We were delighted to have HRH the Duchess of Gloucester join us to hear about the progress being made.

Professor Huw Morris from the Institute of Neurology showed how the PROSPECT study has confirmed PSP is more common than we thought. The Global



Parkinson's Genetics programme is collecting data from many different ethnic backgrounds, including people with PSP, CBD and Multiple System Atrophy (MSA). His team have discovered a new genetic risk factor in people with Parkinson's disease of African ancestry, that's not present in people from Europe.

Dr Diane Swallow presented the latest prevalence data for PSP & CBD in Scotland. Dr Ed Jabbari described his work to discover a new way to diagnose PSP by measuring a protein called LRRK2. He is now exploring whether this test could help to spot disease changes earlier.

PRIZE-WINNING POSTERS

Friday afternoon saw poster presentations (see article on page 19), including large scale genetic studies, Tau studies and synapse density in CBD that indicates CBD patients may need different treatments. Congratulations to Dr Negin Holland and Dr Ivan Martinez-Valbuena, who were awarded joint 'best poster' by the judges!

EXCELLENT CLINICAL CARE

Neurologists Dr Boyd Ghosh and Professor Larry Golbe talked about care for people with PSP & CBD in the UK and the US.

UK-based Dr Ghosh described how care for people with PSP & CBD matters. Patients and their carers have a poor quality of life, and carer quality of life deteriorates as patients with PSP & CBD decline. The economic cost of PSP is higher than many other conditions – the total cost to the UK (NHS) annually for PSP patients was £195 million in 2011, £78 million of those being inpatient costs. These huge costs correlate with other countries and cost increases as patients progress.

There are no NICE guidelines that tell doctors how to care for people with PSP & CBD. This means nothing is statutory, just guidance - and without evidence for what works for PSP & CBD it's very hard to convince NHS managers to provide new initiatives. He proposed a care model that spans earlier diagnosis, early management, complex management and palliative care.

INTERNATIONAL INSIGHTS

Friday afternoon brought talks from Barcelona, India and Malaysia. Dr Yaroslau Compta is investigating proteins present in cerebrospinal fluid from the Barcelona PSP registry. Dr Prashanth Lingappa Kukkle described the Parkinson's Research Alliance of India, while Dr Shen-Yang Lim described PSP research in Malaysia and ethnic differences, as well as differing cultural attitudes to research. Malaysia doesn't have a brain bank for cultural and religious reasons.

EARLY DIAGNOSIS

Professor Irene Litvan from the University of California highlighted how we need to speed up biomarker research and drive forward new treatments for PSP & CBD. By the time people see specialists they can be advanced and have missed the 'window' to take part in clinical trials. Professor Jonathan Rohrer from UCL Queen Square Institute of Neurology in London is using computer modelling to model disease progression - he showed some amazing images of how PSP & CBD spreads across the brain, and how it correlates with the PSP Rating scale doctors use. He believes modelling could accurately stage and subtype people, screen people for eligibility for clinical trials and track disease progression.

WRAPPING UP A FANTASTIC CONFERENCE

Dr Kristophe Diaz closed the conference by showing an extremely moving video featuring people with PSP and their carers, calling on the research community to find treatments. And a plea for researchers to join CurePSP and the Rossy PSP Centre for a PSP & CBD conference in Toronto, 24 to 25 October 2024.

"THERE IS NOTHING MORE IMPORTANT FOR OUR PATIENTS THAN CLINICAL TRIALS. FOR SCIENTISTS, CLINICAL TRIALS MEAN WE CAN TEST IF OUR HYPOTHESES WILL MAKE A DIFFERENCE FOR PATIENTS."

CLINICAL TRIALS FOR PSP & CBD – HOPE FOR THE FUTURE

Clinical trials are a crucial step to bring new treatments to people living with PSP & CBD. They tell us if new treatments work and provide evidence needed for regulators to approve treatment for use. At Neuro 2023, leading researchers summarised the latest on clinical trials for PSP & CBD.

Professor Adam Boxer from the University of California set the scene for the session. "There is nothing more important for our patients than clinical trials," he explained. "For scientists, clinical trials mean we can test if our hypotheses will make a difference for patients."

Professor Gunter Hoglinger from Ludwig-Maximilians University Hospital in Munich described how he was encouraged to see upcoming trials in PSP: "It wasn't the case a while ago - we now need to work together as a community," he said.

In recent years Alzheimer's disease research has shifted towards treatments and it's a similar story for Motor Neurone disease, or Amyotrophic Laterol Sclerosis (ALS) as it's known in the US. Some new treatments have recently been approved for both conditions.

For PSP & CBD, we don't yet have a new treatment, but there has been a dramatic change, with several opportunities in the pipeline. Researchers around the world are working together more closely to find new treatments.

APPROACHES TO DEVELOPING NEW DRUGS

When developing new prevention or treatment strategies, you can hone your approach using a 'molecular clue' involved in disease, such as a gene or protein change. You can also take the 'high throughput' approach - to test lots of compounds and hope one works. Researchers recently discovered the drug Relyvrio using the latter, and this is now approved to treat MND in the US. US MND researchers have also developed the Healey platform, a 'platform trial' which tests multiple drugs at the same time to find new treatments faster.

To run effective trials, we also need 'biomarkers' for PSP & CBD treatments to be developed, such as a protein you can measure in blood or urine that 'flags' disease, helping with diagnosis, predicting a patient's prognosis, and monitoring disease progression. To develop biomarkers, we must understand disease processes. The goal is to find biomarkers that monitor if drugs are working or diagnose disease earlier, when it could be easier to treat.

The biomarker-based approach has been crucial for Alzheimer's disease and MND, but it has taken a long time. In Alzheimer's disease, it took 20 years of trials for scientists to realise drugs were hitting the biomarker required.

Developing drugs for PSP & CBD is challenging. We don't currently have a validated clinical biomarker, and the regulators who approve the drugs have concerns about the PSP Rating Scale. An accelerated drug development strategy – a process to approve drugs faster, with fewer stages to go through – is an option, but it means drug companies have significant hoops to jump through after the drug has been approved instead, making it risky.

HUNTING FOR NEW BIOMARKERS

Although lots of work is happening to discover PSP & CBD biomarkers, we don't have one yet.

One potential biomarker Professor Boxer described is the lysosome – a component of cells which acts like 'rubbish lorries' within cells to clear them of proteins they no longer need. When lysosomes don't work, unwanted molecules build up – and scientists think this process is important in neurodegenerative diseases where unwanted proteins build up in the brain.

Measuring B-type Natriuretic Peptide or BNPs (proteins which tell us how well lysosomes work) in cerebrospinal fluid taken from patients with Tauopathies has discovered lysosomes are dysfunctional. It is possible lysosomes could change early on and spotting this would mean scientists have a target to intervene earlier.

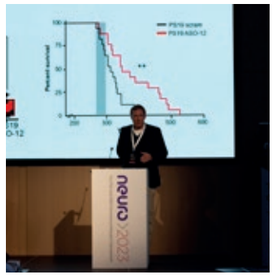
BETTER PSP & CBD UNDERSTANDING IS REVEALING CLUES

Having a better understanding of PSP & CBD means we have a few options to intervene. Many target the protein Tau, which builds up in several diseases including Alzheimer's disease, PSP & CBD and are therefore called 'Tauopathies.'

Potential ways to target Tau include:

1. Silencing the Tau protein: an 'antisense oligonucleotide' against Tau is being tested in a phase 1 trial.
2. Drugs to stop Tau transmission and spread between cells: French company Alzprotect's experimental drug AZP2006 reduced Tau expression and slowed disease progression. The phase 2 trial has been extended.
3. Blocking Tau using antibodies: in the phase 2 PASSPORT PSP trial, gosuranemab profoundly reduced Tau expression but didn't improve survival. Meanwhile drug company UCB is testing bepranemab in a phase 1b trial for PSP (results due in 2024).
4. Stopping Tau being chemically modified – such as phosphorylation that makes Tau more likely to clump. A drug called FNP-233 to block phosphorylation will be tested during a phase 1 PSP clinical trial which is coming soon.

Professor Adam Boxer



Professor Gunter Hoglinger

Dr Colin Ewen

Professor Nigel Leigh

There are also some other potential targets for drugs:

1. Targeting mitochondria, the 'energy stores' in cells which are dysfunctional in PSP. Early studies show this approach is promising in Alzheimer's disease, and we hope a PSP trial will follow.
2. Protein degradation – a drug targeting this and other processes has been approved for MND in the US, and the 'ORION' phase 3 trial will be recruiting PSP patients shortly.

NEW TRIAL ENDPOINTS AND BETTER TRIAL DESIGNS

Researchers are innovative and are coming up with new ways to develop trials to measure the difference drugs could make, but ensuring regulators are still comfortable to approve based on the evidence. This involves exploring new trial designs and new ways to measure drug effects.

Professor Boxer and his research team have been involved in three large multicentre trials for PSP. He also described a new PSP phase 2 trial platform for people with mild to moderate PSP. They are securing funding for where they'll test at least three potential therapies, including targeting the lysosome. The key is a 'clinically meaningful' effect – essentially something that matters to patients.

They want to develop the PSP rating scale, incorporating targets to tell if a drug works, and new ways to monitor progression. They want to explore master protocols inspired by the Healey ALS Platform, and equivalents for Alzheimer's disease too.

Dr Colin Ewen from UCB talked about his company's work involved in optimising clinical trial design in PSP. He described a new phase 3 clinical trial where they have learnt from MND trials and will use a different endpoint (or trial target) that will better reflect whether a drug is successful. They extended the study to 24 months and switched their endpoint to a combined assessment of function and survival. Together, they believe this approach will show whether the drug really worked and can make a difference to the patients.

Professor Boxer and Dr Ewen described how they are developing new ways to measure if patients are responding to treatment, for example by examining gait (walking), finger tapping, eye saccades, and cognition. They use body movement sensors to spot changes in disease progression. These might provide early evidence of success compared to clinical rating scales. The challenge is to convince the regulators to accept them.

HOPE FOR THE FUTURE

It was encouraging to hear so many avenues to explore that could reveal new ways to treat PSP & CBD. Researchers are very optimistic about the future. Based on our improved knowledge, and recent successes with Alzheimer's disease and MND, we could be on the cusp of finding something important for patients with PSP & CBD.

BASED ON OUR IMPROVED KNOWLEDGE, AND RECENT SUCCESSES WITH ALZHEIMER'S DISEASE AND MND, WE COULD BE ON THE CUSP OF FINDING SOMETHING IMPORTANT FOR PATIENTS WITH PSP & CBD.

IMPRESSIVE EFFORTS HAVE BEEN MADE IN THE US TO RECORD THE LIVED EXPERIENCES OF 50 FAMILIES AND WHAT CHANGES THEY'VE MADE TO HELP MANAGE THEIR RELATIVES' CONDITION.

SHAPING RESEARCH WITH PATIENT INVOLVEMENT

Clinical research into specific diseases, conditions, and treatments is conducted every day, and the results help save lives and improve the quality of care for thousands of people each year. But how can people get involved and help shape the research agenda?

The Neuro 2023 symposium session titled ''Lived Experience and Care'' gave the opportunity to share information collected directly from people living with PSP & CBD, carers and families to help shape future research.

The PSP Journey: Insights from Conversations with Patients and Care Partners

Dr Stephanie Oscarson, SJO Research & Consulting LLC, Pennsylvania, USA

Impressive efforts have been made in the US by Dr Oscarson and her team to record the lived experiences of 50 families and what changes they've made to help manage their relatives' condition. 20 different states were represented in this study to provide a glimpse into various ethnic and socio-economic groups. Researchers talked with people about challenges with diagnosis, and then living with PSP & CBD on a day-to-day basis and how that evolves over the course of the condition.

This talk also discussed how we can foster engagement in clinical trials. Interviewees who have been involved in clinical trials shared what could be improved, not just in terms of if the treatment worked or not. They also shared practical issues such as transport, whether the results were shared, and whether there was good support throughout the process.

To draw the talk to a close, Dr Oscarson showed an emotional video summary of the findings to demonstrate patients were extremely eager to share their stories and have a voice.

''WHEN SOMEONE BECOMES SILENCED BY THIS (CONDITION), IT MAKES US ALL (FAMILY) MORE SILENT, MORE SILENT THAN WE SHOULD BE.''

Beyond clinical research, user perspectives

Paul Inness, PSPA Trustee, Milton Keynes, UK

Paul is an ex-carer, having looked after his mum who lived with PSP. He presented a public perspective how research can help improve the wellbeing of people affected and carers.

He untangled what wellbeing can mean, for example ''the best life, based on what we make of it, with help, when we need it''. In the context of PSP or CBD, this could refer to:

- movement
- the enjoyment of music or audiobooks
- the socialisation around food and experience around feeding options
- the importance of rest, especially for carers
- meaningful social interactions; and adequate resources available.

Then Paul presented data derived from PSPA's survey of people living with PSP & CBD which showed how research is one of the charity priorities and 65% of respondents would like to or have signed up to participate in research studies. In summary, Paul's talk made attendees think about how "little things could make a really big difference'' and invited researchers to find solutions to patients' daily challenges with that in mind.

Engaging Patients in Research into PSP & CBD

Riona Fumi, Queen Square Institute of Neurology, University College London, UK

Riona is well known to PSPA, being the Research Coordinator of PROSPECT-M-UK, a nation-wide observational study of people living with atypical Parkinsonism conditions including PSP & CBD. As well as sharing key stats, such as evidence that there is a delay of approximately 2.5 years between the first motor symptoms of PSP and its diagnosis, Riona talked about key learning of working with people living with the condition. This includes ensuring any participants are fully aware that there is no guarantee they will have any individual benefit from taking part in the study, before they sign up to take part. Feedback suggests people feel a huge sense of fulfilment anyway, knowing they're taking part in important research supporting future discoveries, and helping future generations, who will have better quality of life and will be able to better manage their symptoms. Brain donations were also discussed tactfully, considering factors like religion and spirituality, and the views of family and friends.

Learnings About the Clinical and Emotional Journey in PSP

Dr Gesine Respondek, Hoffmann La-Roche, Basel, Switzerland

Dr Respondek, Medical Director at Roche in Basel, recently led a study to map the clinical and emotional journey of people affected by PSP. This study involved PSP experts, key opinion leaders, patients, caregivers, patients' organisations, neurologists and nurses in the UK, France, Italy, Germany, Spain, the USA and Japan. The aim was a better understanding of key challenges and unmet needs. The team identified important breakpoints to tackle in the clinical journey: current support to patients and caregivers is not reaching its potential; diagnostic divergence exists because there is an overlap in symptoms which means there is a low index of suspicion by professionals; consistent management of the conditions and extended dialogue with caregivers following the initial diagnosis could be reached if access to appropriate professionals is granted. In addition, caregivers emerged as invisible and unmentioned heroes. Studies like this one are important to identify targets for potential interventions and to lobby governments to provide better care.

People's lived experiences should be a key driver for health and social care practice and research. These talks demonstrate the importance of projects exploring these experiences in order to prioritise research funding for people's benefit.

PROGRESS TOWARDS DIAGNOSIS OF PSP & CBD

The second day of Neuro 2023 was designed by PSPA and CurePSP to continue to reinvigorate a critical conversation about the challenges of diagnosis PSP & CBD.

Getting a diagnosis is a process to determine the nature of a disease and distinguish it from other possible conditions. It has been defined as a process of information gathering, information integration and interpretation, to determine a working diagnosis. Completing a clinical history and interview, conducting a physical exam, performing diagnostic testing is what general practitioners and neurologists do when they need to provide care for people with Atypical parkinsonism symptoms.

Dr Maura Malpetti - Neuroinflammation in PSP and Related Conditions: Evidence From PET, Blood and Post-mortem

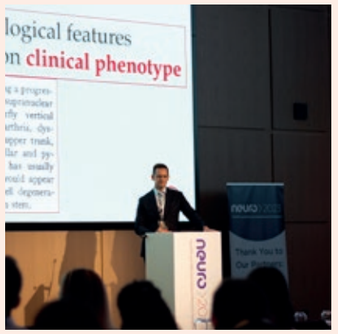
One of the other potential culprits of PSP & CBD symptoms is inflammation and was mentioned all through the symposium, in particular by Dr Maura Malpetti, a post-doctoral research fellow at the Cambridge Centre for FND and Related Disorders. She discussed neuroinflammation in PSP and related conditions: Evidence from PET, Blood and Post-mortem. Brain inflammation can be detected in multiple ways, and she showed how specific areas of inflammation of the brain, as shown in PET scans, could aid the diagnosis and follows the progression of disease. This means that markers of inflammation, also available in blood tests, could in the future help to diagnose PSP & CBD and research is ongoing to understand which specific markers can be used.

Overall, these talks provided hope that the diagnostic challenges professionals face will be overcome in the near future by a combination of clinical signs and assessment, more precise fluid biomarkers, and more insightful imaging techniques.

Professor Irene Litvan - Update on CBD Clinical Criteria

Irene Litvan, Professor of Neurology at the University of California, provided an update on CBD clinical criteria. One of the main points of her presentation was that in the diagnosis of CBD exclusion criteria are as important as inclusion ones. This means that when a professional assesses a patient, they need to ask about their symptoms and makes some performance tests to see signs of the conditions, the clinician also needs to exclude other causes of said symptoms and signs. The list of excluded causes includes Lewy Body Disease, MSA, MND, Alzheimer's Disease or lesions like focal tumours. To exclude those conditions, the routine assessments should be enough: blood and spinal fluid tests, and imaging. Professor Litvan showed results of studies where different ligands (substances that can be injected in the blood to make cells more visible in MRIs or PET scans) were tested to prove which one is more reliable. As she pointed out ''improving the diagnostic criteria for CBD is crucial for accurately diagnosing and differentiate it from other conditions. It requires a multidisciplinary/multimodal approach and ongoing research efforts''.

Professor Gabor G. Kovacs - Novel Approaches to tackle PSP



Gabor G. Kovacs, Professor at the Department of Medicine/Neurology at the University of Toronto, presented a summary of novel approaches to tackle PSP. He pointed at the neuro pathological features of PSP (what is not working properly in the brain cells) mentioning alterations are similar in patients with PSP, but the expression of those changes on body activities can be very different. This makes diagnosis even more complex. The several forms of PSP have been classified in eight distinctive clinical subtypes and some people don't even have symptoms, but the pathological cells are found in their brain after passing away. Some of the potential ways to diagnose these different forms were mentioned, complementary to the ones already in use, but novel approaches are still at lab level and more research is needed to make those available at clinics.

Dr Diane Swallow - Diagnostic Journey in PSP & CBD

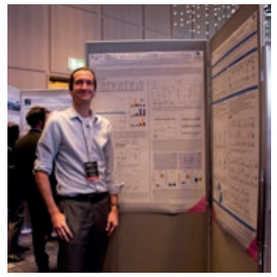
Dr Diane Swallow, Neurologist based at the University of Aberdeen, Scotland, showed results of her PSPA co-funded study on the Diagnostic Journey in PSP & CBD. She looked at a group of people living with PSP & CBD compared to people with Parkinson's disease. She found that there is a delay in diagnosis due to patients' related concerns (the time of recognising the problem and deciding to seek healthcare input) and healthcare system-dependent delays (the process named above that is responsible of most of the latency). The delay is of 3.3 years for PSP and 2.6 years for CBD. Waiting times for a specialist movement disorder review is longer for people living with PSP & CBD compared to people affected by Parkinson's, potentially for mis-attributing symptoms to other causes.

Dr Edwin Jabbari - Novel Fluid Biomarker Approaches to Enhance Diagnosis and Probe Treatment Targets

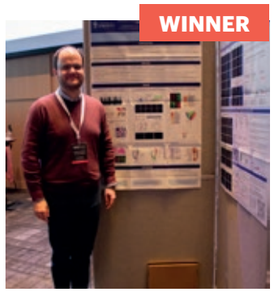
Dr Edwin Jabbari, from the University College London Queen Square Institute of Neurology, London, who was a PSPA funded Research Fellow 2016 to 2018, talked about the work towards Novel Fluid Biomarker Approaches to Enhance Diagnosis and Probe Treatment Targets. There is a need for early and accurate diagnosis via indicators found in blood, spinal fluid or saliva, called biomarkers, that can also act as targets for developing treatment. Even though Alzheimer's disease may share some of the causes of disease with PSP & CBD, markers that work for Alzhiemer's disease didn't show any benefit for PSP & CBD. Dr Jabbari has been using genetics to discover treatment targets, especially non-Tau ones. The UCL team and collaborators looked into the genome of patients and found a specific area called LRRK2 that changes in PSP and could be a potential marker of disease. More work needs to be done to create a test to easily measure the LRRK2 changes in body fluids.

neuro 2023 POSTER PRESENTERS

We were incredibly lucky to hear from four brilliant speakers at the symposium who were presenting their posters. All four covered a wide variety of research questions.

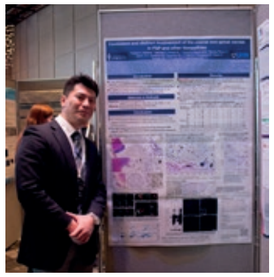


Dr Kurt Farrell



WINNER

Dr Ivan Martinez-Valbuena



Dr Hidetomo Tanaka

WINNER

Dr Negin Holland

'Integrative genetic, transcriptomic, histological, and biochemical analysis of PSP implicates glial activation and new risk genes'
Dr Kurt Farrell, Icahn School of Medicine at Mount Sinai, New York.

They conducted the largest Genome Wide Association Study (GWAS) of PSP to date and found six independent PSP risk loci which correlated to five known genes and one novel gene. After fine-mapping of the significant loci the genes MOBP, STX6, RUNX2, SLCO1A2, and C4A were prioritized as potentially causal. The study also showed a distinctive oligodendrocytic signature that distinguishes PSP from other neurodegenerative diseases.

'Molecular subtyping of PSP: a proof of concept'
Dr Ivan Martinez-Valbuena, Rossy Institute, University of Toronto, Canada. **WINNER**

The study used 4R Tau seeding amplification assays to examine 4R-Tau's ability to spread through the brain, examining 20 brain regions of 25 different PSP patients. They showed that high-molecular weight Tau has a greater seeding capacity and that its prevalence in various regions correlates with the susceptibility of those regions to PSP. Therefore, PSP has multiple molecular drivers and shows we need better molecular classification of PSP which would hopefully enable more personalised therapies.

'Consistent and distinct involvement of the cranial and spinal nerves in PSP and other Tauopathies'
Dr Hidetomo Tanaka, University of Toronto.

This study was looking to clarify the involvement of Tau pathology in the peripheral nervous system (PNS). The study showed for the first time the seeding capacity of Tau to the PNS where extensive Tau deposits were present for the majority of PSP cases, whereas Tau pathology was not evident in the PNS of Alzheimer's Disease cases.

'Differential patterns of in vivo synaptic loss, in relation to Tau accumulation and grey matter atrophy, in amyloid negative vs. positive CBD'
Dr Negin Holland, University of Cambridge - **WINNER**

Dr Holland tested whether amyloid which is seen in Alzheimer's disease and 1/3 of CBD cases affected synaptic loss which often correlates to cognitive function. It was explained that using MRI and PET imaging they showed that amyloid negative cases showed higher synaptic loss severely affecting the anterior and subcortical regions of the brain.

Distinct patterns of synaptic loss, and atrophy show differences in the pathogenic processes according to whether CBD is likely to be caused by Alzheimer's disease or CBD.

WANT TO TAKE PART IN RESEARCH?

PSPA
CREATING A BETTER FUTURE FOR PEOPLE LIVING WITH PSP & CBD

EXPRESS YOUR INTEREST IN RESEARCH WITH PSPA!

PSPA works closely with researchers across the UK who undertake studies into PSP & CBD.

We can help link you to study coordinators who can provide information and support to help you make the decision about whether you want to take part in research. This research could include:

- **Taking part in clinical trials, when a new drug is tested or repurposed**
- **Feeding back via patient and carers questionnaires**
- **Blood and tissue banking collection and banking for future research**
- **Brain scans**
- **Testing new technologies**

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