This table lists disorders that can mimic PSP. PLEASE READ THESE NOTES BEFORE USING THE TABLE.

- **"Mimic PSP" means that the disorder can have limitation or slowing of downward gaze in at least a few cases. I chose downgaze loss because it's PSP's most specific feature. In no other disorder is the downgaze loss as consistent or as severe relative to upgaze loss as it is in PSP.**
- **This table shows only the differences between the listed condition and PSP. But that doesn't mean that the listed condition otherwise can mimic classic PSP closely. In fact, many people with PSP itself don't have some of the classic features, especially in the early stages.**
- **For many of these diseases, there's little or no Parkinsonism (i.e., general slowing and muscle rigidity). That is not noted in the table because even some people with genuine PSP don't have Parkinsonism early on.**
- **The columns show the**
  - **names of the disorders sorted by category and alphabetically within each category**
  - **points from the general and neurological history that differ from those of PSP**
  - **points from the general and neurological exam that differ from PSP**
  - **a few notes on curative or neuroprotective treatment**
- **PSP experts don't test for these disorders in people with clear signs of PSP who don't have any features on history, exam or brain MRI that are atypical for PSP. So, the vast majority of people who meet, or almost meet, criteria for PSP don't need to be tested for any of these things beyond:**
  - **a good general medical history**
  - **a good general medical and neurological physical exam**
  - **usually a brain MRI without contrast**
- **At each follow-up visit, the neurologist should keep all of these diagnostic alternatives in mind even if there had been no previous evidence for them.**
- **Treatment is listed if and only if it applies to the specific disease as a cure or to slow progression. For such diseases, the listing is highlighted. The symptomatic treatments used in PSP can as a rule be used for the same symptoms in any disease.**
- **Treatments are listed here only if they are generally accepted as effective. Treatments in pre-clinical testing or clinical trials are not listed.**
- **As medicine advances, some of the information listed here (in March 2023) may become obsolete.**
- **To save space, I don't explain many of the technical terms or abbreviations. All physicians will understand them, however.**
- **Parkinson's disease is included here not because it can cause downgaze abnormalities (it doesn't), but because it's the disorder most frequency mis-diagnosed in people who eventually prove to have PSP.**
- **If you leave constructive criticism in the comments area, I'll consider using them in my updates of this document.**

Mimics	Findings in the mimic that are absent, rare or mild in PSP			Specific treatment, if any
	History	Physical/neuro exam	Ancillary tests	
Degenerative				

Corticobasal degeneration	Onset in one upper or lower extremity	Less dementia and balance problem and more asymmetry than PSP; cortical signs, especially sensory, apraxic and language common	MRI: asymmetric frontal, temporal, and/or parietal in most; perfusion SPECT or FDG PET: asymmetric reduced activity	None
Dementia with Lewy bodies	Onset with important cognitive or behavioral features; fluctuating confusion, stupor or coma	Classic Parkinsonian rest tremor; good levodopa response; dysautonomia, delusions and hallucinations important	FDG PET scan showing reduced occipital and normal frontal activity	None
Frontotemporal lobar degeneration	Usually starts with disinhibition or language deficits	Disinhibition usually worse than in PSP; language deficits often prominent; motor deficits usually less than in PSP	On gene sequencing, 20% have a mutation in MAPT, GRN, C9org72, VCP, CHMP2B, TARDBP, RUS, SQSTM1, UBQLN2, TBK1, TREM2 or CHCHD10. MRI, FDG PET and perfusion SPECT show relatively normal midbrain.	None
Globular glial tauopathy	Distinguishable from PSP only on autopsy, though an FTD type exists also.			
Lytico-bodig	Chamorro ancestry; location on Guam	Muscle atrophy common	No clear way to distinguish from PSP.	None
Motor neuron disease with congophilic angiopathy	Muscle weakness with reflex changes	In late stages, fasciculations and pyramidal signs	MRI: deep white matter ischemic changes. Nerve conduction study: reduced compound muscle action potentials	None
Multiple-system atrophy	Autonomic symptoms often occur early	Cerebellar deficits other than gait; autonomic deficits other than constipation and bladder; minimal to no cognitive loss; neck anteroflexion common	MRI: atrophy of cerebellum and pons but not midbrain, with “hot cross bun sign” in pons and “putaminal rim”; autonomic testing diffusely positive in many	None

Pallidal degeneration	Very slow progression	Chorea in some	MRI: little or no midbrain atrophy	None
Parkinson's disease	Marked, years-long response to levodopa in most	Downgaze spared; limb rigidity at least as severe as nuchal rigidity; tremor is complex; dementia is mild and global, not mostly frontal	MRI: midbrain nearly normal in size; atrophy is milder and less frontal than in PSP	Levodopa and deep brain stimulation prolong survival in addition to reducing symptoms.
Structural				
Normal-pressure hydrocephalus	No problems with sleep or behavior; Cognition and bladder are disproportionate issues	Gait usually "magnetic" or otherwise apraxic.	MRI: Ventricles enlarged without proportionate cortical atrophy	CSF drainage, ventricular shunt
Pineal region masses or third ventricular enlargement	Headache or lethargy in some	Fundoscopic signs of high intracranial pressure in some	MRI: Mass at posterior third ventricle compressing midbrain; may or may not enhance	Lesion excision, shunt
Metabolic or Genetic				
Alzheimer's with presenilin 1 mutations	Young adult onset, autosomal dominant family history in most	Fragments of PSP syndrome, sometimes including gaze palsy	"Likely pathogenic" PSEN1 mutation on sequencing; CSF consistent with Alzheimer's; normal DaT scan	None
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)	A series of cerebral infarctions, some large; migraine, reversible encephalopathy and psychiatric disturbances common; family history in most	Only a few cases reported mimicking PSP; signs of other strokes on exam; downgaze loss occurs, but not disproportionately to upgaze	MRI: Multiple or confluent areas of high T2	Mutation in NOTCH3 gene
Frontotemporal lobar degeneration, familial types	see Degenerative			

Gaucher disease types 3a, 3b or 3c	Onset usually in infancy or childhood; slow progression	Enlargement of liver/spleen; severe skeletal abnormalities; myoclonus; ataxia	Low platelets/lymphocytes; high angiotensin-converting enzyme; high ferritin; polyclonal gammopathy; Low WBC glucocerebrosidase activity; GBA gene mutation. Bone imaging: skeletal lesions, marrow infiltration on cranial MRI	GBA enzyme replacement helps non-neurological features only
Huntington's disease	Onset usually in 30s-40s; family history in most	Chorea in most; rigidity/bradykinesia mainly in younger-onset individuals	MRI: caudate atrophy; HD gene test: >39 CAG repeats	None
Niemann-Pick disease type C	Onset in middle age very rare; psychiatric history; suggestive family history in some	Psychosis/schizophrenia, ataxia, dystonia prominent; hepatospleno-megaly in some	Plasma oxysterols; lyso-sphingolipids; NPC1, NPC2 gene sequencing; if inconclusive, bone marrow filipin test; MRI: severe white matter disease on diffusion imaging	Miglustat, but not in those with advanced neurological involvement or dementia
Spinocerebellar ataxias	Onset usually younger than PSP; family history in most	Ataxia most prominent; other features variable; parkinsonian features rare	Gene tests for SCA types 2, 3 and 8	None
Tay-Sachs disease, adult-onset	Psychosis common; Ashkenazi Jewish ancestry common	Hypometric vertical saccades	Low blood hexosaminidase activity; if that's equivocal, heterozygous HEXA gene mutation	None
Wernicke encephalopathy	Nutritional disturbance, usually from alcohol abuse, but also starvation, GI disease, pregnancy, AIDS, malignancy, et al	Ataxia, mostly of gait/balance; combinations of ocular motor loss; often with Korsakoff amnestic encephalopathy in advanced cases; bilateral vertical gaze palsy is rare	Low thiamine or thiamine pyrophosphate level; CT: hemorrhages in many; MRI: high T2, low T1 lesions in brainstem, cerebellum, cerebral cortex; mamillary body atrophy if chronic	Thiamine; general dietary and nutritional support
Wilson's disease	History of liver disease in most; Onset almost never after age 50	Kayser-Fleischer rings in 98% with neuro signs; liver signs; any sort of movement disorder	Low serum ceruloplasmin, abnormal liver function tests; high urinary copper excretion;	D-penicillamine or trientine; zinc salts long-term and low copper diet for longer-term

			Abnormal liver/spleen on imaging; liver biopsy or ATP7B gene test if uncertain	
Immune				
Anti-IgLON5 disease	REM and non-REM parasomnias and sleep apnea very common; in 25%, progression to disability over a few months	Chorea in a third; otherwise often a close PSP mimic	Antibodies to IgLON5; video-polysomnography may be helpful	Corticosteroids, IgG, plasma exchange and/or other immunomodulators
Paraneoplastic syndromes	Cancer history in most; progression over months, not years	Evidence of cancer in some	Paraneoplastic antibody screen; many associated rarely with PSP-like syndrome	Immunotherapyas above, but usually not very effective
Postencephalitic parkinsonism	History of encephalitis	Many forms; vertical gaze palsy is usually in attacks lasting minutes to hours	None	None specific, though responds well to levodopa
Vascular				
Lacunar states ("vascular PSP")	History of stroke risk factors, especially hypertension; course can stabilize for years	Gait disproportionately affected; asymmetric pyramidal signs are frequent	MRI: chronic vascular lesions, especially in basal ganglia and upper brainstem	Treat the treatable risk factors: hypertension, diabetes, hyperlipidemia
Post-aortic surgery	Starting a few days after apparently uncomplicated major aortic surgery with hypothermia	Gaze, gait and speech (ataxic) most common	MRI: no more vascular damage than typical for population with aortic disease	None
Infectious				
Whipple's disease	Chronic diarrhea, abdominal pain, weight loss, arthritis	Oculo-masticatory myorhythmia in 20%; cognitive loss, ataxia myoclonus, nystagmus, SIADH, obstructive sleep apnea, seizures, etc.	Whipple bacteria on duodenal biopsy; anemia; CSF: PCR for Whipple bacterium; MRI: enhancing area in hypothalamus; lack of response to	IV antibiotics for CNS involvement

		(Little/no rigidity or bradykinesia)	immunomodulators hints at dx	
Neurosyphilis	Isolated case reports only; more rapid progression than PSP; history of syphilis in nearly all	Highly variable	If serum RPR or VDRL positive or if suspicion is high, then CSF: FTA ABS or TP-PA; MRI: multiple small infarctions in basal ganglia; midbrain not atrophic	Antibiotics
AIDS	PSP-like syndrome can be the initial manifestation	Other signs of infection	HIV titer	Antiretroviral treatment likely effective
Toxic				
Guadeloupean tauopathy	Residence on Guadeloupe or nearby islands. Hallucinations, REM behavioral disorder and dysautonomia common.	Cortical myoclonus	MRI: abnormalities in temporal, occipital, limbic and cerebellum, not much in midbrain	None
Prion				
Creutzfeldt-Jakob disease	Clear progression over months, not years	Dementia is disproportionate. Myoclonus is prominent.	CSF RT-QuIC for prion protein. When familial, PRNP gene mutation	No treatment, but prevention of transmission is important