Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome):

Report of the NINDS-SPSP International Workshop*

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Article abstract—To improve the specificity and sensitivity of the clinical diagnosis of progressive supranuclear palsy (PSP, Steele-Richardson-Olszewski syndrome), the National Institute of Neurological Disorders and Stroke (NINDS) and the Society for PSP, Inc. (SPSP) sponsored an international workshop to develop an accurate and universally accepted set of criteria for this disorder. The NINDS-SPSP criteria, which were formulated from an extensive review of the literature, comparison with other previously published sets of criteria, and the consensus of experts, were validated on a clinical data set from autopsy-confirmed cases of PSP. The criteria specify three degrees of diagnostic certainty: possible PSP, probable PSP, and definite PSP. *Possible PSP* requires the presence of a gradually progressive disorder with onset at age 40 or later, either vertical supranuclear gaze palsy or both slowing of vertical saccades and prominent postural instability with falls in the first year of onset, as well as no evidence of other diseases that could explain these features. *Probable PSP* requires vertical supranuclear gaze palsy, prominent postural instability, and falls in the first year of onset, as well as the other features of possible PSP. *Definite PSP* requires a history of probable or possible PSP and histopathologic evidence of typical PSP. Criteria that support the diagnosis of PSP, and that exclude diseases often confused with PSP, are presented. The criteria for probable PSP are highly specific, making them suitable for therapeutic, analytic epidemiologic, and biologic studies, but not very sensitive. The criteria for possible PSP are substantially sensitive, making them suitable for descriptive epidemiologic studies, but less specific. An appendix provides guidelines for diagnosing and monitoring clinical disability in PSP.

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Progressive supranuclear palsy (PSP), also called Steele-Richardson-Olszewski syndrome, is one of the most common atypical parkinsonian syndromes. PSP was well described as a clinicopathologic entity in 1964,[1,2] although a few single clinical or pathologic reports were previously published.[3-6] The estimated prevalence of PSP is 1.39 per 100,000 inhabitants after age adjustment to the U.S. population.[7,8] However, this is probably a considerable underestimate, as diagnosed cases are often not recognized until the disease has run half its course,[9] and probably many more patients die without a diagnosis, or have a misdiagnosis, usually Parkinson's disease (PD).

Currently, there is no biologic marker for the diagnosis of PSP. Neuropathologic examination remains the "gold standard" for its definitive diagnosis. Preliminary National Institute of Neurological Disorders and Stroke (NINDS) neuropathologic criteria for the diagnosis of PSP and related disorders were recently proposed.[10,11] The NINDS neuropathologic criteria[11] specified two subtypes of PSP: typical and combined. (The subtype of atypical PSP originally proposed[10] is omitted from this discussion because it was found not to be reliable.[11]) *Typical PSP* conforms to the original description of Steele et al.[1] The neuropathologic characteristics of PSP include a high density of neurofibrillary tangles and neuropil threads in the basal ganglia and brainstem with a characteristic distribution.[10-14] Neuropil threads are filamentous structures scattered throughout the neuropil, occurring independently of neurofibrillary tangles and indicating a diffusely distributed disease of the

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cytoskeleton.[12] Tau-positive astrocytes or processes in areas of involvement help to confirm the diagnosis.[10,13,14] These characteristic pathologic findings are accompanied by a relatively nonspecific and variable neuronal loss and gliosis. *Combined PSP* is restricted to the coexistence of neuropathologically typical PSP and vascular lesions in the brainstem and basal ganglia.[11] Otherwise, when vascular lesions are found in areas distinct from these characteristically affected in PSP, or other CNS disorders occur, the diagnosis should be typical PSP plus the associated disease.[11,15] Patients with a neuropathologic diagnosis of PSP may also have other associated neurodegenerative disorders.[16] Neuropathologists, therefore, may be routinely confronted with complicated PSP cases, and could benefit from the use of standardized criteria for PSP diagnosis.

Neuropathologically confirmed cases of corticobasal ganglionic degeneration (CBGD), dementia with Lewy bodies, cerebrovascular disease, subcortical gliosis, prion disease, and multiple system atrophy have been clinically misdiagnosed as PSP.[17-25] In a recent study,[26] in which retrospectively collected and abstracted clinical and laboratory data on 105 cases of parkinsonism or dementia were presented to six neurologists for "blind" diagnosis, false-positive diagnoses accounted for up to 24 to 50% of the PSP diagnoses. In addition, neuropathologically confirmed cases of PSP may be confused clinically with other syndromes in which the clinical features overlap with those of PSP, such as PD, CBGD, multiple system atrophy, and Alzheimer's disease (AD).[27-31] Misdiagnosis not only hinders the study of PSP, but also work on disorders with which it is confused. Currently, there is no effective treatment for PSP.[32]

The recruitment of a population of patients with an accurate diagnosis of PSP is essential for therapeutic and epidemiologic research and for the confident comparison of the findings from different studies. This effort depends on the availability of standard clinical criteria for the diagnosis of PSP. There are several published sets of criteria for the clinical diagnosis of PSP[33-38] but, though some of them are reliable, they incorporate many false-negative or false-positive cases.[26] On May 5 and 6, 1995, the NINDS and the Society for Progressive Supranuclear Palsy, Inc. (SPSP) sponsored the NINDS-SPSP international workshop to develop an accurate and universally accepted set of criteria for the diagnosis of PSP.

This paper presents the consensus findings on the diagnosis of PSP resulting from the workshop and reviews the main studies that led to their development. We describe the common and uncommon clinical features of PSP, review the validity of previously published criteria, and report on the validity of the NINDS-SPSP clinical criteria as determined in a well-characterized data set.

Common clinical features of PSP. The medical history and physical examination are most relevant for making the clinical diagnosis of PSP, but the lack of systematic evaluation of patients and overlap of symptoms make the early diagnosis difficult. Therefore, the following description of the typical clinical features of PSP is based mainly on cases with known neuropathology.[39-42]

The onset of symptoms in PSP is insidious, and the evolution of symptoms may vary. The mean age at PSP onset ranges from 55 to 70 years,[39-42] with a few cases beginning as early as 45 years of age. The first symptoms of PSP are usually postural instability and falls, which occur either at the onset of the disease (in 63% of the cases reviewed[42]) or during the first year (in 69% of the cases[39]). Cognitive or behavioral changes usually begin in the first year (in 52% of the cases[39]), but rarely occur at the disease onset (in 8% of the cases[42]). After postural instability, dysarthria is the second most common symptom of PSP (in 33% of cases at onset[42] and 40% during the first year[39]), and bradykinesia is the third most common problem (in 13% of cases at onset[42] and 22% during the first year[39]).

Visual disturbances (e.g., diplopia, blurred vision, burning eyes, and light sensitivity) are also early symptoms (in 13% of newly diagnosed PSP cases[42] and during the first year in 64%[39]). Characteristically, supranuclear gaze deficits in PSP involve initially either downward or upward gaze and, later, horizontal gaze. Vertical supranuclear palsy, the hallmark of the disease, may be present at the disease onset, but in many cases may only be detected several years later, or may never develop.[6,41] Because limitation of upward gaze is more common than limitation of downward gaze in neurodegenerative disorders, and because there is also a certain degree of upward gaze restriction with aging, limitation of downward gaze is considered more specific for the diagnosis of PSP.[33,41,43]

Early in the course of the disease, pursuit eye movements may become saccadic; voluntary saccades may become slow with preserved range of motion, or hypometric saccades may develop. In addition, patients may fail to suppress the vestibuloocular reflex, and may have abnormalities in convergence.[44] Later signs include slowing of eye opening or eye closure, slowing of eyelid saccades (i.e., eyelid movement occurring when subjects with supranuclear palsy attempt to make a vertical saccade), and an inability to suppress a blink to a bright light, (i.e., a "visual" rather than a somatosensory glabella, or Meyerson, sign) (personal communication, D.S.Z.).

The first clinical visit to a tertiary center occurs a mean of 1.5 to 3.7 years after the onset of PSP symptoms.[42] In 16 cases of PSP confirmed by pathologic examination, Colosimo et al.[41] reported that within 3 years of onset 94% had bilateral parkinsonism and instability, 81% symmetrical onset, 50% vertical supranuclear palsy, 56% axial "dystonia," and 50% had cognitive impairment. At the first visit, in the study by Litvan et al.,[42] PSP patients had gait disorder and postural instability, a history of falls, bilateral bra-

Table 1 *Salient features of PSP in five autopsy-confirmed series*

Features	Litvan et al.[42] (n = 24)*	Colosimo et al.[41] (n = 16)†	Collins et al.[38] (n = 12)‡	Verny et al.[57] (n = 21)§	DeBruin and Lees[40] (n = 90)**
Parkinsonism					
Bradykinesia	21 (88)	—	11 (100)††	20 (95)	60 (67)
Gait disorder	23 (96)	—	12 (100)	19 (90)	63 (71)
Falls	20 (83)	—	12 (100)	19 (90)	54 (61)
Rigidity	16 (77)	—	—	—	52 (58)
Neck dystonia	5 (21)	9 (56)	4 (33)††	7 (33)	43 (48)
No levodopa benefit	9/11 (82)‡‡	12 (75)	7 (64)††	17 (81)	—
No tremor	19 (79)	10 (63)	9 (75)††	14 (67)	75 (83)
Other					
Vertical supranuclear palsy	19 (79)	8 (50)	11 (100)††	19 (90)	61 (69)
Frontal lobe abnormalities	11 (46)	8 (50)	—	17 (81)	34 (37)
Extensor plantar response	5 (21)	—	8 (66)††	11 (52)	30 (34)
Dysarthria	18 (75)	—	11 (100)††	19 (90)	60 (67)
Bulbar palsy (dysphagia and dysarthria)	4 (17)	—	6 (55)††	—	51 (57)
Cerebellar signs	2 (8)	—	1 (8)	—	6 (7)

Values are number and percent of patients with PSP features for the first visit in Litvan et al.[42] or the last visit in the other studies.[38,40,41,57]

* Nine women, 15 men; mean disease duration, 6.6 years.
† Sex not specified; mean disease duration, 6.7 years.
‡ Three women, nine men; mean disease duration, 5.3 years.
§ Fifteen women, six men; disease duration not specified.
** Thirty-four women, 51 men; mean disease duration, 5 years.
†† Data missing for one patient.
‡‡ Number and percent of patients in total number of patients treated with levodopa.

dykinesia, a predominant akinetic-rigid disease course, vertical supranuclear palsy, dysarthria, dysphagia, axial rigidity, neck dystonia, frontal lobe type symptoms, and personality changes involving mostly apathy and depression (table 1). The presence of "staring," nonblinking facies (in 92% of cases), and sitting "en bloc" (in 30% of cases) are also characteristic of PSP.[38] In contrast with the hypomimia of PD, the facial expression of patients with PSP is often described as "worried" or "astonished."[45]

In general, the early symptoms and signs of PSP steadily worsen. Gait abnormalities with postural instability and bradykinesia are observed in most patients at the last visit (table 1). The mean survival of PSP from disease onset is 5 to 6.7 years (range, 1 to 13 years) in autopsy series[38-42] and 5.9 to 6.9 years (range 1 to 17) in clinical ones.[7-9] The most common cause of death is pneumonia.[42]

Uncommon clinical features of PSP. Features of PSP that deviate from the usual disease course, and do not support the diagnosis, include onset of symptoms before age 40 or a disease duration of more than 20 years. However, there are other uncommon features that do not exclude the diagnosis of PSP: late onset of postural instability and falls, mild asymmetric parkinsonism, and absence of cognitive disturbances.[38,42] Infrequently, PSP may present with absence of gaze restriction, pure akinesia, severe dementia, or a family history of PSP.[46-55] It is unclear whether these unusual features have any biologic significance since, in a small series,[56] no histologic distinction could be made between cases of PSP with vertical supranuclear palsy, a sign that is considered to be essential for the diagnosis, and cases without it.

Proposed NINDS-SPSP criteria. The NINDS-SPSP criteria were developed in two phases. In the first phase, previously published criteria for the clinical diagnosis of PSP[33-35] were validated by six neurologists, who were unaware of the diagnosis, using clinical information retrospectively abstracted from clinical records of patients with autopsy-confirmed cases of dementia or parkinsonism provided by seven medical centers specializing in neurodegenerative disorders.[26] The diagnoses of these cases were based on the NINDS neuropathologic criteria,[11] which have been shown to have substantial interobserver reliability. Because the previously published clinical criteria[33-35] were found to be suboptimal, new prelimi-

Table 2 Features distinguishing PSP-related disorders from PSP

Corticobasal ganglionic degeneration
Alien limb syndrome
Severe limb apraxia (inability to use correctly mimed objects, or perform symbolic gestures on command)
Cortical sensory deficits
Markedly asymmetric onset of bradykinesia
Focal frontal or temporoparietal atrophy
Parkinson's disease
Asymmetric onset of bradykinesia symptoms
Tremor-dominant disease
Marked and prolonged levodopa benefit
Dementia with Lewy bodies
Hallucinations or delusions unrelated to dopaminergic therapy
Cortical dementia, especially aphasia
Alzheimer's disease
Cortical dementia (severe amnesia and aphasia, or agnosia, NINCDS-ADRDA criteria)
Multiple system atrophy
Prominent cerebellar symptomatology or unexplained early and prominent incontinence, impotence, or marked postural hypotension*
Multiinfarct parkinsonism
Multiple strokes, one of which involves the brainstem and basal ganglia
Whipple's disease
Ocular-masticatory myorhythmia, laboratory confirmation (e.g., polymerase chain reaction), if indicated
Postencephalitic parkinsonism
History of encephalitis, oculogyric crisis
Jakob-Creutzfeldt disease
Disease course of <1 year, myoclonus, EEG abnormalities

* Mild, or late onset urinary disturbances occur in some PSP patients.

nary clinical criteria were proposed and validated in the same data set.[26]

In the second phase, the preliminary clinical criteria were revised by the consensus of experts (movement disorder specialists, neuroophthalmologists, behavioral neurologists, and neuropsychologists) experienced with the diagnosis of PSP. These experts, meeting in plenary session, refined the criteria by characterizing the common and uncommon clinical features of PSP, as discussed earlier, differentiating the features of PSP and related disorders (table 2), and reviewing the relevant literature. Finally, NINDS-SPSP criteria, specifying mandatory inclusion and exclusion criteria, as well as supportive criteria, were adopted (table 3). These criteria were evaluated in a well-characterized data set containing information commonly available in carefully made records. The data set comprised 83 cases of autopsy-confirmed parkinsonian disorders (table 4), including PSP (n = 24), CBGD (n = 11), PD (n = 11), dementia with Lewy bodies (n = 14), multiple system atrophy (n = 15), and Pick's disease (n = 8). Patients were selected from the research and clinical neuropathologic files of seven medical centers in Europe and the United States by neuropathologists[42] who used the NINDS neuropathologic criteria for the diagnosis of PSP and related disorders for their diagnoses.[10,11] The patient records were abstracted by neurologists who followed strict instructions such as to record as missing any features that were not explicitly described in the records and to record clinical descriptions uniformly, according to specific definitions provided. The sensitivity, specificity, and positive predictive values for the diagnosis of PSP were chosen as measures of validity. Sensitivity is defined as the percentage of cases with a clinical diagnosis of PSP using a set of criteria among all PSP cases confirmed by neuropathologic examination. Specificity is the percentage of cases without a clinical diagnosis of PSP among all non-PSP cases confirmed by neuropathologic examination. Positive predictive value is the percentage of autopsy-confirmed PSP cases among all cases with a clinical diagnosis of PSP using a set of criteria. The validity of the NINDS-SPSP criteria, compared with that of previously proposed criteria,[33-38] is shown in table 5.

Discussion. This is the first attempt to develop criteria for the diagnosis of PSP following a programmatic effort that included the standardization of neuropathologic[11] as well as clinical criteria.[26] In spite of the thorough process used, the validity of the NINDS-SPSP criteria needs to be tested in prospective studies.

The possibility of detecting and validating the clinical criteria in a well-characterized data set with known neuropathologic diagnosis allowed us to concentrate on the early symptoms of the disease. Early postural instability with falls and neuroophthalmologic findings helped us to avoid the usual misdiagnosis of PSP as PD. Moreover, falls occurring during the first year in a patient with either upward or downward gaze supranuclear palsy, *but without any of the exclusionary features*, strongly indicated the diagnosis of PSP, because none of the patients with this cluster of features had any other disease. However, in our study, upward-gaze abnormalities were moderately to severely restricted (at least 50% of the normal range) to eliminate age-related impairments. Further, when we included only downward-gaze palsy as one of the criteria for probable PSP, there was no effect on specificity, but the sensitivity decreased to 38%, compared with 50% when vertical gaze palsy was used. The result was similar for possible PSP.

Even though the features proposed for the diagnosis of probable PSP are highly specific (100%), they are not sensitive enough, as they can detect only half of the patients at the first visit. Thus, the NINDS-SPSP criteria for the diagnosis of *probable* PSP are suitable for clinical drug trials or studies on the biol-

Table 3 *NINDS-SPSP clinical criteria for the diagnosis of PSP*

PSP	Mandatory inclusion criteria	Mandatory exclusion criteria	Supportive criteria
Possible	Gradually progressive disorder Onset at age 40 or later	Recent history of encephalitis Alien limb syndrome, cortical sensory deficits, focal frontal or temporoparietal atrophy	Symmetric akinesia or rigidity, proximal more than distal Abnormal neck posture, especially retrocollis
	Either vertical (upward or downward gaze) supranuclear palsy* or both slowing of vertical saccades* and prominent postural instability with falls in the first year of disease onset	Hallucinations or delusions unrelated to dopaminergic therapy Cortical dementia of Alzheimer's type (severe amnesia and aphasia or agnosia, according to NINCDS-ADRA criteria)	Poor or absent response of parkinsonism to levodopa therapy* Early dysphagia and dysarthria
	No evidence of other diseases that could explain the foregoing features, as indicated by mandatory exclusion criteria	Prominent, early cerebellar symptoms or prominent, early unexplained dysautonomia (marked hypotension and urinary disturbances)*	Early onset of cognitive impairment including at least two of the following: apathy, impairment in abstract thought, decreased verbal fluency, utilization or imitation behavior, or frontal release signs*
Probable	Gradually progressive disorder	Severe, asymmetric parkinsonian signs (i.e., bradykinesia)	
	Onset at age 40 or later	Neuroradiologic evidence of relevant structural abnormality (i.e. basal ganglia or brainstem infarcts, lobar atrophy)	
	Vertical (upward or downward gaze) supranuclear palsy* *and* prominent postural instability with falls in the first year of disease onset*	Whipple's disease, confirmed by polymerase chain reaction, if indicated	
	No evidence of other diseases that could explain the foregoing features, as indicated by mandatory exclusion criteria		
Definite†	Clinically probable or possible PSP *and* histopathologic evidence of typical PSP[10]		

* See Appendix for testing guidelines. Upward gaze is considered abnormal when pursuit or voluntary gaze, or both, have a restriction of at least 50% of the normal range.

† Definite PSP is a clinicopathologic diagnosis.

ogy of the disease, when it is essential to exclude subjects with illnesses other than PSP. On the other hand, the NINDS-SPSP criteria for the clinical diagnosis of *possible* PSP, which are more sensitive (detected 83% of the patients at the first visit 3 years after onset) but less specific (false-positive ratio of 17%), are more suitable for descriptive epidemiologic studies or clinical care, when it is important to identify all, or nearly all, cases of PSP even at the cost of including a few false-positive cases.

Slowing of vertical saccades is suggested as an early sign of PSP (see Appendix), but missing data precluded us from evaluating its predictive value in this data set. However, 13% percent of the PSP patients whose condition was not detected with the NINDS-SPSP criteria for possible PSP had postural

Table 4 *Characteristics of the 83 cases studied*

Disorder*	No. of cases	Age at onset (yr)	Time from symptom onset to first examination (yr)	Time from symptom onset to death (yr)
PSP	15M/9F	63 ± 2	3.7 ± 0.5	6.6 ± 0.7
Corticobasal ganglionic degeneration	6M/5F	62 ± 3	2.8 ± 0.6	7.8 ± 0.9
Parkinson's disease	10M/1F	54 ± 3	6.8 ± 2.1	15.6 ± 2
Dementia with Lewy bodies	9M/5F	66 ± 3	3.2 ± 0.7	7.5 ± 2
Multiple system atrophy	9M/6F	55 ± 3	3.8 ± 0.7	67 ± 0.6
Pick's disease	4M/4F	66 ± 4	3.4 ± 0.7	6.9 ± 1

Values are mean ± SEM.

* Clinicopathologic diagnosis.

PSP = progressive supranuclear palsy.

Table 5 Validity of PSP diagnostic criteria at the first visit

Criteria	Sensitivity (%)*	Specificity (%)*	Positive predictive value (%)*
NINDS-SPSP			
Probable	50	100	100
Possible	83	93	83
Blin et al.[34]			
Probable	21	100	100
Possible	63	85	63
Lees[33]	58	95	82
Golbe and Davis[35]	50	98	92
Tolosa et al.[37]			
Probable	54	98	93
Possible	54	98	93
Collins et al.[38]			
Possible	42	92	67
Verified	25	100	100

* See Methods for definitions.

instability with falls within 1 year of onset. Therefore, alternative, untested criteria for possible PSP, in the absence of supranuclear limitation of vertical gaze, are slow vertical saccades together with early postural instability with falls (table 3). Because slowing of vertical saccades was not part of the clinical criteria tested in the present study, this feature needs to be subjected to a similar validation study.

The exclusionary criteria (table 3) are important because they provide the specificity for the diagnosis of PSP. For example, in possible PSP, the omission of the exclusionary criteria decreases the specificity to 89% and the positive predictive value to 77%.

The supportive criteria (table 3) are included to remind physicians of important features often associated with PSP, but that are neither essential nor sufficient for the diagnosis. Some of these features, such as retrocollis, occur infrequently. Others, such as a poor response to levodopa or frontal lobe symptoms, may become more relevant for the diagnosis when tested prospectively. Similarly, there may be other features, such as early palilalia, that could be identified and tested for diagnostic relevance.

The proposed NINDS-SPSP criteria improve upon previously published sets of criteria.[26] Prospective studies are needed to determine whether ancillary studies can further improve the diagnosis of PSP. These investigations should validate the usefulness of (1) neuropsychological studies of frontal lobe dysfunction,[58-63] (2) PET studies to determine frontal cortex metabolism and striatal dopamine D2-receptor function,[64-72] (3) recording of event-related potentials to assess normal early N1 component and delayed P2 and P300 components,[73-75] (4) electrophysiologic testing of the auditory startle response,[76,77] (5) recording of eye movements to detect early abnormalities,[43,44,78] (6) MRI to detect brainstem atrophy and to rule out other disorders,[79-81] and (7) polysomnographic studies to detect abnormalities of rapid-eye movement sleep.[82-85]

Ideally, the proposed NINDS-SPSP criteria will assist in identifying biologic markers that in turn will yield an earlier diagnosis of this disorder.

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Appendix: Guidelines for testing. *Testing eye movements.* Limitation of the range of voluntary downward vertical gaze, which is overcome by reflexive stimulation, is the established ocular motor criterion for the diagnosis of PSP. However, slowing of either upward or downward vertical saccades, before the range of downward gaze becomes restricted, is an early sign of PSP that may be as specific as an actual limitation of gaze (D.S.Z., unpublished data). The slowing of saccades can be best elicited by having the patient make voluntary saccades on command between stationary targets located straight ahead and down. In some PSP patients, limitation of upward gaze may occur before limitation of downward gaze. Other common ocular motor signs of PSP are (1) greater involvement of vertical than horizontal eye movements, (2) excessive frequency or amplitude of square-wave jerks (saccadic intrusions on fixation that take the eyes away from and, after a brief intersaccadic interval of several hundred milliseconds, back to the target), (3) slowness of eyelid opening or closure, and (4) difficulty performing the antisaccade task (looking in the direction opposite to a novel visual stimulus). Recording of eye movements may help differentiate PSP from CBGD, striatonigral degeneration, and PD,[78] but in practice such measures can usually be obtained only in the horizontal plane (few laboratories are capable of performing quantitative oculography in the vertical plane). The typical pattern in PSP includes an increase in the percentage of errors in the antisaccade task, hypometric saccades but with normal latencies, and impaired pursuit.[78] With vestibular and optokinetic stimulation, the initiation of quick phases is impaired, leading to a tonic deviation of the eyes in a lateral position in the orbit.

Testing posture and balance. Postural reflexes should be tested with the subject standing with the eyes open and the feet slightly separated. After testing of a possible spontaneous tendency to fall, the tendency to fall after a backward pull should be tested. If the subject has retropulsion but recovers unaided, or falls if not caught by the examiner, the postural stability test is considered abnormal. Item 43 of the the Unified Parkinsonism Disability Rating Scale[86] could be used to test postural stability. PSP patients typically have a stiff gait with the legs extended at the knee (not flexed, as is typical in PD patients) and pivoting (rather than en bloc shuffle) when turning.

Testing response to levodopa therapy. The response of the parkinsonism to levodopa therapy should be tested with at least 25/250 mg of carbidopa/levodopa administered three times a day for at least 2 months. The response to levodopa is considered poor when the extrapyramidal

features fail to show marked improvement, or the therapeutic effect is transient (i.e., lasts less than a year). In PSP patients, dyskinesia rarely, if ever, develops, even at high (1 g) levodopa dosages but dystonia may occur.

Neurobehavioral testing. Patients with PSP typically have cognitive deficits and personality changes suggestive of frontal lobe dysfunction.[58-62,87] The deficits include decreased verbal fluency, concreteness in thinking, impaired reasoning, slowed information processing, lack of insight, poor information retrieval, impaired control over attention or execution of sequential actions, and problems in shifting back and forth between two different tasks. The cognitive changes may be severe enough to warrant the diagnosis of dementia. Personality changes may include apathy, reflecting a lack of concern about personal behavior or the behavior of others, or disinhibition, often appearing as bulimia, inappropriate sexual behaviors, or aggression, which occasionally are among the first signs of PSP.

The following bedside testing can assess for neurobehavioral changes typical of PSP by asking the patient to (1) interpret a proverb or deduce the conceptual relationship between two different objects or items, as in the Similarities subtest of the Wechsler Adult Intelligence Scale (WAIS-R), (2) provide the maximum number of words beginning with a given letter in 1 minute, as a measure of verbal fluency, (3) reproduce with one hand a motor sequence that tests executive functions, and (4) tap once when the examiner taps twice and vice versa, as a test of inhibition of task interference. In addition, observe the patients for signs of apathy or aggressive and disinhibited conduct and for a tendency to prehend (grab) involuntarily objects placed in front of them.

The following neuropsychological examination may be helpful in better defining and quantifying PSP patient deficits by administering tests such as: (1) the Mattis Dementia Rating Scale to evaluate global cognitive-intellectual efficiency, (2) the Wisconsin Card Sorting Test, Picture Arrangement Subtest, and Similarities Subtest from the WAIS-R to assess concept formation and reasoning, (3) the Stroop Test to test inhibitory function, (4) the Trail-Making Test (Parts A and B), the Choice Versus Simple Reaction Times Test, and the Paced Auditory Serial Attention Task to measure attentional control and cognitive speed, (5) the Grober-Buschke Word List Learning Test, the California Verbal Learning Test, or the Rey Auditory Verbal Learning Test to test memory, and (6) the Token Test, the Comprehension Subtests of the Boston Diagnostic Aphasia Examination, the Benton Visual Perception Battery, and the Test of Limb Apraxia to exclude other neurodegenerative disorders with extrapyramidal features. A description of these tests can be found in Lezak.[88]

Given the physical restrictions of some PSP patients (e.g., restricted eye movements and impaired motor agility), some of the procedures may require modification. Few tests assessing the cognitive functions associated with the frontal lobe have large normative population standards, so performance on these "frontal lobe" tests should be interpreted with caution.

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