University Hospitals Plymouth NHS Trust

Neuro-Orthoptics in Progressive Supranuclear Palsy

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Learning outcomes

1. Gain an understanding of general and ocular features of PSP.

2. Recognise the value of MDT approach in atypical Parkinsonian disorder, to aid earlier suspected diagnosis of PSP.

3. Apply knowledge of neuroanatomy to understand the pathogenesis for ocular signs in PSP.

4. Examine and evaluate optical management for PSP.

What is PSP?

Atypical Parkinsonian disorder: neurodegenerative – build of tau protein (tauopathy).

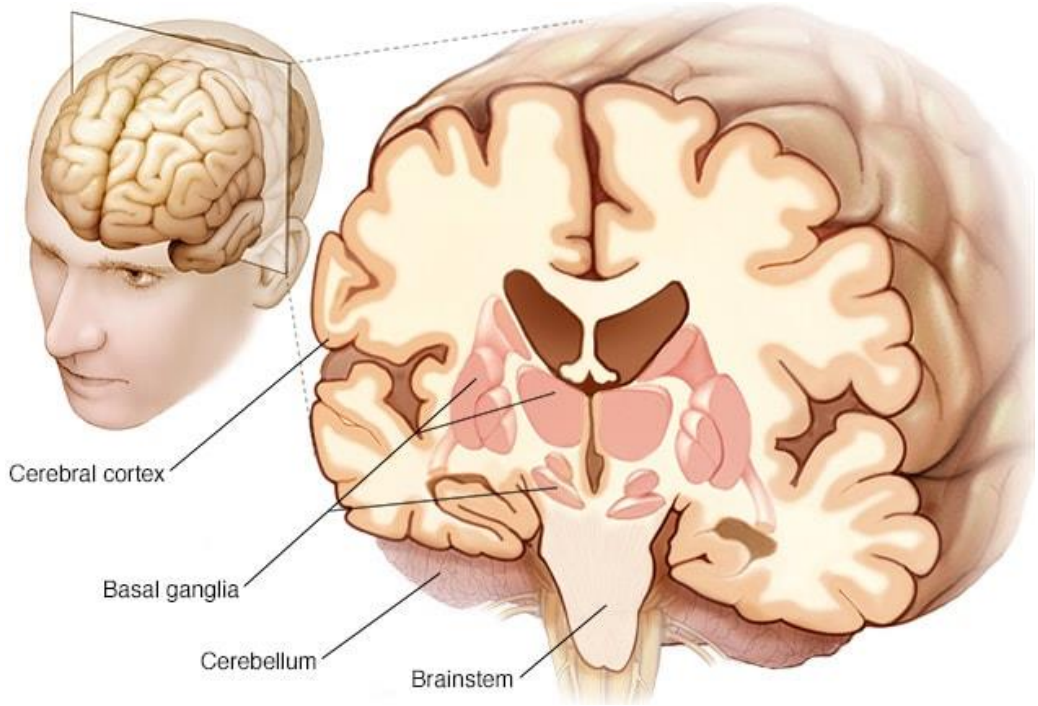
Clinical diagnosis only – no known biomarkers.

Oculomotor dysfunction: most sensitive and specific diagnostic sign. *(Respondek, 2017).*

Prognosis – 6 -12 years fatality *(Williams DR, 2009).*

PSP prevalence – 6.4 per 100,000 (*Shrag A, 1999*).

PD prevalence – 139 per 100,000 (*Porter et al, 1999*).



General Signs – MDT approach required

General motor issues: Postural instability, bradykinesia, rigidity and incontinence - OT and physio input.

Bulbar dysfunction:

Dysarthria – slow/slurred/quiet – voice banking – SALT input.

Dysphagia – choking, drooling – altered diet – SALT and dietician input.

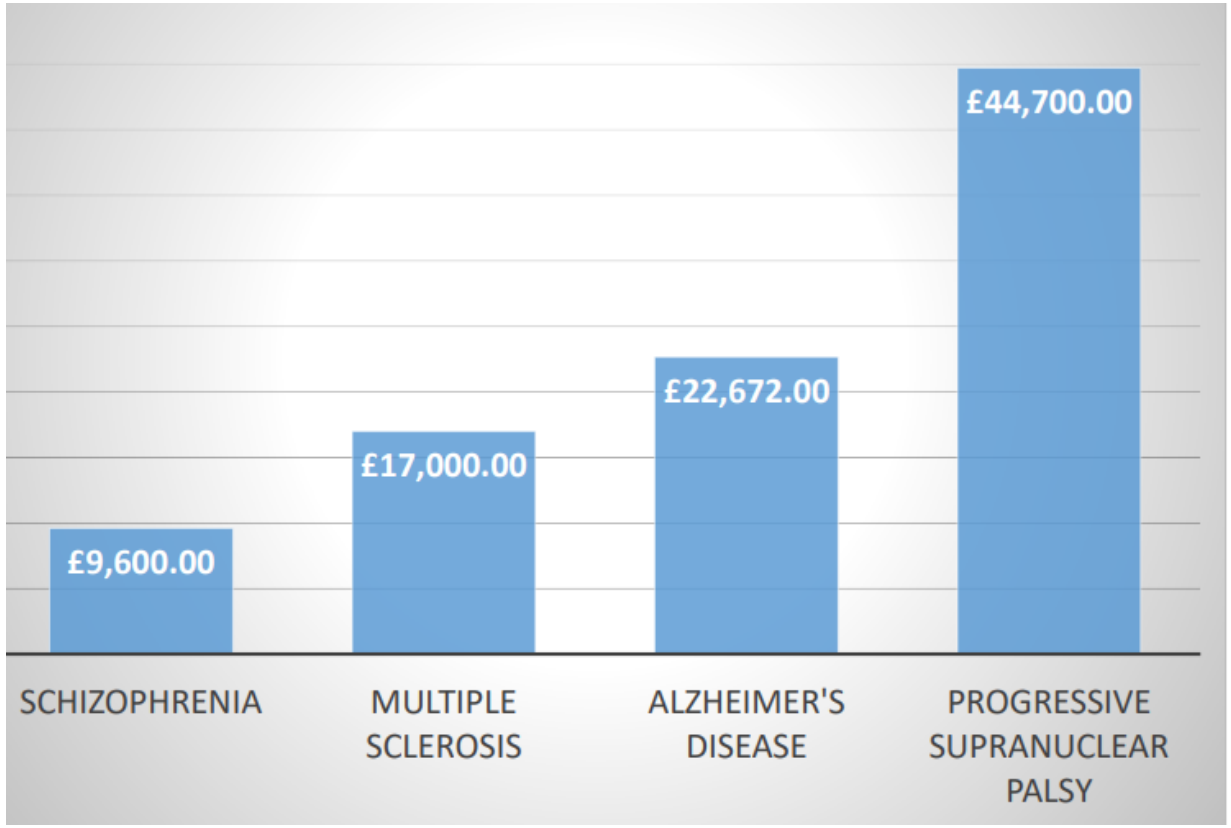
Dementia: Cognitive dysfunction, amnesia and depression - neuro-psychological input.

Frontal Lobe deficit: Personality change, irritability, impulsiveness, apathy - neuro-psychological input.

Oculomotor dysfunction – orthoptic and oculoplastic input.

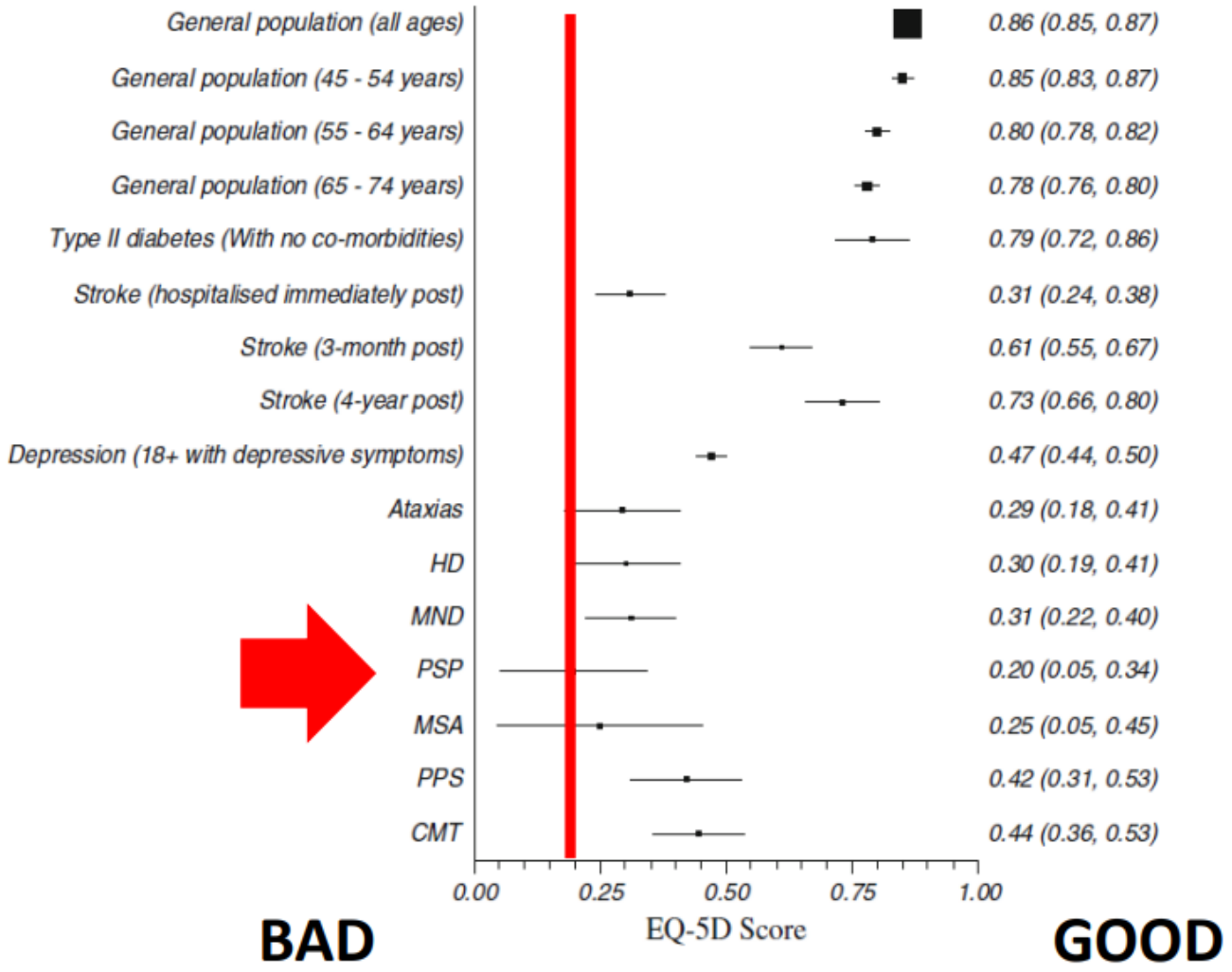
Overlap with Parkinsonian signs – neurology input.

Economic Cost



McCrone et al, 2011

QOL



Calvert M et al, 2013

Oculomotor dysfunction

Vertical supranuclear gaze palsy
Slow velocity vertical saccades
Impaired vergence
Lid signs: • Apraxia of eyelid opening • Reduced blink rate • Blepharospasm
Macro square wave jerks

A unique set of tests required to identify these signs.

Diagnostic criteria

O1:
Vertical supranuclear gaze palsy

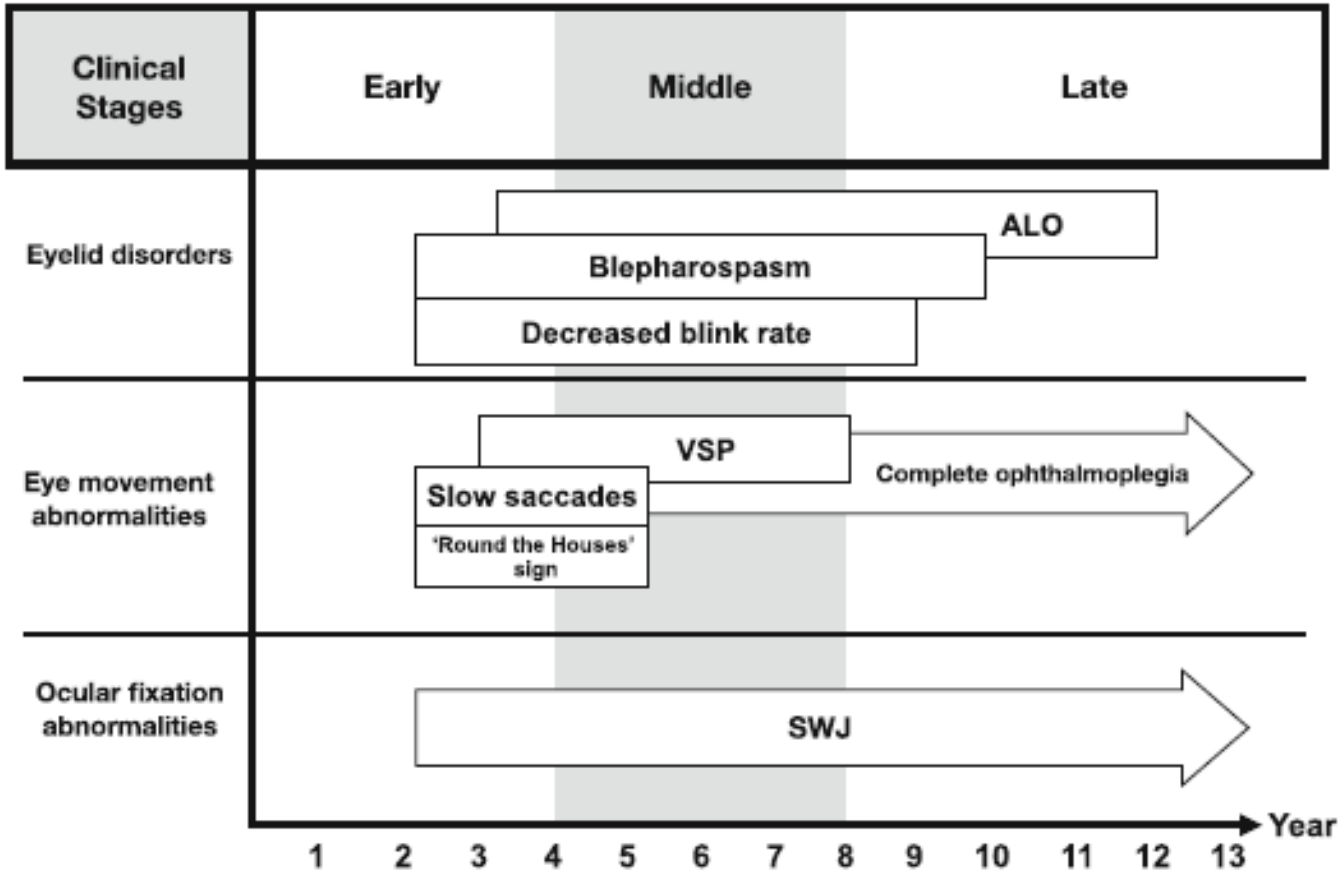
O2:
Slow velocity of vertical saccades

O3:
Frequent macro square wave jerks or "eyelid opening apraxia"

Hoglinger et al, 2017

Diagnostic Certainty	Definition	Combinations	Predominance Type	Abbreviation
Definite PSP	Gold standard defining the disease entity	Neuropathological diagnosis	Any clinical presentation	def. PSP
Probable PSP	Highly specific, but not very sensitive for PSP	(O1 or O2) + (P1 or P2)	PSP with Richardson's syndrome	prob. PSP-RS
	Suitable for therapeutic and biological studies	(O1 or O2) + A1	PSP with progressive gait freezing	prob. PSP-PGF
		(O1 or O2) + (A2 or A3)	PSP with predominant parkinsonism	prob. PSP-P
		(O1 or O2) + C2	PSP with predominant frontal presentation	prob. PSP-F
Possible PSP	Substantially more sensitive, but less specific for PSP	O1	PSP with predominant ocular motor dysfunction	poss. PSP-OM
	Suitable for descriptive epidemiological studies and clinical care	O2 + P3	PSP with Richardson's syndrome	poss. PSP-RS
		A1	PSP with progressive gait freezing	poss. PSP-PGF
		(O1 or O2) + C1	PSP with predominant speech/ language disorder[a]	poss. PSP-SL
		(O1 or O2) + C3	PSP with predominant CBS[a]	poss. PSP-CBS
Suggestive of PSP	Suggestive of PSP, but not passing the threshold for possible or probable PSP	O2 or O3	PSP with predominant ocular motor dysfunction	s.o. PSP-OM
		P1 or P2	PSP with predominant postural instability	s.o. PSP-PI
	Suitable for early identification	O3 + (P2 or P3)	PSP with Richardson's syndrome	s.o. PSP-RS
		(A2 or A3) + (O3, P1, P2, C1, C2, CC1, CC2, CC3, or CC4)	PSP with predominant parkinsonism	s.o. PSP-P
		C1	PSP with predominant speech/ language disorder	s.o. PSP-SL
		C2 + (O3 or P3)	PSP with predominant frontal presentation	s.o. PSP-F
		C3	PSP with predominant CBS	s.o. PSP-CBS

Timing of presentation of signs



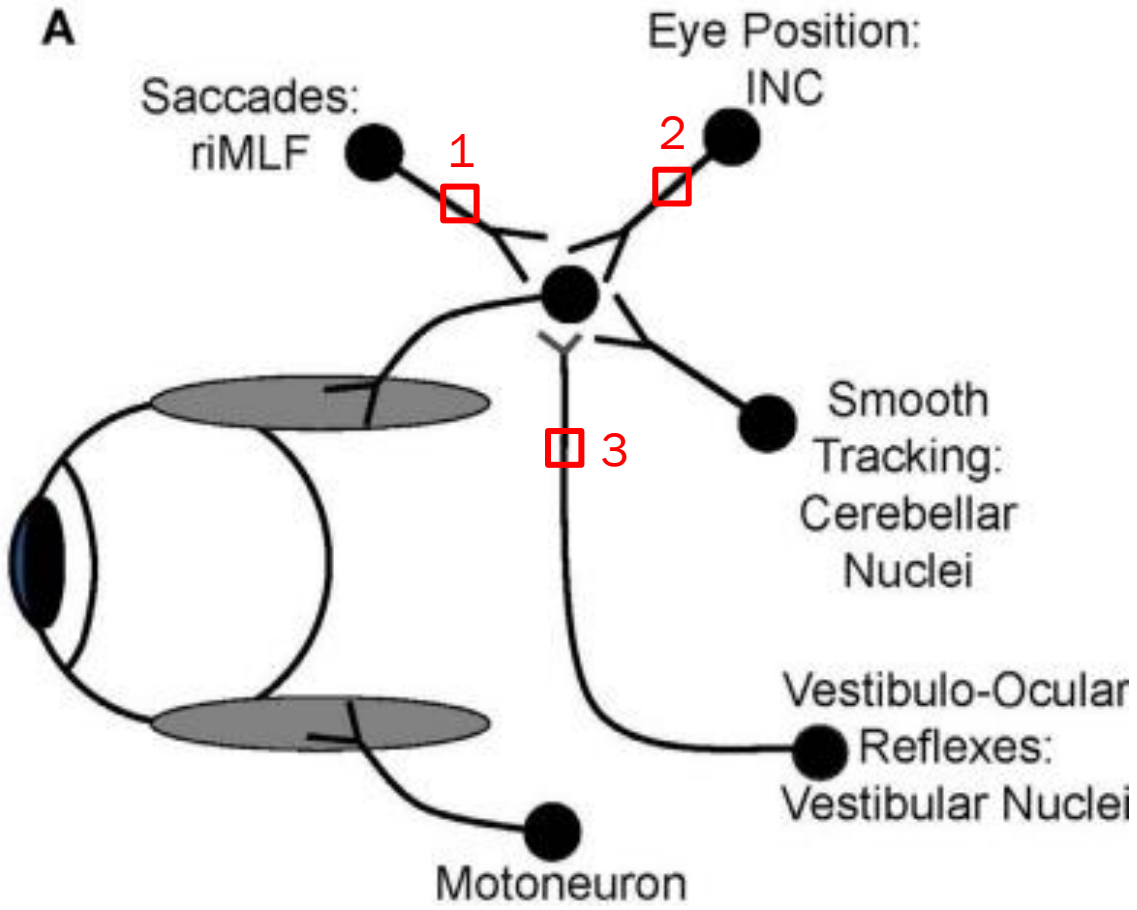
Phokaewvarangkul and Bhidayasiri, 2019.

Patient symptoms

Diplopia/blurred vision – 61%
Photophobia – 43%
Difficulty reading – but unsure why.
(*Nath et al, 2003*)

Symptoms not always reported – thorough case history important!

What does supranuclear mean?

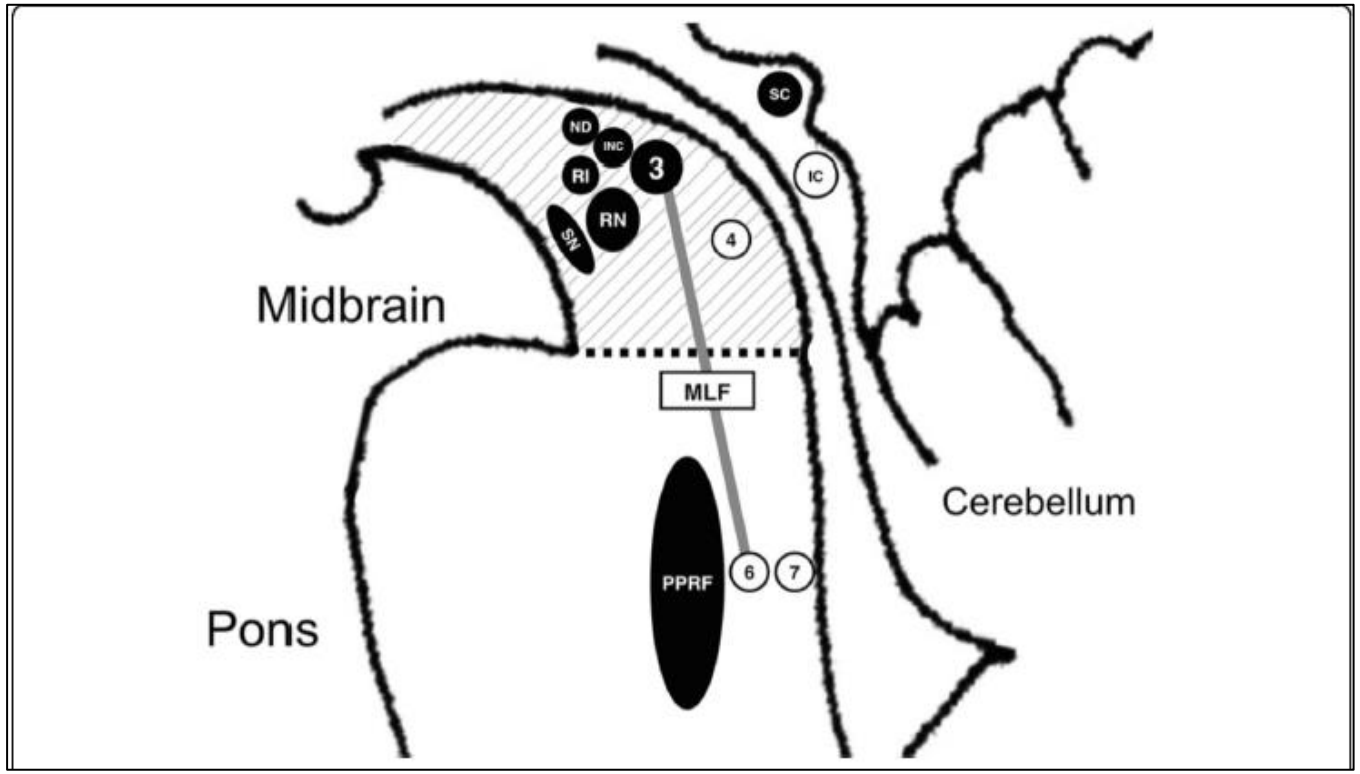


Chen et al, 10

Eye movement pathophysiology

Vertical = Midbrain

Horizontal = Pons



Phokaewvarangkul and Bhidayasiri, 2019.

Saccades

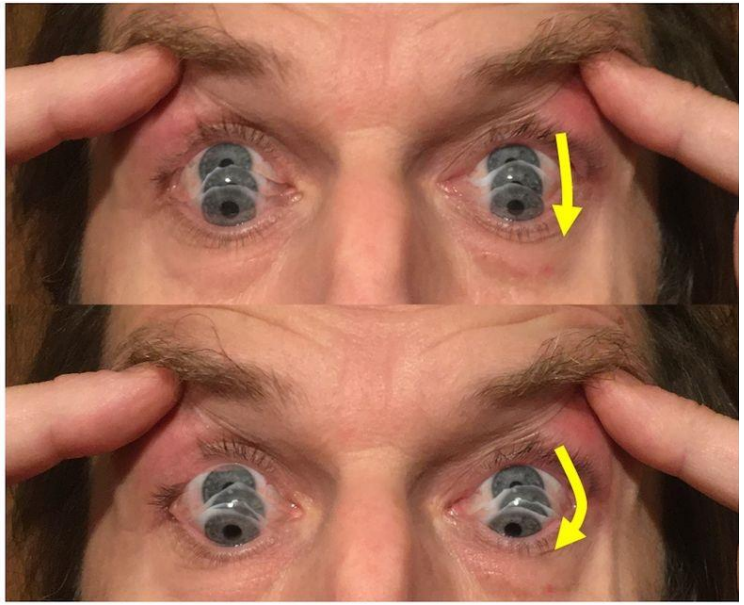
Pathophysiology – excitatory burst neurons:

- Vertical (primarily affected) – RiMLF in midbrain.
- Horizontal – PPRF in pons.

What do you assess?

- Velocity, accuracy, conjugacy
- ‘round the houses’ sign.
- Eye tracker helpful.

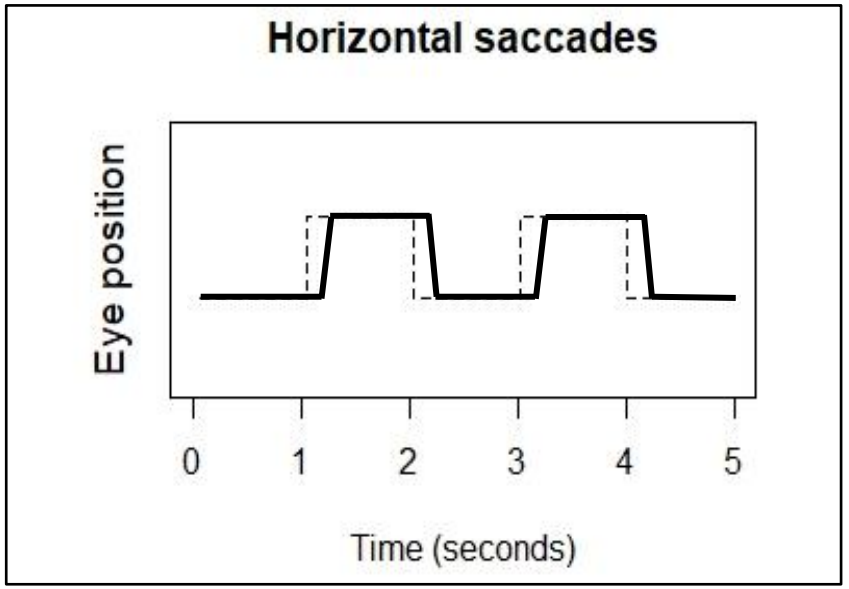
1. Early stage: low velocity vertical saccades.
2. Middle stage: multiple hypometria, low velocity.
3. Late stage: absent.



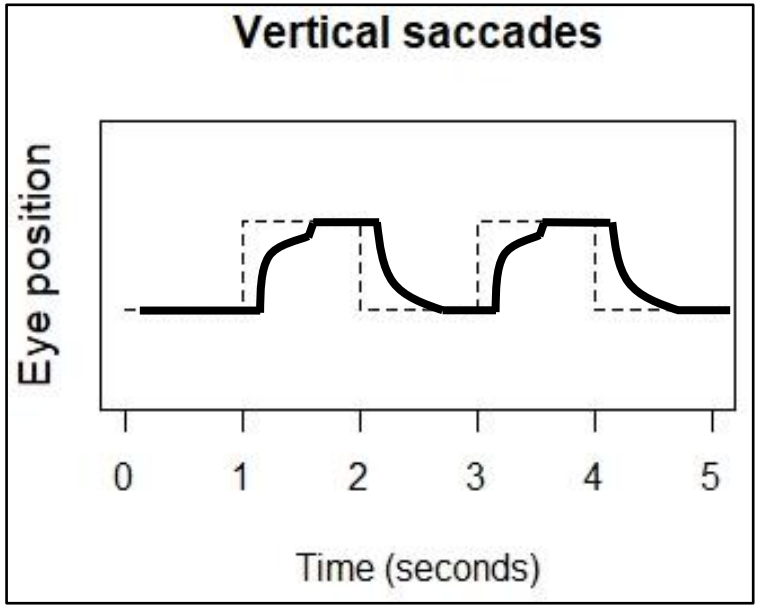
Rowe JB, 21

Saccades – eye tracking

- Objectively assesses eye movement waveform - Eyelink 1000+ infrared eye tracker.



Horizontal - okay



Up – slow + hypometric.
Down – slow.

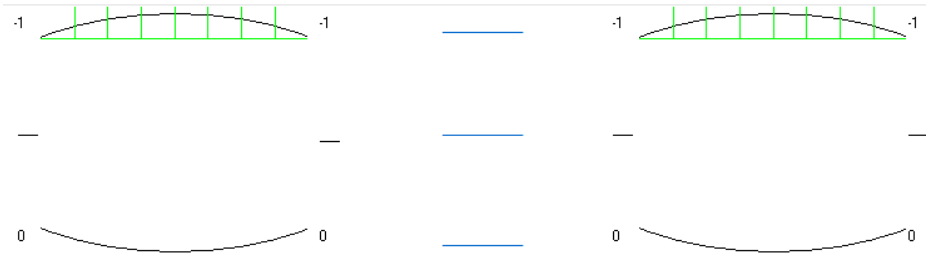
Eye position – ocular motility

Pathophysiology – positional step neurons.

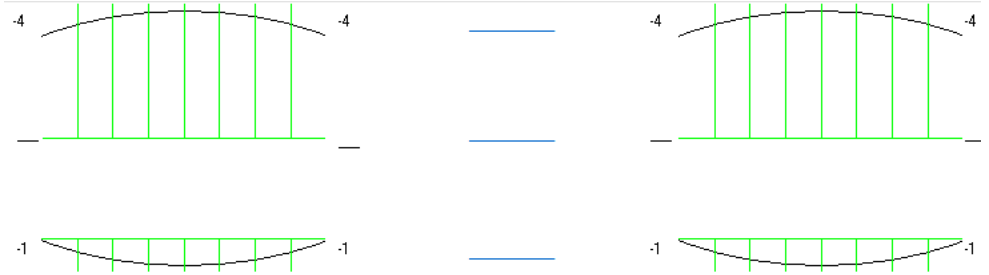
- Vertical – INC in midbrain.
- Horizontal – NPH in pons.

Vertical affected first and symmetrical.

Important to differentiate from physiological upgaze limitation (*Clarke et al, 2002*).



Common in elderly



Uncommon

Vestibular ocular reflex (VOR)

Spared until later in the disease until gaze palsy becomes nuclear – complete ophthalmoplegia.

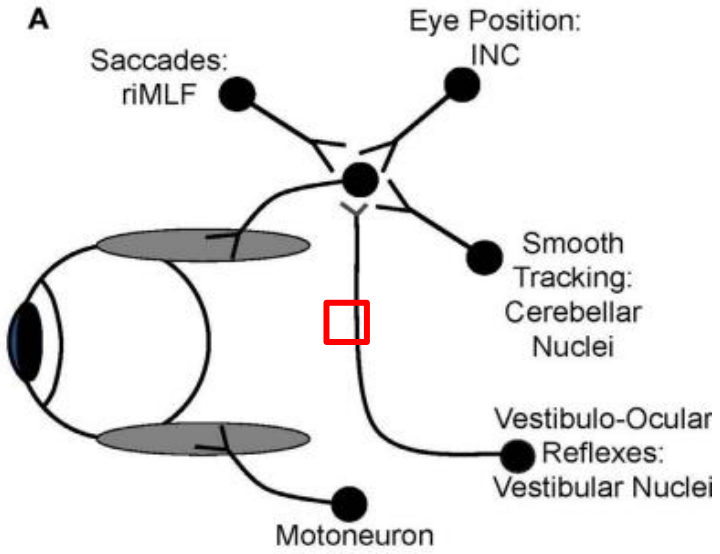
Pathophysiology

- 4 vestibular nuclei in pons and upper medulla.

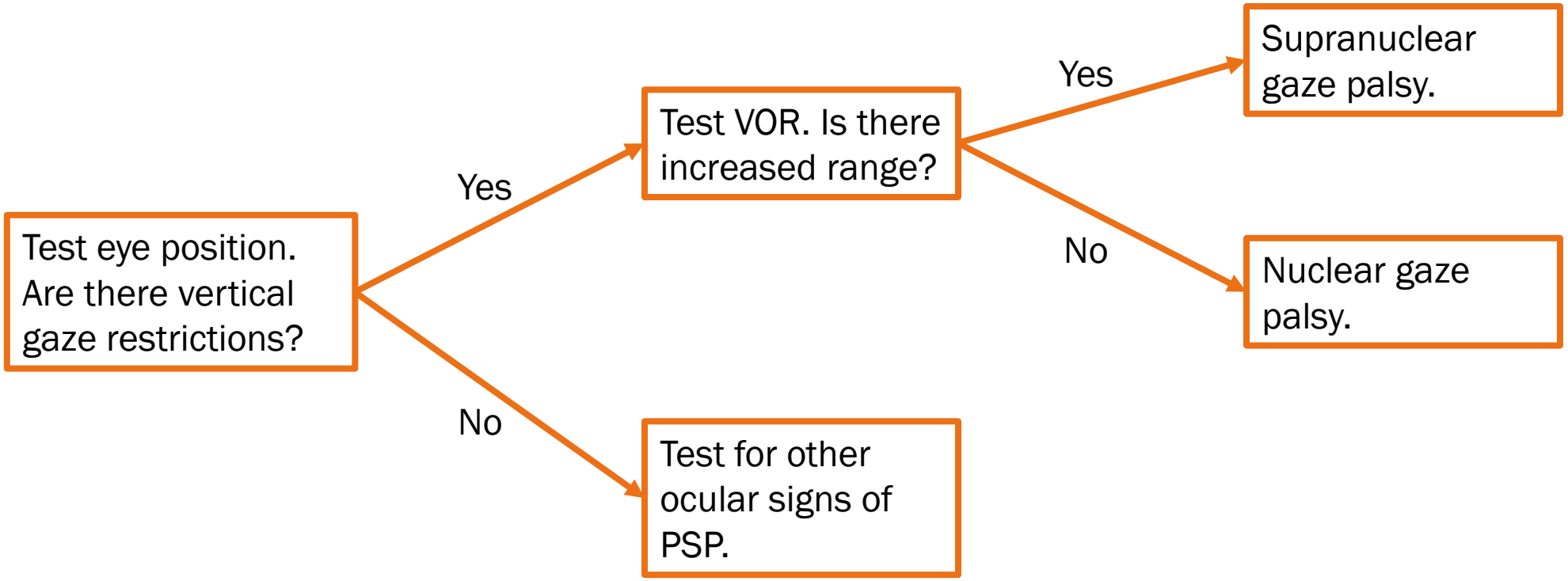
How do you test this?

- Dolls head manoeuvre.

Difficult with axial rigidity.



Vertical supranuclear gaze palsy



Eyelid signs

Decreased blink rate – staring.

- Typical blink rate = 12-15 per minute (*Abusharha, 2017*).
- PSP = 1.9 per minute (*Reddy et al, 2013*).
- Eye lubricants essential.

Blepharospasm

- Spontaneous eyelid contracture.
- Treatment: Botulinum toxin good success (*Barclay and Lang, 1997*).

Lid opening apraxia

- Delay in opening lids after closure.
- Frontalis overaction to force lid open can give look of astonishment.

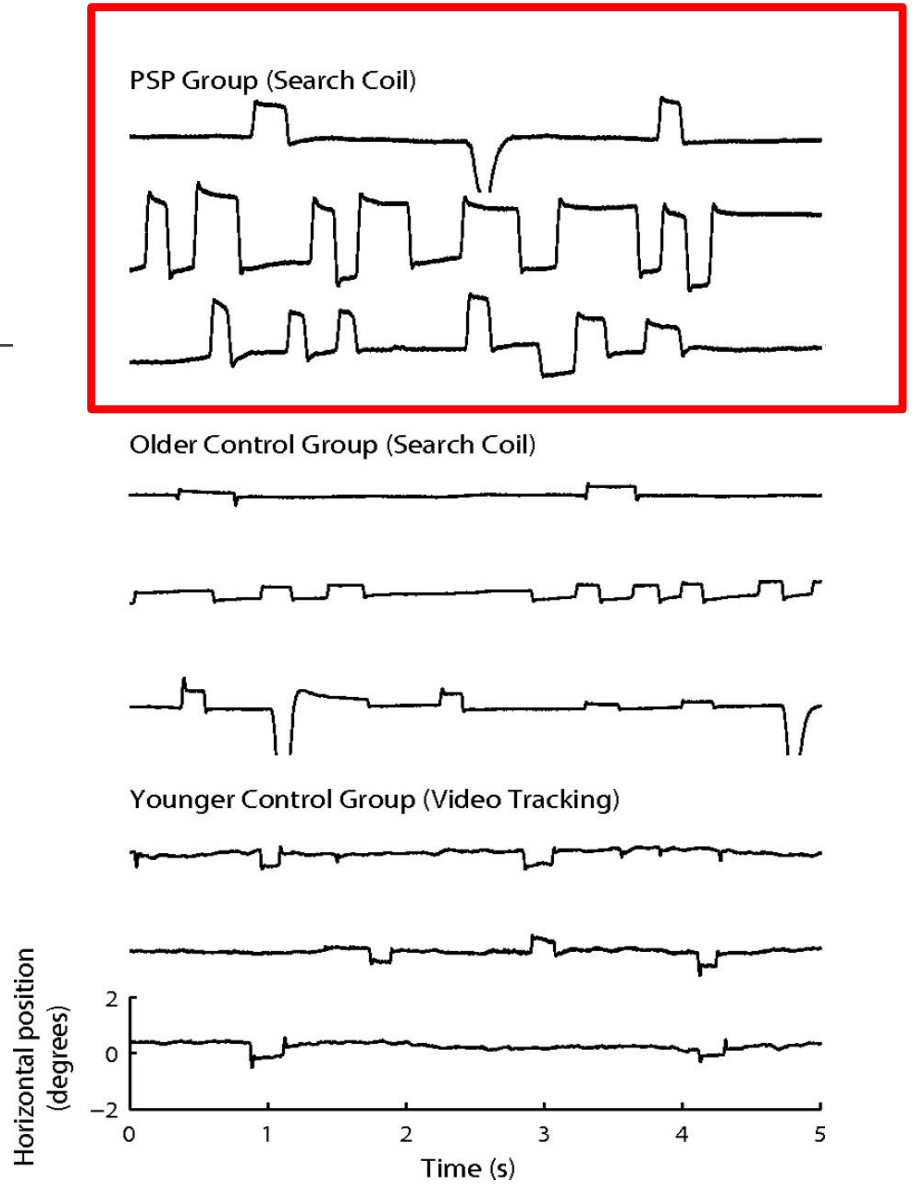
Symptoms – photophobia, dry eye.

Fixation

Macro square waved jerks

- Amplitude 0.7 deg in control vs 1.4 in PSP.
- Frequency 11.5/min in control vs 48/min in PSP.
- Eye tracking helpful.

Otero-Millan et al, 2011

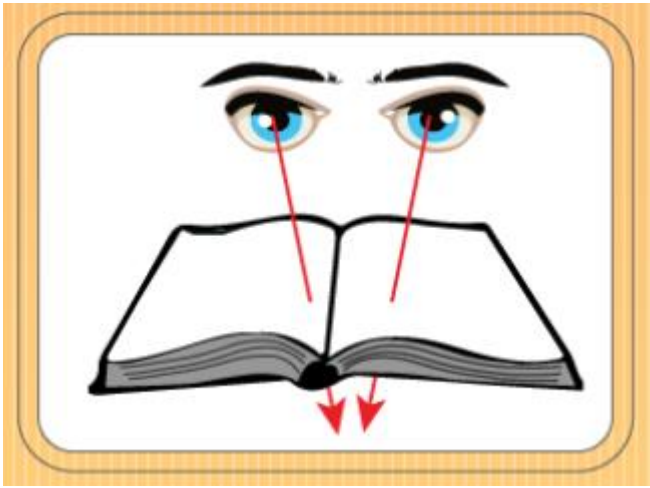


Vergence

Pathophysiology – supraocular motor area next to 3rd nerve nucleus in midbrain.

Symptom – diplopia, confusion or difficulty reading.

Important to differentiate from primary convergence insufficiency!



Ocular management

- Restricted ocular motility
  - Single vision lenses.
  - Compensatory strategies.
  - Prism glasses.
- Photophobia
  - Tinted lenses.
  - Compensatory strategies.
- Diplopia/confusion
  - Prisms (Fresnel, incorporated).
  - Occlusion (patch, frosted tape, permanent frosting, occlusive contact lens).

Other Parkinsonian disorders

Parkinson's disease

- Hypometric saccades, impaired pursuit, impaired vergence, macro SWJ.

Multiple system atrophy

- Gaze evoked nystagmus, down beat nystagmus, rebound nystagmus, impaired pursuit, macro SWJ, hypometric saccades.

Dementia with Lewy body's

- Saccade latency, accuracy, peak velocity and antisaccade affected – horizontal and vertical.
- Rarely supranuclear vertical gaze palsy.

Corticobasal syndrome

- Increased saccade latency and anti-saccade difficulties.
- Can occasionally present with slow velocity vertical saccade, VSGP or similar eyelid signs to PSP.

Eye movement assessment essential for differential diagnosis.

Summary

- PSP is a serious neuro-degenerative condition requiring a multi-disciplinary approach for diagnosis and care.
- Identifying oculomotor signs is key for diagnosis and differentiation between other atypical Parkinsonian conditions.
- Ocular management can help ease symptoms and improve quality of life.

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Thank you for listening

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References

Respondek G, Kurz C, Arzberger T, Compta Y, Englund E, Ferguson LW, Gelpi E, Giese A, Irwin DJ, Meissner WG, Nilsson C, Pantelyat A, Rajput A, van Swieten JC, Troakes C, Josephs KA, Lang AE, Mollenhauer B, Müller U, Whitwell JL, Antonini A, Bhatia KP, Bordelon Y, Corvol JC, Colosimo C, Dodel R, Grossman M, Kassubek J, Krismer F, Levin J, Lorenzl S, Morris H, Nestor P, Oertel WH, Rabinovici GD, Rowe JB, van Eimeren T, Wenning GK, Boxer A, Golbe LI, Litvan I, Stamelou M, Höglinger GU; Movement Disorder Society-Endorsed PSP Study Group. Which ante mortem clinical features predict progressive supranuclear palsy pathology? Mov Disord. 2017 Jul;32(7):995-1005.

Williams DR, Lees AJ PSP: clinicopathological concepts and diagnostic challenges. Lancet Neurolo. 2009.

Schrag A, Ben-Shlomo Y, Quinn NP. Prevalence of progressive supranuclear palsy and multiple system atrophy: a cross-sectional study. Lancet 1999; 354: 1771–75.

PORTER, B., MACFARLANE, R., UNWIN, N. & WALKER, R. 2006. The prevalence of Parkinson's disease in an area of North Tyneside in the North-East of England. *Neuroepidemiology,* 26**,** 156-61.

McCrone P, Payan CAM, Knapp M, Ludolph A, Agid Y, Leigh PN, et al. The Economic Costs of Progressive Supranuclear Palsy and Multiple System Atrophy in France, Germany and the United Kingdom. PLOS ONE 2011; 6: e24369

Calvert M, Pall H, Hoppitt T, Eaton B, Savill E, Sackley C. Health-related quality of life and supportive care in patients with rare long-term neurological conditions. Qual Life Res 2013; 22: 1231–1238.

Schmotz C, Richinger C, Lorenzl S. High Burden and Depression Among Late-Stage Idiopathic Parkinson Disease and Progressive Supranuclear Palsy Caregivers. J Geriatr Psychiatry Neurol 2017; 30: 267–272.

Höglinger GU, Respondek G, Stamelou M, Kurz C, Josephs KA, Lang AE, Mollenhauer B, Müller U, Nilsson C, Whitwell JL, Arzberger T, Englund E, Gelpi E, Giese A, Irwin DJ, Meissner WG, Pantelyat A, Rajput A, van Swieten JC, Troakes C, Antonini A, Bhatia KP, Bordelon Y, Compta Y, Corvol JC, Colosimo C, Dickson DW, Dodel R, Ferguson L, Grossman M, Kassubek J, Krismer F, Levin J, Lorenzl S, Morris HR, Nestor P, Oertel WH, Poewe W, Rabinovici G, Rowe JB, Schellenberg GD, Seppi K, van Eimeren T, Wenning GK, Boxer AL, Golbe LI, Litvan I; Movement Disorder Society-endorsed PSP Study Group. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord. 2017 Jun;32(6):853-864.

Phokaewvarangkul O, Bhidayasiri R. How to spot ocular abnormalities in progressive supranuclear palsy? A practical review. Transl Neurodegener. 2019 Jul 10;8:20.

References cont…

Nath U, Ben-Shlomo Y, Thomson RG, Lees AJ, Burn DJ. Clinical features and natural history of progressive supranuclear palsy: a clinical cohort study. Neurology. 2003 Mar 25;60(6):910-6.

Chen AL, Riley DE, King SA, Joshi AC, Serra A, Liao K, Cohen ML, Otero-Millan J, Martinez-Conde S, Strupp M, Leigh RJ. The disturbance of gaze in progressive supranuclear palsy: implications for pathogenesis. Front Neurol. 2010 Dec 3;1:147.

Rowe JB, Holland N, Rittman T, Progressive supranuclear palsy: diagnosis and management. *Practical Neurology* 2021;**21:**376-383

Clark RA, Demer JL. Effect of aging on human rectus extraocular muscle paths demonstrated by magnetic resonance imaging. Am J Ophthalmol. 2002 Dec;134(6):872-8.

Abusharha AA. Changes in blink rate and ocular symptoms during different reading tasks. Clin Optom (Auckl). 2017 Nov 20;9:133-138.

Reddy VC, Patel SV, Hodge DO, Leavitt JA. Corneal sensitivity, blink rate, and corneal nerve density in progressive supranuclear palsy and Parkinson disease. Cornea. 2013 May;32(5):631-5.

Barclay CL, Lang AE. Dystonia in progressive supranuclear palsy. J Neurol Neurosurg Psychiatry. 1997 Apr;62(4):352-6.

Otero-Millan J, Serra A, Leigh RJ, Troncoso XG, Macknik SL, Martinez-Conde S. Distinctive features of saccadic intrusions and microsaccades in progressive supranuclear palsy. J Neurosci. 2011 Mar 23;31(12):4379-87.