

Research Strategy



Would you like to contribute to the research agenda?

The PSP Association's Research Strategy has been developed in consultation with people with PSP and CBD, their carers, healthcare professionals, researchers and other interested parties. It sets out the broad focus for our research for the five-year period from January 2011 to December 2015.

However, the world of science and healthcare is continually evolving and we must remain flexible and in a position to anticipate, identify and respond to the needs of people with PSP and CBD with a view to commissioning research that has potential to make a real difference to people's lives. To do this effectively, it is essential that we remain engaged with all our stakeholders over the research agenda.

The PSP Association therefore actively encourages and welcomes your comments and suggestions for future research topics ***at any time***.

Please send your comments, views and ideas for research that you believe could make a difference to the lives of people with PSP and CBD (marked 'Research Topics') to:

The Research Department,
The PSP Association, PSP House,
167 Watling Street West, Towcester,
Northamptonshire NN12 6BX

Or email to: psp@pspeur.org

Research Strategy



CONTENTS

	Page
Executive summary	3
PSP – The challenge we face	5
Context – PSP research	6
The PSP Association’s Research Strategy	11
Care and treatment	13
Cause and prevention	15
Cure	17
Delivering The PSP Association’s Research Strategy	18

Since 2005 The PSP Association has provided support for people with corticobasal degeneration (CBD) a closely related disease. Reference to PSP in this document should be read where appropriate as PSP and CBD.

Research Strategy



EXECUTIVE SUMMARY

1. The PSP Association is the only UK charity dedicated to helping all those affected by PSP (Progressive Supranuclear Palsy). Its mission is: 'The conquest of PSP'. A key objective of The PSP Association is to promote and sponsor research.
2. Research into PSP has a relatively short but distinguished history in the UK. The PSP Association has played a key role in championing PSP research worldwide since its formation in 1994.
3. The PSP Association is the single major UK provider of funds for PSP research and has invested more than £2.5 million into research aimed at improving our knowledge about PSP, its prevalence, cause(s), potential treatment and cure. Research funded by The PSP Association has been of the highest scientific quality and the findings have been acknowledged as of great importance by the international research community.
4. In 2002 The PSP Association established the Sara Koe PSP Research Centre (SKRC) at the Institute of Neurology, 1 Wakefield Street, London. This is the only research centre in the world dedicated to PSP research. The Centre is co-located with the Rita Lila Weston Research Institute at the Institute of Neurology, University College London creating a nucleus of world renowned clinical expertise and research excellence. The SKRC also houses The PSP Association's Brain Bank, a vital resource for research into PSP.
5. In 2010 The PSP Association conducted a public consultation exercise to seek the views of people with PSP, their carers, health and social care professionals, researchers and other interested parties on its Draft Research Strategy for the five year period from January 2011 to December 2015. All feedback was considered in detail and where appropriate the Draft Research Strategy amended accordingly. The Research Strategy was approved by the PSP Association's Board of Trustees in November 2010.
6. The aim of the Research Strategy is to contribute to delivery of The PSP Association's mission through an effective programme of research focusing on three key areas, closely coordinating with other international research into the disease.
These are:
 - Care and treatment
 - Cause and prevention
 - Cure
7. Investment in research in these three key areas has the potential to yield significant improvements for people with PSP.

8. Not enough is known yet about PSP to restrict our future research endeavour to finely tuned specific research priorities. However, four broad priority areas have been identified where the outcome of research is felt most likely to have the greatest potential to improve the lives of people with PSP.

These priority areas are where research aims to:

- Achieve earlier and better diagnosis of PSP
- Develop an effective treatment for PSP
- Improve the day to day management of the symptoms of PSP thereby improving the quality of life of those living with PSP
- Determine the cause(s) of PSP

9. The PSP Association's future focus will be on research where the outcome has potential to make a difference to people's lives to be derived within the short term (3 - 5 years), medium term (5 - 7 years) or longer term (10 years and beyond). The PSP Association takes the view that basic scientific research into neurodegenerative disease is more appropriately funded by other organisations. Accordingly, research applications to The PSP Association will be considered for funding on the basis of their scientific merit and on the potential difference the outcome of that research could make to the lives of people with PSP.

10. Investing in research projects to explore new areas, and in people, to develop the best PSP researchers for the future, has been central to The PSP Association's work in the past and will continue to be the case.

11. Crucial to the success of the new Research Strategy is that we communicate effectively about PSP research – especially that funded by The PSP Association and in the context of PSP research worldwide. As a charity The PSP Association is reliant on donations. Research is the one area to which many people want to give money but they also want to know that their money is being well spent and used to make a difference to the lives of people with PSP. It is therefore imperative that we communicate information about new research projects, about emerging findings from ongoing research, and the outcome of completed research in a timely and appropriate manner.

12. The PSP Association will work collaboratively and will co-fund, co-ordinate and promote research with a view to maximising the difference research can make to the lives of people with PSP. Research undertaken will be closely coordinated with other research worldwide.

13. The PSP Association will actively seek out, initiate and promote new and exciting partnerships with other charities, government bodies, the NHS, industry and others both nationally and internationally, with a view to maximising the impact of research on PSP.

13. The PSP Association will campaign to influence government policy to increase the amount of money allocated to PSP research.

14. The PSP Association is committed to putting research into practice for the benefit of people with PSP. Accordingly, The PSP Association will identify and work with relevant partners to ensure research outcomes are taken into consideration in future changes to clinical practice, healthcare and government policy.

PSP – the challenge we face

- PSP is a progressive degenerative brain disease.
- The areas of the brain most affected by PSP are the upper part of the brain stem and its connections with the frontal lobe where cell death results in the development of the predominant symptoms - problems with balance and movement, vision and speech.
- People with PSP gradually lose their ability to walk, talk, see and swallow. In the late stages of the disease, people are unable to move or communicate and are confined to a wheelchair or are bed-bound. For the most part, people remain mentally alert although difficulties with some aspects of thinking and decision making can occur. Changes in behaviour with mood swings and depression are common.
- PSP is believed to be slightly commoner in men and to affect all races.
- There is no effective treatment to slow or halt the progression of PSP and no known cure.
- PSP causes significant morbidity and reduces both quality and length of life.
- Life expectancy is some 7 to 9 years from the onset of the disease and between 2 and 6 years from diagnosis.
- The only known risk factor for PSP is age; most cases occur over the age of 60.
- PSP is frequently misdiagnosed as Parkinson's disease, a stroke or a brain tumour because of the slowness of movement and balance problems, and as Alzheimer's disease because of changes in mood, intellect and personality. PSP is often undiagnosed in the elderly, especially those living in residential care homes.
- Data held by The PSP Association indicates that 3 out of every 4 people with PSP are initially misdiagnosed and often repeatedly misdiagnosed with another medical condition.
- Public awareness of PSP is low and awareness about the disease and the needs of patients amongst health and social care professionals is often limited.
- The cause of PSP remains unknown but it is thought to result from a combination of genetic and environmental factors.
- Leading neurologists believe there are at least 4000 people in the UK with PSP and possibly more than 10,000. The number of people with CBD is uncertain but it is less frequent than PSP. A proportionally similar number of cases of PSP are reported for France, Italy and the United States.
- The number of people in the UK with PSP is set to rise with the changing demographics and our aging population. PSP will also increase in developing countries as life expectancy increases.
- The cost to the NHS for the care of people with PSP has not yet been quantified. In considering the cost of care it should be remembered that a significant proportion of the cost is borne not by the state but by the patient's family in that family members function as unpaid carers or secure private nursing care.

Context - PSP research

The human and health burden of PSP is immense and the economic cost considerable. Research is essential if the burden to families and society is to be lessened.

Research into PSP has a relatively short but distinguished history in the UK and The PSP Association has played a key role in championing PSP research since its formation in 1994. The PSP Association is the single major UK provider of funds for PSP research and has invested more than £2.5 million into research aimed at improving our knowledge about PSP, its prevalence, cause(s), potential treatment and cure. Research funded by The PSP Association has been of the highest scientific quality and the findings have been acknowledged as of great importance by the international research community.

In 2002 The PSP Association established the Sara Koe PSP Research Centre (SKRC) at the Institute of Neurology, 1 Wakefield Street, London. This is the only research centre in the world dedicated to PSP research. The Centre is co-located with the Rita Lila Weston Research Institute at the Institute of Neurology, University College London creating a nucleus of world renowned clinical expertise and research excellence. The SKRC also houses The PSP Association's Brain Bank, a vital resource for research into PSP.

Since 2005 The PSP Association has provided support for people with corticobasal degeneration (CBD) a closely related disease. Reference to PSP throughout this document should therefore be read where appropriate as PSP and CBD.

There are many examples of groundbreaking research funded by The PSP Association, some of which are outlined in the boxes below. The aim of The PSP Association's research programme is to make a significant difference to the lives of people with PSP. With regard to research outcomes it is important to note that success, in terms of 'the benefit to peoples health', is seldom immediate – it can often take some considerable time for the significance and impact of research findings to be fully realised.

Investing in people, in order to develop the best PSP researchers for the future has always been central to The PSP Association's work. Accordingly, The PSP Association offers research-training opportunities in the form of PhD Studentships and Research Fellowships aimed at young clinicians or scientists at different stages in their careers. These individuals often go on to a lifetime's work committed to research aimed at improving the lives of people with PSP. The PSP Association is committed to investing in young researchers for the future as the only way to beat PSP is through increased research capability and capacity.

Over the past sixteen years most of the research funded by The PSP Association has been oriented at answering fundamental questions about PSP. The newness of the research field dictated a focus on a range of essential 'need to knows'. For example: What causes PSP? What changes take place in the brain in PSP? What role do our genes play in PSP? How many people in the UK have got PSP? Is it possible to develop

a test for PSP so as to get earlier and better diagnosis? Can we develop an effective treatment to slow or halt disease progression? Research has provided significant advances in our knowledge of PSP but all these questions remain relevant today.

The PSP Association receives no money from government and is wholly dependent on the generosity of its benefactors to fund vital research. Its resources are limited and going forward the charity's challenge is to ensure it focuses on those areas of research that have the potential to make the biggest difference to the lives of people with PSP. To help meet this challenge the charity considered it essential that its future research agenda was informed by the views and needs of people with PSP, their carers, health and social care professionals, researchers and other interested parties. Accordingly, in 2010 The PSP Association conducted a public consultation exercise on its Draft Research Strategy for the five year period from January 2011 to December 2015.

The public consultation exercise ran for a period of 20 weeks from Monday 24th May to Friday 8th October 2010. It was widely advertised – on the homepage of The PSP Association's website, in mailings to supporters, health and social care professionals, in relevant publications and at external meetings and events. The Draft Research Strategy was available to download from The PSP Association's website and available as hard copy on request. Submissions to the consultation exercise were accepted electronically and in hard copy.

The consultation exercise giving people the opportunity to input to the future Research Strategy was widely welcomed by all parties. Feedback on the Draft Research Strategy was overwhelmingly constructive. All feedback was considered in detail and where appropriate the Research Strategy was amended accordingly.

The Research Strategy was approved by The PSP Association's Board of Trustees in November 2010.

A Decade of Discovery

Some Examples of Research Funded by The PSP Association

How many people in the UK have PSP?

Supported by a research grant from The PSP Association in 1998, Dr Uma Nath at the University of Newcastle undertook a groundbreaking epidemiological study and provided for the first time ever, a figure for the number of people in the UK who have PSP.

Dr Nath's 'Russian doll' study derived a PSP prevalence of 6.5 cases per 100,000 of the population and demonstrated that PSP prevalence varied depending on the intensity and thoroughness of the data collection. Through her work Dr Nath provided evidence that many cases of PSP are misdiagnosed and that PSP is under-recorded as the cause of death on death certificates making it appear less common than it really is.

Dr Nath's findings are supported by a similar though less comprehensive study carried out in primary health care in the London area by Dr Anette Schrag in 1998. Most authorities now believe that the PSP prevalence figure of 6.5 cases per 100,000 of the population as reported by Dr Nath, is likely to be a very conservative figure and that there might be twice as many patients with PSP in the community i.e., in excess of 10,000 cases .

Knowledge of the number of people with PSP is essential for health and social care planning purposes. If government does not know how many people are living with PSP it cannot effectively plan to ensure there is adequate provision to meet peoples needs.

Developing a diagnostic test for PSP

Many diseases can be diagnosed by testing the blood or urine for the presence of specific substances – called biomarkers. There is no such test for PSP but if a test existed it would eliminate much of the stress and anxiety that accompanies patients frequent and often multiple misdiagnoses. Over the past decade The PSP Association has funded a programme of work by Drs Giovannoni, de Silva and Luk at the Sara Koe PSP Research Centre in London, aimed at finding a biomarker and developing a test for PSP. This research has shown that the defective tau protein, which builds up in the brain and forms the neurofibrillary tangles, leaks into the cerebro-spinal fluid (CSF) and that its presence in the CSF may support a clinical diagnosis of PSP. The healthy brain contains about equal amounts of two forms of tau protein know as 3R-tau and 4R-tau. In PSP there is more 4R-tau and it is this distinguishing feature that the researchers are looking to detect in the CSF. However, the level of tau protein in the CSF is 1000 to 10000 times more dilute than in the brain and it has proved challenging to refine the test to make it sufficiently sensitive to detect the very low levels of tau in the spinal fluid. The researchers are currently working with a commercial company to develop a kit for PSP testing. The availability of such a test would be an enormous step forward in our quest for earlier and better diagnosis of PSP.

Use of high powered MRI scans to detect changes in the brain

The substantia nigra, subthalamic nucleus and the pedunculo pontine nucleus which are discrete regions in the base of the brain, are damaged in PSP. Conventional MRI scans (1.5 Tesla) are unable to pick out these areas in any detail and are therefore of no use to diagnose PSP or to monitor changes in the brain over time.

Over the past decade The PSP Association has funded a programme of research undertaken by Dr Dominic Paviour and Dr Luke Massey under the supervision of Professor Nick Fox, Professor Tarek Yousry and Professor Andrew Lees at the Sara Koe PSP Research Centre aimed at exploiting the use of much higher powered MRI scans (9.4 Tesla) and MR sequences as a means to detect subtle changes within the brain. The hope is that these newer scanning techniques will enable doctors to make earlier diagnoses and be able to distinguish PSP from other brain diseases.

Using the high powered scans the researchers have found detectable differences in the subthalamic nucleus in patients with PSP compared to those with other neurodegenerative diseases such as Parkinson's disease.

In due course, high powered scans may give us a tool with which to monitor disease progression and determine the effectiveness of any new treatments that become available.

In June 2008 Dr Luke Massey won the '*International Movement Disorder Society's 2008 Junior Award for Excellence in Clinical Research*' for his work on high powered MRI scanning. This is the most prestigious award in the world for young clinical researchers in the field of movement disorders and was won by Luke in the face of strong worldwide competition.

What role do our genes play in PSP?

In 1994 when The PSP Association was established, almost nothing was known about the role of genes in PSP. Over the past decade our knowledge in this area has grown significantly through research carried out worldwide, with major contributions from that sponsored by The PSP Association, particularly the work of our former Research Fellows - Dr Huw Morris who worked at the Institute of Neurology, UCL in London and is now based at the University Hospital of Wales, and Dr Rohan de Silva at the Sara Koe PSP Research Centre.

As a result of this work we now know that:

- There is a gene responsible for making tau protein (the MAPT gene)
- One form of the tau gene (called H1) is more common in people with PSP
- Having the H1 form makes you more susceptible to developing PSP than if you have the H2 form
- H1 makes more of the 4R form of tau than H2 (and the tangles in PSP contain more 4R than 3R tau)

In 2009 an international collaborative PSP whole genome project, funded by Cure PSP, found evidence for 2 new 'hot spots' associated with PSP and CBD. PSP brain tissue for this study was provided by The PSP Association's PSP Brain Bank housed at the Sara Koe PSP Research Centre in London.

Developing an effective treatment for PSP

PSP is thought to cause or result from the hyperphosphorylation of tau protein. When hyperphosphorylated, the tau molecules become 'sticky' and clump together forming neurofibrillary tangles in the brain. Several enzymes can phosphorylate tau but the enzyme called glycogen synthase kinase-3 (GSK-3) has been proposed as the main enzyme involved. The development of drugs which inhibit the production and action of GSK-3 is therefore seen as a possible means of treating PSP. The PSP Association has funded research aimed at developing two drugs to treat PSP, both of which target GSK-3.

Lithium safety and tolerability trial (Joint UK (PSPA) &USA (NIH) project)

Lithium has been used since the 1940s to treat manic depression and is known to have a neuro-protective effect. High levels of lithium in the blood can however cause serious side effects. A safety and tolerability trial in which lithium was administered to PSP patients was therefore undertaken in 2009 as the first step in developing lithium as a potential treatment for PSP. Unfortunately, the side effects of lithium at the doses used in the trial were found to be significant and the trial was terminated early.

Sodium valproate safety and tolerability trial

Sodium valproate is a drug used to treat epilepsy and is thought to have neuroprotective effects. A safety and tolerability trial of sodium valproate in people with PSP is currently underway. So far sodium valproate seems to be well tolerated but work is ongoing. The outcome of this trial is not expected until December 2010.

The PSP Association Brain Bank

In 2002 The PSP Association established the Sara Koe PSP Research Centre (SKRC) at the Institute of Neurology in London. This is the world's only research centre dedicated to PSP research. The PSP Association Brain Bank is located at the SKRC. This tissue resource forms part of the Queen Square Brain Bank for neurological disorders and contains more than two hundred brains of PSP patients who have donated their brains for research. It also has a collection of thirty CBD brains available for research scientists to study.

Samples of tissue from the brains of people who have died from PSP and CBD are essential for research aimed at improving our understanding of what happens during the disease process. The PSP Association Brain Bank provides an invaluable resource for researchers across the world.

Tissue from the PSP Brain Bank has contributed to many groundbreaking PSP research studies across the world including the recent (2010) International Collaborative PSP Whole Genome Project.

For more examples of groundbreaking research funded by The PSP Association please go to our website www.pspeur.org

The PSP Association's Research Strategy

For the five year period January 2011 – December 2015

We do not know what causes PSP. The only known risk factor is age as PSP occurs mainly but not exclusively in later life. Our increased longevity and aging population therefore brings with it a challenge – an increase in the number of people with PSP. The only way to tackle this challenge is to improve our knowledge about what causes PSP, to develop an effective treatment that slows or stops its progression, and ultimately, to find a cure. For this, research is essential and at the heart of The PSP Association.

The PSP Association's mission is: 'The conquest of PSP'.

The aim of The PSP Association's Research Strategy is to:

Contribute to delivery of the mission through promotion, sponsorship and oversight of an effective programme of research focusing on three key areas:

Care and Treatment

Cause and Prevention

Cure

The Research Strategy sets out the broad framework for PSP research with a focus on research opportunities within the three key areas. Details of these three key areas and the research opportunities that exist within each are given in the following pages.

Research opportunities represent areas where there are gaps in our current knowledge and which, if advanced by investment in research, have the potential to yield significant improvements for people with PSP and for those who may be at risk of developing PSP. Our knowledge about PSP is poor by comparison with that for many other disease areas e.g., cancer, heart disease, diabetes, and as such, the list of research opportunities is wide-ranging. The PSP Association will consider applications for research funding across all of these areas.

The PSP Association's future focus will be on research where the outcome of that research has potential to make a difference to peoples lives to be derived within the short term (3 - 5 years), medium term (5 -7 years) or longer term (10 years and beyond). The PSP Association takes the view that basic scientific research into neurodegenerative disease is more appropriately funded by other organisations. Accordingly, research applications to The PSP Association will be considered for funding on the basis of their scientific merit and on the potential difference the outcome of that research could make to the lives of people with PSP.

Research Priorities

Not enough is known yet about PSP to restrict our future research endeavour to finely tuned specific research priorities. However, four broad priority areas have been identified where the outcome of research is felt most likely to have the greatest potential to improve the lives of people with PSP.

These priority areas are where research aims to:

- Achieve earlier and better diagnosis of PSP
- Develop an effective treatment for PSP
- Improve the day to day management of the symptoms of PSP thereby improving the quality of live of those living with PSP
- Determine the cause(s) of PSP

It is important to note that The PSP Association will remain sensitive to new ideas and will not rule out applications for novel work outside the scope of the *Research Strategy*. Applications of this kind will need to devote particular attention to showing how a successful project would benefit people with PSP. Applications would be expected to be exceptional. In the first instance researchers should discuss their proposed work with the Director of Research.

Care and treatment

PSP is a very individual disease and no two patients are the same. Different people experience differences in the symptoms they exhibit at different stages of the disease. Some of the symptoms of PSP are common to a number of other conditions including other neurodegenerative diseases. As such, obtaining a correct diagnosis especially during the early stages can be difficult and people with PSP are often misdiagnosed as having atypical Parkinson's syndrome, Alzheimer's, a stroke or depression. The lack of a definitive diagnostic test for PSP (e.g., a blood, urine or cerebrospinal fluid test) presents a major obstacle for patients and the medical profession. At present, absolute confirmation of a diagnosis of PSP can only be achieved by post-mortem examination of brain tissue although the disorder can be strongly suspected on clinical grounds.

Currently, there is no treatment that can slow or halt the progression of PSP. At present there are only two commercially funded PSP clinical research trials underway: the Noscira funded clinical trial of NP-12 (also known as Nypta); and the Allon Therapeutics Ltd funded clinical trial of Davunetide (also known as NAP and AL-108). Both of these clinical trials involve small numbers of patients and aim to determine the tolerability and efficacy of two new drugs as potential treatments for PSP. All other (and very limited) research effort oriented at developing an effective treatment for PSP has focused on the potential of drugs used to treat other conditions as a treatment for PSP (e.g., lithium or valproic acid, which are used to treat depression and bi-polar disorder; and methylene blue, a drug used to treat urinary tract infections). The development of accurate and sensitive ways to monitor the progression of PSP, especially once effective treatments become available, will be of enormous benefit in patient management and in measuring the efficacy of treatments administered at different stages of the disease.

People with PSP and their carers manage the symptoms of PSP on a day to day basis. In the main this involves adopting strategies which enable the person with PSP and/or their carer to deal with the effects that the death of neurons in the brain has on the movement of muscles throughout the body e.g., on muscles in the eyelids causing them to remain open or closed for too long thereby requiring the use of eye drops to relieve dry sore eyes or the use of devices to help hold the eyelids open; and on muscles in the tongue and throat leading to difficulties with speech requiring support from speech and language therapists, and with chewing and swallowing requiring food to be softened and liquids to be thickened to prevent choking. In some instances medication may be used to help relieve symptoms such as neck stiffness or body rigidity.

There is little evidence regarding the benefits or otherwise of physiotherapy and different forms of physical exercise in slowing down the progression of PSP or in helping to manage the symptoms, especially in relation to problems with balance and movement. Until very recently the value of dietary supplements in the treatment of PSP was not universally recognised e.g., Coenzyme Q10.

We know that PSP is a very individual disease yet we have little or no evidence-based information on what works well for some people or less well for others, at what stages and the reasons why. We also lack information on the effects of PSP on different groups in the population e.g., are there differences in those who are relatively younger or older at

disease onset or diagnosis; and does gender, race, or the existence of co-morbid conditions make a difference? In the case of co-morbid conditions (e.g., heart disease, cancer, mental illness, depression) there is no information on how treatment for these diseases may impact on the progression of PSP. Furthermore, the appropriate management of PSP patients as in-patients for surgical or other procedures is a hitherto neglected area for consideration.

How a person with PSP is treated by health and social care professionals in their locality, especially given the low levels of awareness about PSP and the lack of established best practice in the care and treatment of PSP, can have a significant impact on their quality of life. Variability in the availability and quality of services across the UK resulting from the way in which Primary Care Trusts choose to implement national guidelines are further factors affecting quality of life.

PSP is a terminal illness and as such good palliative and end of life care is essential. In recent years there have been significant advances in palliative and end of life care for cancer but evidence based good practice for palliative care in the management of patients with neurological disease is lacking. Only very recently has it been recognised that there is a need to make available hospice beds for patients with neurological disease. However, the needs of patients with neurological disease are very different from those with cancer. There is therefore a need to develop evidence based good practice for palliative and end of life care for people with PSP.

At present much variation and inequality exists across the UK in the care and treatment of people with PSP. More research is needed to develop evidence based good practice to ensure that everyone with PSP has access to the best possible care and treatment at every stage in the disease process.

Research opportunities – for care and treatment

- Development of a diagnostic test for PSP (for earlier and better diagnosis)
- Development of an effective treatment for PSP (i.e., drugs that slow or halt disease progression)
- Improvement in the day to day management and control of symptoms (to include the development of new drugs and establishment of the efficacy of commonly used symptomatic drug treatments (e.g., amantadine and l-dopa) currently used but lacking an evidence base; development of devices and patient-aids and determination of the effectiveness of procedures such as deep brain stimulation in symptom management)
- Development of effective ways to monitor disease progression/regression
- Optimising mental health and well being (e.g., effective treatment and management of depression and behaviour change)
- Development of more effective speech and swallowing treatment strategies

- Role of diet (including nutrition), physical exercise and lifestyle factors in disease progression
- Role of dietary supplements (e.g., glutathione)
- Role of complementary therapies in patient management
- Establishment of good practice for palliative and end of life care
- Establishment of quality of life and well-being measures for people with PSP to gauge the impact of PSP on a regular basis with a view to improving quality of life
- Establishment of evidence based good practice across all aspects of the care and treatment of people with PSP
- Service organisation and delivery (in primary and secondary care settings)

Research Outcome

Establishing evidence-based good practice with improvements in care and treatment will help people with PSP to live longer and with improved quality of life.

Cause and Prevention

We need to understand what causes PSP in order to find effective ways of preventing it from developing in those at risk. Understanding what causes PSP will also help us work towards effective treatments and a cure.

Current thinking is that the development of PSP is linked to the appearance of tau protein deposits (neurofibrillary tangles) in the brain. Tau protein in the neurofibrillary tangles differs from that normally found in brain cells in that it is 'hyperphosphorylated' (i.e., contains more phosphorus). Hyperphosphorylation causes the tau protein to become sticky and to clump together forming the neurofibrillary tangles. As yet, we do not know if it is the neurofibrillary tangles themselves that cause the death of neurons and hence the development of PSP or whether their appearance is merely a marker for some other PSP-causing phenomenon occurring in the brain. At present much research effort is centred around tau production and on the development of drugs which will prevent the harmful clumping of abnormal tau protein in vulnerable nerve cells. This current focus should not preclude the pursuit of other promising lines of enquiry.

Research opportunities

Identification and understanding of the causes of PSP

- Epidemiological studies – to establish the distribution and determinants of PSP within the population
- Understanding how PSP is caused by
 - Environmental factors (e.g., pollutants or neuro-toxins), geographic isolates and clusters
 - Genetic factors
 - Immune system/infection (viral, bacterial, prion)
 - Trauma (blow to head)
 - Physiological factors (inflammation)
 - Other (e.g., drugs used to treat other conditions)

Identification and understanding of molecular and cellular aspects of PSP including:

- Distribution and variation in brain cell degeneration throughout the brain
- Neurone function and physiology
- Neuroglial cell function and physiology (astrocytes, oligodendroglia and microglia)
- Neurotransmitter synthesis and secretion
- Tau biology
- Other

Prevention of PSP

- Development of effective ways to identify people at risk of developing PSP
- Development of effective interventions to prevent those at risk from developing PSP

Research Outcome

The loss of life and reduced quality of life experienced by an increasing number of people who have PSP is unacceptable. Advances in our knowledge of what causes PSP and the development of effective ways to prevent (and treat) it, will have enormous impact on peoples lives as well as reducing the burden on carers and healthcare systems worldwide.

Cure

Currently there is no cure for PSP. It is important to note that a cure for PSP will not necessarily originate from work undertaken in the field of PSP research. Developments and discoveries take place in other areas of science and medicine – it is the import and application of these developments to PSP that may yield dividends. It is also possible that a cure for PSP may originate from work undertaken to better understand and establish the causes of PSP. It is impossible to predict how, when or where a cure may be found.

Research opportunities – for cure

- Pump prime novel areas of work which challenge conventional thinking about PSP and a possible cure
- Development of new and/or experimental therapies which have longer term potential for developing a cure including:
 - stem cell research
 - donor tissue transplantation
 - other (e.g., xenotransplantation)

Research Outcome

A cure would rapidly take us to the desired state - a world without PSP. In the absence of a cure The PSP Association will continue to work towards one.

Delivering the Research Strategy

A number of important principles will underpin delivery of the *Research Strategy*. These are as follows.

Research management processes

The PSP Association will operate best practice in all matters relating to its research management processes. The PSP Association will be open and transparent, fair and objective at all times. Details of all new research grants awarded and of the membership of the Research Advisory Panel (composed of eminent research clinicians and scientists from across the world) which helps The PSP Association make informed decisions about the research it funds, will be published on the website.

Research funding modes

Responsive mode

Responsive mode funding gives The PSP Association the ability to respond rapidly to the best ideas from the research community and to provide the most appropriate support to take the ideas forward. As such, The PSP Association will continue to fund most of its research in responsive mode.

Applicants to the responsive grant scheme will need to familiarise themselves with the *Research Strategy* and be able to demonstrate:

- That their research maps onto one of the areas of research opportunity as outlined in the *Research Strategy*
- The relevance of their work to people with PSP
- The potential difference the outcome of their research could make to the lives of people with PSP and over what timescale, ie in the short term (3-5 years), medium term (5-7 years) or longer term (10 years and beyond) and
- The ways in which the success of their research can be measured

Proactive mode

The PSP Association will look to actively commission research in any area where there is clearly identified need to address a specific topic area.

Research schemes

The PSP Association currently operates a mainly responsive research grant funding scheme. The charity's research budget is set to grow in the near future. At that point we will review the research funding scheme and where appropriate introduce new funding schemes to ensure delivery of the *Research Strategy*.

Investing in people

Investing in people to develop the best PSP researchers for the future is central to The PSP Association's *Research Strategy*. The PSP Association will offer research-training opportunities in the form of PhD Studentships and Research Fellowships aimed at young clinicians or scientists at different stages of their careers. The PSP Association considers this to be of fundamental importance as these individuals often go on to a lifetime's work committed to research in the laboratory and/or the clinic aimed at improving the lives of

people with PSP, developing an effective treatment, preventing PSP from developing in those at risk and to finding a cure.

Communication

As a charity The PSP Association receives no money from government and is reliant on donations. Research is the one area to which many people want to give money but they also want to know that their money is being well spent and used to make a difference to the lives of people with PSP. It is therefore imperative that we communicate information about new research projects, about emerging findings from ongoing research, and about the outcome of completed research to all our supporters in a timely and appropriate manner.

Getting research into practice

The PSP Association is committed to putting research into practice for the benefit of people with PSP. The PSP Association will identify and work with relevant partners to ensure research outcomes are taken into consideration in future changes to clinical practice, healthcare and government policy.

Income generation to fund research

Publicising the success of our research will encourage more people and other organisations to support The PSP Association and help to grow our income - and the greater our income, the more money we will have for research, and more research means the greater the difference we can make to the lives of people with PSP.

In future, a condition of research funding from The PSP Association will be that researchers are required to work with The PSP Association's Director of Research and its press office to promote a flow of newsworthy information ensuring regular media attention on PSP.

Intellectual property rights

The PSP Association seeks to participate in any financial rewards arising from the research it funds. This may involve the shared ownership of any Intellectual Property Rights or a share of future royalties arising. Any such proceeds would be re-invested by The PSP Association in its funding of future research projects.

The PSP Association's research ethos

The PSP Association will work collaboratively and will co-fund, co-ordinate and promote research with a view to maximising the difference research can make to the lives of people with PSP. Research undertaken will be closely coordinated with other research worldwide.

In implementing its *Research Strategy* The PSP Association will actively seek out, initiate and promote new and exciting partnerships with other charities, government bodies, the NHS, industry and others, both nationally and internationally, with a view to maximising the impact of research on PSP.

The PSP Association will campaign to influence government policy to increase the amount of money allocated to PSP research.

Working for a world free of PSP

The PSP Association

Registered charity numbers: England & Wales 1037087 / Scotland SC041199