Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Summary

Our understanding of progressive supranuclear palsy (PSP) disease onset and diagnosis is undergoing significant advancements owing to the coordinated efforts of groups of international neurologists who are experts in their field.

Given that PSP is an irreversible neurodegenerative condition, it is critical to address the health issues of PSP patients as early as possible to delay disease progression and to potentially improve outcomes. Towards this end, physicians and neurologists must be made aware of the latest advances in predictive diagnostic criteria for PSP, disease management, and also to have an understanding of the latest therapeutic strategies under investigation.

We propose to address these physician educational needs via an expert-driven CME-certified curriculum that reviews progressive supranuclear palsy diagnosis, treatment options, and the latest experimental therapeutic investigations.

Educational Objectives and Agenda

Educational Objectives

The educational objectives for the proposed activity are based on the identified gaps and needs, and will allow us to measure improvements in the participants' knowledge and competence.

After participating in the activity, the learners are expected to be better able to:

1. Identify patients with progressive supranuclear palsy (PSP) based on their presentation, symptoms, and laboratory test results.
1. Monitor PSP disease progression and assess the potential therapeutic benefits to risks of symptomatic, supportive, and palliative care approaches for patients with PSP.
2. Recognize the potential impact of emerging tau-targeted therapies under investigation in clinical trials on the future management of PSP.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Agenda

The Live Webcast and onDemand Activity will be held over the course of 1.0 credit hour; this program will feature insight from a leading expert in the management of progressive supranuclear palsy. This activity will be the basis of the material developed for the live, local interventions, updated as appropriate in order to capture new evidence or therapeutic advances.

10 min - Welcome, Introduction, Pre-Polling
After welcoming participants, the faculty expert will briefly review the topics that will be covered during the activity. The audience will also be polled on their knowledge and competence in the diagnosis and management of progressive supranuclear palsy in an era of refinement of clinical predictors of PSP and emerging tau-targeted experimental therapies.
20 min - Recognizing and Diagnosing Progressive Supranuclear Palsy
In the first segment, the faculty expert will begin with a brief overview of the symptomatology, incidence, and prevalence of PSP. The pitfalls associated with current clinical recognition. This will be followed by a review of differential diagnosis of PSP relative to other neurodegenerative diseases along with the latest criteria encompassing the spectrum of PSP clinical phenotypes.
20 min - Management and the Potential Treatment of Investigational Approaches for Progressive Supranuclear Palsy
This segment will start with a review of the benefits, risks, and limitations of current treatment options for the management of PSP. Next, focus will be shifted review the role of the tau protein in the neuropathogenesis of PSP. This will include a review of the current data related to emerging tau-targeted therapies for the treatment of PSP. This section will conclude with a discussion of the potential implications for these emerging therapies on the future management of PSP.
10 min - Take-Home Strategies, Ask an Expert Q&A, Conclusions
In the final segment, the faculty expert will summarize the key objectives and take-home points discussed during the activity. Before closing the event, the presenter will address questions submitted from the online audience (live webcast). The audience will also be polled on changes in knowledge and competence.

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Practice Aids Examples of Practice Aid downloadable point-of-care tools for this proposed activity may include the following:

- Infographic-like charts summarizing key information on clinical presentation, diagnostic criteria, monitoring of disease progression, and management of symptoms for progressive supranuclear palsy.
- Diagrams illustrating the process of disease monitoring with management of symptoms and consideration of experimental tau-targeted therapies for patients with progressive supranuclear palsy.

Faculty Considerations

The faculty will be selected based on expertise, research, and published data. Faculty selection will also take into account the ability of particular experts to stimulate interactivity in the learning experience through their presentation style. All final decisions regarding activity faculty will be made by Medical Learning Institute.

Potential Chair and Faculty Members include, but are not limited to:

Mellissa J Armstrong, MD
Director, Mangurian Clinical-Research Center for Lewy Body and Parkinson's Disease Dementia
Department of Neurology
University of Florida College of Medicine
Gainesville, Fl

Irene Litvan, MD
Director, Movement Disorders Center
Department of Neurology
University of California
San Diego, Ca

Lawrence I. Golbe, MD
Department of Neurology
Robert Wood Johnson University Hospital
New Brunswick, NJ

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Adam Boxer, MD, PhD
Professor of Neurology
Department of Neurology
University of California
San Diego, Ca

Keith A. Josephs, MD
Professor of Neurology
Department of Neurology
Mayo Clinic
Rochester, Mn

David J. Irwin, MD
Assistant Professor of Medicine
Department of Neurology
University of Pennsylvania Perelman School of Medicine
Philadelphia, Pa

Gil Rabinovici, MD
Professor of Neurology
Department of Neurology
University of California
San Francisco, Ca

Shashank Agarwal, MD
Assistant Professor of Neurology
Department of Neurology
New York Medical Center
New York, NY

Onur Melen, MD
Assistant Professor or Neurology
Department of Neurology
Northwestern Feinberg School of Medicine
Chicago, Il

Eric Eggenberger, DO
Department of Neurology
Mayo Clinic
Jacksonville, Fl

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

APPENDIX

Summary of Gaps and Needs with Related Educational Objectives for the Proposed Intervention

The different elements of this needs assessment demonstrate that significant gaps and unmet needs exist and further education is needed for optimal early recognition and management of patients with progressive supranuclear palsy, which are summarized in the following sections.

A. Summary of Progressive Supranuclear Palsy Disease Landscape

Progressive supranuclear palsy is a rare neurodegenerative disorder characterized by excessive accumulation of tau protein leading to development of neurofibrillary tangles with neurodegeneration that presents most commonly with vertical supranuclear gaze palsy, postural instability, Parkinsonism, and a range of other symptoms involving neurological dysfunction. The cause of PSP is unknown and the only established risk factor is advanced age. No reports of diagnosed PSP has been observed for greater than 40 years of age. However, ongoing research supports that environmental exposure to heavy metals and drinking well water may increase the risk for developing PSP. [1,2] The average age at symptom onset is 65 years and disease duration to death averages 6 years, with a range of 2 to 17 years.[3] Death is usually caused by an inability to move involving dysphagia and frequent infections. Disease prevalence for PSP is approximately 5-7 in 100,000 or about 4-6% of patients with Parkinsonism diagnosis.[4]

The most frequently reported symptoms at onset of PSP are postural instability with falls, unsteady gait, bradykinesia, a wide range of ocular motor defects, subtle personality changes (apathy, disinhibition), cognitive slowing, executive dysfunction (difficulty planning, multitasking), slow, ataxic, spastic and hypophonic speech, dysphagia and impaired ocular movement [5] PSP is typically initially subdivided into the classic more common Richardson Syndrome type (PSP-RS) or Parkinsonism type (PSP-P). Patients with the classic PSP-Richardson syndrome usually develop their first symptoms in their mid-60s and the condition gradually progresses to death over an average of 7 years.[6] Clinical subtypes of PSP-P and PSP-pure akinesia with gait freezing have a more benign course with a survival period of a decade or more.

PSP was first recognized in 1963 and support groups have been focused on assisting individuals with professionally guided healthcare for over 25 years, but PSP-specific treatment to date has been limited and primarily focused on managing symptoms.[6,7] Given that PSP is a progressive irreversible neurodegenerative disease, it is critical that diagnosis is made as early as possible in order to attempt to make changes, implement symptom management strategies, or consider experimental therapies as early as possible in efforts to delay disease progression.[8] Over the course of disease progression there are many members of the multi-disciplinary health team

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

that must assist in treating PSP patients and associated family members. Publicly accessible resources and telehealth options have recently been developed towards addressing these needs.[7,9]

Three international clinical trials involving treating PSP patients with riluzole, tideglusib, or davunetide have been completed to date. They did demonstrate small beneficial effects, but all failed to show efficacy on endpoints. However, there have been significant advances in our understanding of the etiology of PSP over the past decade that have lead to development of tau-targeted therapies designed to halt the propagation and accumulation of tauopathies. These tau-targeted therapies are currently under investigation in clinical trials.[10,11]

B. Optimal/Desired State of Practice

General practitioners and neurologists should possess the necessary knowledge and competence to suspect, identify, and diagnose progressive supranuclear palsy. This should include the ability to effectively assess the potential benefits and clinical shortcomings of current symptomatic and supportive care approaches for PSP patients.

C. Gaps Based on Current Practice

Current research suggests that general practitioners and neurologists likely do not possess the knowledge and awareness of the latest PSP diagnostic criteria and disease monitoring advances. Moreover, there is a low level of understanding of the potential for tau-emerging therapies for patients with progressive supranuclear palsy. [8,11,12]

D. Underlying Unmet Needs

Neurologists and general practitioners need to improve knowledge and understanding of:

- Progressive supranuclear palsy clinical presentation, variability, and expected prognosis.
- The benefits and limitations of current symptomatic and supportive care options available for progressive supranuclear palsy patients.

General practitioners and neurologists managing patients with progressive supranuclear palsy need to improve competence in:

- Methods of monitoring PSP disease progression as related to the potential impact of current symptomatic and supportive care approaches
- The role of tau protein in PSP pathogenesis and the potential impact of tau-targeted therapies for halting PSP disease progression.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

E. Educational Gaps Grid

To address the gaps and unmet needs related to treatment of progressive supranuclear palsy, we are proposing the development of a live/on-demand educational platform (please see the section of the proposal titled “Educational Rationale, Design, and Features” for further details) with the following learning objectives and goals:

Proposed educational objectives (*as a result of participating in this activity, the learners are expected to be better able to)*:	**Relevant outcome level*** (*this learning objective will measure a change in*)**: ABMS, IOM, & National Quality Strategy (NQS)**	**competencies & domains** (*the proposed activity based on these learning objectives will address the following competencies*)**:**
1. Identify patients with PSP based on their presentation, symptoms, and laboratory test results.	Knowledge (Level 3)	**ABMS:** ☒ Patient care ☒ Medical knowledge ☒ Interpersonal & communication skills **IOM:** ☒ Provide patient-centered care ☒ Work in interdisciplinary teams ☒ Employ evidence-based practice **NQS:** ☒ Making Care Safer ☒ Patient and Family Engagement ☒ Communication and Care Coordination ☒ Prevention and Treatment Practices
2. Monitor PSP disease progression and assess the potential therapeutic benefits to risks of symptomatic, supportive, and palliative care approaches for patients with PSP.	Competence (Level 4)	
3. Recognize the potential impact of emerging tau-targeted therapies under investigation in clinical trials on the future management of PSP.	Knowledge (Level 3)	

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

F. Details of Underlying Unmet Needs & Proposed Educational Objectives

The following sources were used in this gap analysis and needs assessment:

- Review of published evidence in progressive supranuclear palsy
- Expert groups on the advances and challenges in the clinical diagnosis and management of progressive supranuclear palsy

Lack of awareness among neurologists and family practitioners is one of the limitations to advancing PSP therapy. As a rare disorder, PSP is potentially an over-looked diagnosis. Currently, the pre-symptomatic phase of PSP can only be identified post mortem by evidence of neuropathological histological changes. This combined with the additional complexity of differentially diagnosing a disease whose only established risk factor is advanced age, has led to the development of expert driven initiatives to identify clinical features of PSP earlier in disease progression.[8] This has led to advancements in the refinement of mandatory inclusion and exclusion criteria for diagnosing PSP earlier in the neurodegenerative sequelae.

General practitioners or neurologists are likely to be the first healthcare professionals to observe the symptoms of progressive supranuclear palsy. Delays in diagnosis due to a lack of awareness of clinical presentation and knowledge of when to suspect and consider a PSP diagnosis will prevent proper prognosis and disease management. It is critical that diagnosis is made as early as possible in order to attempt to make changes, implement symptom management strategies, or consider experimental therapies as early as possible in efforts to delay the progression of irreversible neurodegenerative disease progression.[8]

Knowledge and understanding of the potential for halting the excessive tau protein accumulation that causes neurofibrillary tangle neurodegeneration has advanced significantly over the past decade. Several clinical trials are currently targeting the tau protein and preliminary data suggests these therapies may delay neurodegeneration in PSP patients. Evidence supporting the following gaps were obtained from review of published research on educational gaps in progressive supranuclear palsy.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Educational Need 1: Need to Identify patients with progressive supranuclear palsy based on their presentation, symptoms, and laboratory test results.
Learning Objective 1: Summarize the distinguishing clinical presentation, symptoms, and laboratory tests required for making a diagnosis of progressive supranuclear palsy.

Supranuclear palsy diagnosis is a rare disease whose differential diagnosis is further complicated by a completely unknown etiology. The advanced age of onset in the 6th decade of life can make the differential diagnosis even more challenging. To some extent, the early diagnosis of PSP remains an active area of research. For all of these reasons progressive supranuclear palsy diagnosis is consistently delayed.

Currently, the 1996 dated clinical criteria proposed by the National Institute of Neurological Disorders and Stroke and Society for PSP (NINDS-SPSP) has been the most widely used criteria for the ante mortem diagnosis of PSP.[13] However, diagnosis on this basis is typically made 3 to 4 years after onset of first classic symptoms involving falls and supranuclear gaze palsy.[14] Accordingly, early and reliable diagnosis of PSP remains a major clinical challenge. The International Parkinson and Movement Disorder Society-endorsed PSP Study Group (MDS-PSP) was established to provide an evidence- and consensus-based revision of the NINDS-SPSP criteria.[8,15] While the NINDS-SPSP criteria focused on two core functional domains (ocular motor dysfunction, postural instability), the MDS-PSP criteria added two further domains (akinesia, cognitive dysfunction). The MDS-PSP emphasized that brain imaging can be helpful in ruling out other diagnosis. Patients diagnosed with PSP exhibit demonstrable midbrain atrophy or hypometabolism and/or striatal dopaminergic degeneration increases the diagnostic confidence in patients presenting with clinical features. Only limited PSP diagnostic imaging data are currently available. Future imaging techniques based on more PSP-specific imaging data studies and possibly the successful development of *in vivo* Tau-PET imaging may help confirm and establish *earlier* diagnosis.

Clinicopathological studies have led to the recognition of other clinical phenotypes associated with PSP-tau pathology that are most distinct in the first 2 years of presentation. PSP-RS is the most diagnosed common form followed by PSP-P, which may be observed in up a one-third of the cases.[6] A multi-center clinicopathological series reported clinical heterogeneity beyond a pure Richardson syndrome in the majority (87%) of cases within the first two years of presentation.[16] Nearly 40% of cases could not be classified into a particular phenotype. This study suggested that heterogeneous presentations may be more common in PSP than has previously been indicated.

Collectively, published research indicate that physicians and neurologists need to increase their awareness of the symptoms, clinical presentation, and available diagnostic testing of progressive supranuclear palsy so that management and potential treatment can be initiated as soon as possible.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Educational Need 2: Monitor PSP disease progression and assess the potential therapeutic benefits to risks of symptomatic, supportive, and palliative care approaches for patients with progressive supranuclear palsy.
Learning Objective 2: Weigh the potential therapeutic benefits versus risks with consideration of the most common types of symptomatic and supportive care for PSP patients.

Pharmaceutical treatments are limited as there is no treatment specifically indicated for PSP. Disease management is primarily symptomatic, supportive, and palliative for PSP patients. Specialists frequently use levodopa at up to 1000mg daily doses to manage symptoms. This can help, but benefits are more transient than with Parkinson's disease and levodopa has no demonstrable impact on disease duration.[17] Zolpidem, a GABA agonist, may improve motor function, dysarthria and ocular abnormalities in PSP patients according to anecdotal evidence from a case report, but further clinical evidence is lacking.[18]

Botulinum toxin injection can be used to alleviate eye closure symptoms in patients with eyelid blepharospasm, while regular administration of artificial tears can help relieve eye irritation and dryness. The potential value of physical therapy is of increasing interest particularly given evidence of benefit for individuals with Parkinson disease. Other more practical household concerns should be reviewed with patients on an individual need basis and may include installing grab bars in hallways and bathrooms, using a walker that is weighted, and removing items that are hard to see without looking downward.

Neurologists and physicians managing patients with PSP should be made aware of resources that have been specifically developed for nurses and other healthcare team members involved in the management of PSP patients. This includes accessible telehealth resources specifically developed to assist nurses with knowledge, guidance, and resources for patients and families living with PSP.[9] The Cure PSP organization has an extensive updated guidebook written by healthcare professionals that covers PSP-specific relevant aspects of speech therapy, physical therapy, occupational therapy, social work, and advance family planning with palliative care.[7]

Experts stress that management of progressive supranuclear palsy require a multidisciplinary care approach, with treatment strategies incorporating combined efforts from multiple specialties. Moreover PSP patients need a healthcare team that is attuned to the specific, special needs of the individual PSP patient. Neurologists and general practitioners should be aware of these publicly accessible resources available to help increase the quality of life, safety, and the optimal management of PSP.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Educational Need 3: Need to recognize the potential impact of emerging tau-targeted therapies under investigation in clinical trials on the management of progressive supranuclear palsy.
Learning Objective 3: Cite current data on approved therapies for the treatment of progressive supranuclear palsy.

While no specific and effective treatment for PSP have been established to date, there have been significant advances made in our understanding of the pathogenesis of PSP as related to the tau protein. Tau is a highly soluble protein that is predominately found in neurons, where it functions to modulate the physical stability of microtubules. In disease, tau protein accumulates excessively to form neurofibrillary tangles that are associated with neurodegeneration. The mechanisms by which tau abnormalities lead to cell dysfunction and death are not well entirely understood, but passive immunization with anti-tau monoclonal antibodies has been demonstrated to suppresses tau pathology and to improves cognitive or motor function in tau transgenic mouse models.

Two IgG4 humanized N-terminal tau directed monoclonal antibodies were developed, BIIB092 and Abb-8E12, have progressed to Phase 2 clinical trials for PSP.[10,11] Analysis showed that these antibodies bind and neutralize extracellular Tau but not intracellular tau *in vitro* in pluripotent stem cells derived from familial AD patients. BIIB092 entered its phase I trial in 2014 (clinicaltrials.gov, NCT02294851) and was reported to be safe it was safe and well tolerated in PSP. In 2015, entered phase I trial that evaluated safety and tolerability of multiple ascending doses in 48 mild-moderate PSP patients (including 12 receiving placebo) in their first 5 years of the disease (clinicaltrials.gov, NCT02460094). The primary results confirmed its general safety and the CSF pharmacodynamics (eTau concentration) were indicative of efficacy by a mean CSF free eTau suppression of 90–96% at day 29 and 91–97% at day 85 after treatment with the intravenous infusions of 150–2100 mg antibody every 4 weeks [19] (clin icaltrials.gov, NCT02460094). These patients continued participating in a long-term BIIB092 intravenous monthly administration. A phase II double-blind, placebo-controlled trial of BIIB092 on an estimated 396 PSP patients has started in 2017 and data are expected in 2020 ([20]; clinicaltrials.gov, NCT03068468).

Other advances made in our basic understanding of the PSP tauopathy with respect to Alzheimer's disease may provide greater insight into how we may uniquely address PSP tauopathy in the future. Alzheimer's disease is a tauopathy like PSP, but it is occurs with much higher prevalence than PSP. Functional MRI studies comparing Alzheimer's disease (AD) to PSP suggest that PSP afflicted tissues suffer from weak connectivity, high metabolic demand, and a lack of trophic support, while for AD there is no such correlation.[21]

Similarly, studies of tauopathy within the subtypes of PSP have been informative. Both PSP-P and PSP-pure akinesia with gait freezing subtypes have a more benign disease progression with a longer survival period that also correlates with an overall tau burden less than those in PSP-RS.[6] Moreover studies indicate the distribution of abnormal tau is relatively more restricted to the brain stem in PSP-P.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

Blocking the spread of tauopathy represents a very promising developing therapeutic approach for patients with progressive supranuclear palsy. Studies to date support that BIIB092 is safe and likely effective in delaying tauopathy in PSP patients. Neurologists and general practitioners need to understand the role of tau in PSP pathogenesis and be made aware of potential positive impact of tau-targeted therapies currently under investigation in clinical trials.

References

1 Caparros-Lefebvre, D.*, et al.* A geographical cluster of progressive supranuclear palsy in northern France. *Neurology* 2015; **85**, 1293-1300.
2 Litvan, I.*, et al.* Environmental and occupational risk factors for progressive supranuclear palsy: Case-control study. *Mov Disord* 2016; **31**, 644-652.
3 Golbe, L.I., Davis, P.H., Schoenberg, B.S. & Duvoisin, R.C. Prevalence and natural history of progressive supranuclear palsy. *Neurology* 1988; **38**, 1031-1034.
4 Jackson, J.A., Jankovic, J. & Ford, J. Progressive supranuclear palsy: clinical features and response to treatment in 16 patients. *Ann Neurol* 1983; **13**, 273-278.
5 Golbe, L.I. & Ohman-Strickland, P.A. A clinical rating scale for progressive supranuclear palsy. *Brain* 2007*;* **130**, 1552-1565.
6 Ling, H. Clinical Approach to Progressive Supranuclear Palsy. *J Mov Disord* 2016; **9**, 3-13.
7 *The Cure PSP Guidebook.* 2018. https://www.psp.org/iwanttolearn/#page-section-the-curepsp-guidebook
8 Hoglinger, G.U.*, et al.* Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. *Mov Disord* 2017; **32**, 853-864.
9 Dunlop, S.R., Kent, V.P., Lashley, M. & Caruana, T. The Cure PSP Care Guide: A Telephonic Nursing Intervention for Individuals and Families Living With Progressive Supranuclear Palsy. *J Neurosci Nurs* 2016; **48**, 105-106.
10 Boxer, A.L.*, et al.* Advances in progressive supranuclear palsy: new diagnostic criteria, biomarkers, and therapeutic approaches. *Lancet Neurol* 2017; **16**, 552-563.
11 Shoeibi, A., Olfati, N. & Litvan, I. Preclinical, phase I, and phase II investigational clinical trials for treatment of progressive supranuclear palsy. *Expert Opin Investig Drugs* 2018; **27**, 349-361.
12 Wiblin, L., Lee, M. & Burn, D. Palliative care and its emerging role in Multiple System Atrophy and Progressive Supranuclear Palsy. *Parkinsonism Relat Disord* 2017; **34**, 7-14.
13 Litvan, I.*, et al.* Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): report of the NINDS-SPSP international workshop. *Neurology* 1996; **47**, 1-9.
14 Respondek, G.*, et al.* Accuracy of the National Institute for Neurological Disorders and Stroke/Society for Progressive Supranuclear Palsy and neuroprotection and natural history in Parkinson plus syndromes criteria for the diagnosis of progressive supranuclear palsy. *Mov Disord* 2013; **28**, 504-509.
15 Respondek, G.*, et al.* Which ante mortem clinical features predict progressive supranuclear palsy pathology? *Mov Disord* 2017; **32**, 995-1005.
16 Lang, A.E. Clinical heterogeneity in progressive supranuclear palsy: challenges to diagnosis, pathogenesis and future therapies. *Mov Disord* 2014; **29**, 1707-1709.
17 Testa, D.*, et al.* Comparison of natural histories of progressive supranuclear palsy and multiple system atrophy. *Neurol Sci* 2001; **22**, 247-251.
18 Cotter, C., Armytage, T. & Crimmins, D. The use of zolpidem in the treatment of progressive supranuclear palsy. *J Clin Neurosci* 2010; **17**, 385-386.

Needs Assessment Sample: **Diagnostic Considerations and Potential Treatments for Progressive Supranuclear Palsy**

W. Todd Penberthy, PhD
WTPENBER@GMAIL.COM
1(407)951-1624

[19] Qureshi I, G.M., Tirucherai G, et al. Multiple ascending dose study of the tau-directed monoclonal antibody BMS-986168 in patients with progressive supranuclear palsy. in *2017 International Congress of Parkinson's Disease and Movement Disorders* (Vancouver, Canada, 2017).

[20] Dam, T., Boxer, A., Golbe, L.I., Höglinger & Huw, R.M. Efficacy and Safety of BIIB092 in Patients with Progressive Supranuclear Palsy: PASSPORT Phase 2 Study Design (P6.073). *Neurology* **90**(2018).

[21] Cope, T.E.*, et al.* Tau burden and the functional connectome in Alzheimer's disease and progressive supranuclear palsy. *Brain* 2018**; 141**, 550-567.