A 80-year-old female with severe cognitive impairment and left dominant parkinsonism

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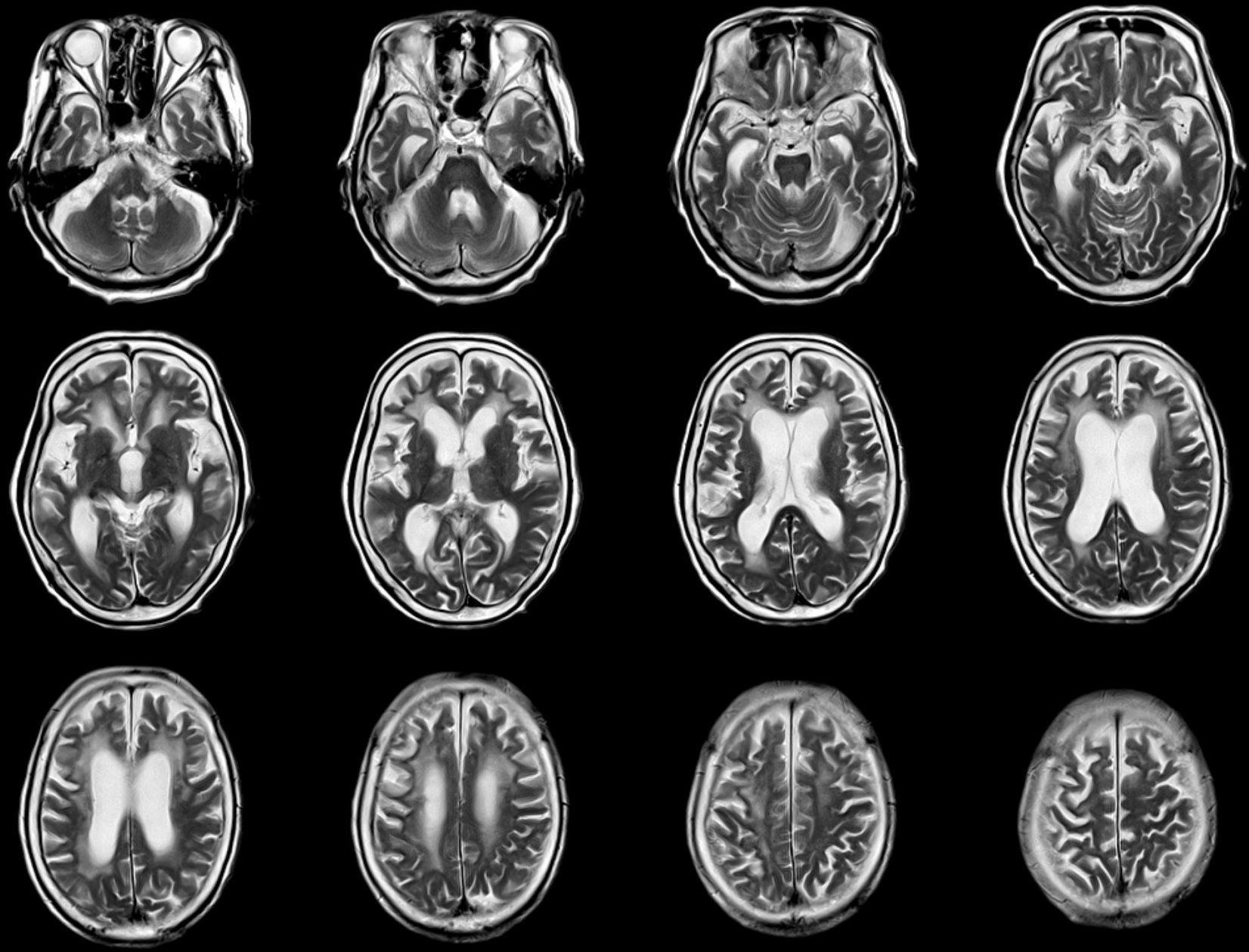
Case; 80-year-old female

Chief complain: cognitive impairment and parkinsonism

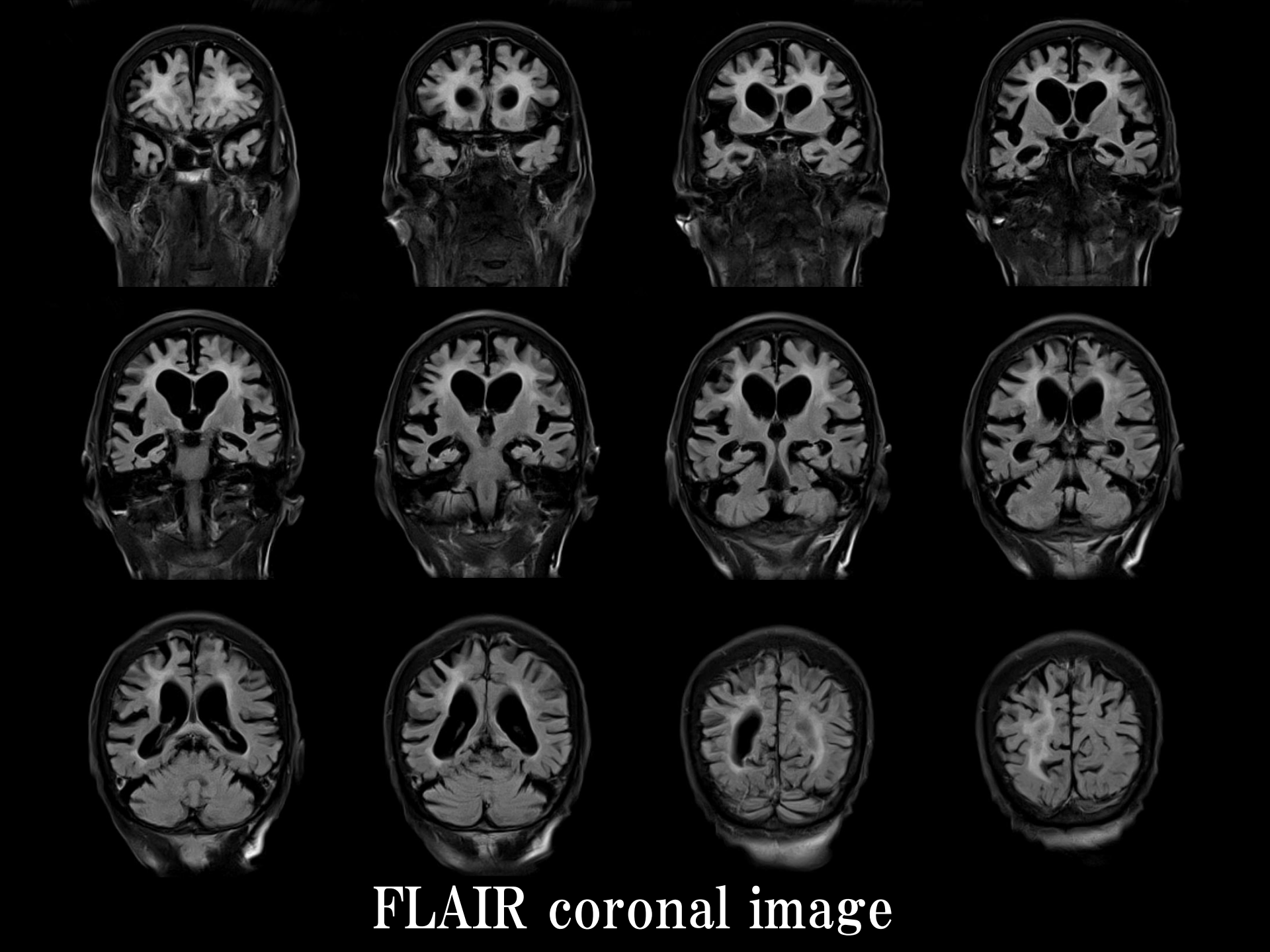
Case history: Patient suffered from cognitive impairment 5 years ago. Additionally, abnormal behaviors developed 3 years prior to the examination.

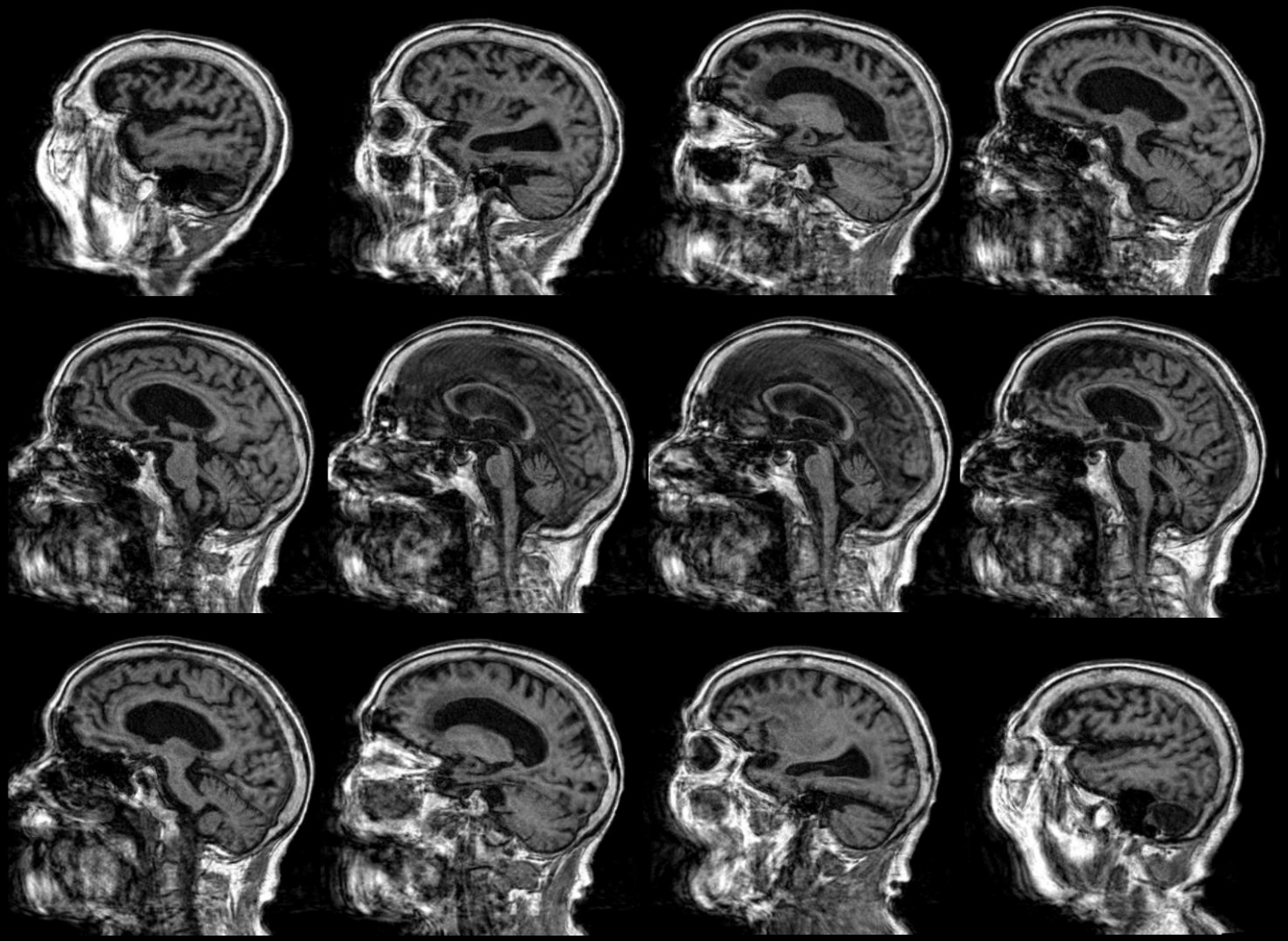
Neurological findings:

- Severe cognitive impairment (MMSE 5/30)
- Impairment of gait and postural reflex
- Tendency to fall
- Left dominant limb rigidity
- No symptoms suggesting aphasia, ataxia and oculomotor disturbance



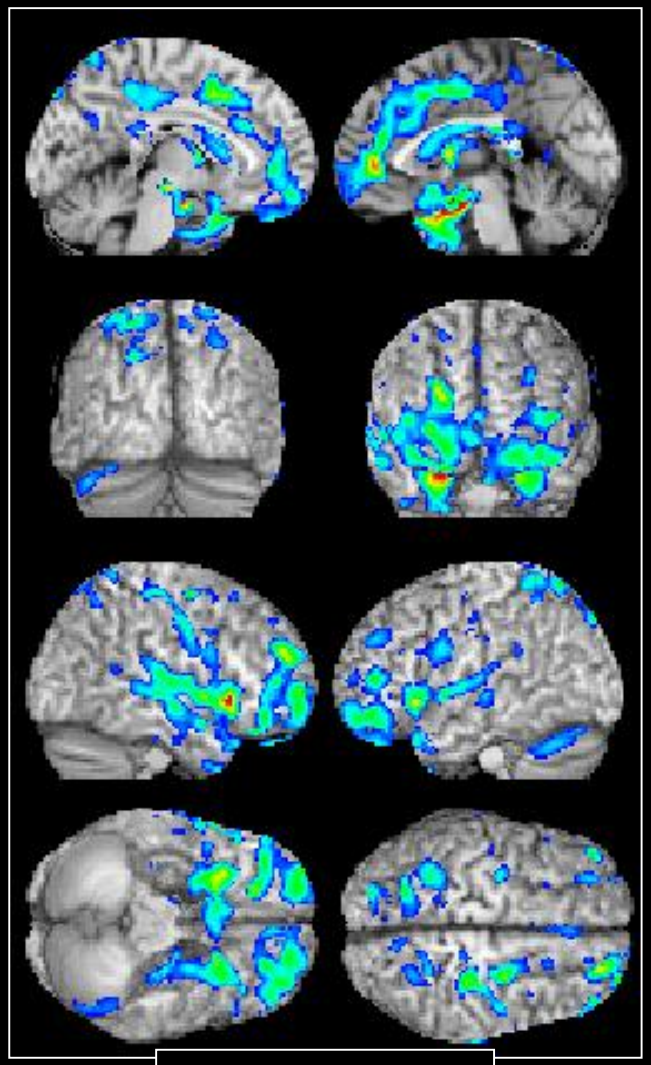
T2W axial image


FLAIR coronal image

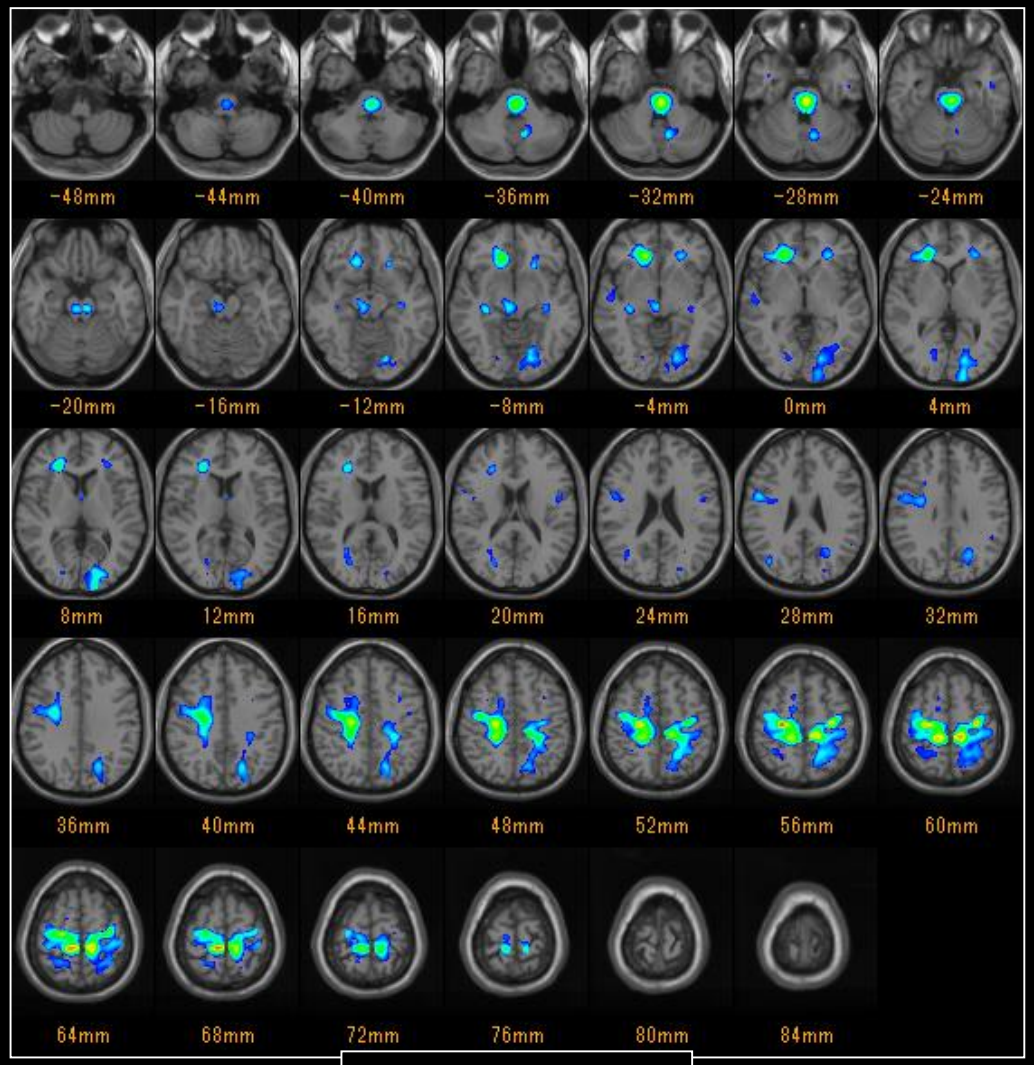


MPRAGE sagittal image (R→L)

- Midbrain (M) = 61.4 mm^2
- Superior cerebellar peduncle = 3.2 mm
- Middle cerebellar peduncle = 7.8 mm
- Pons (P) = 437.5 mm^2
- M/P = 0.14
- MR parkinsonism index = 17.4



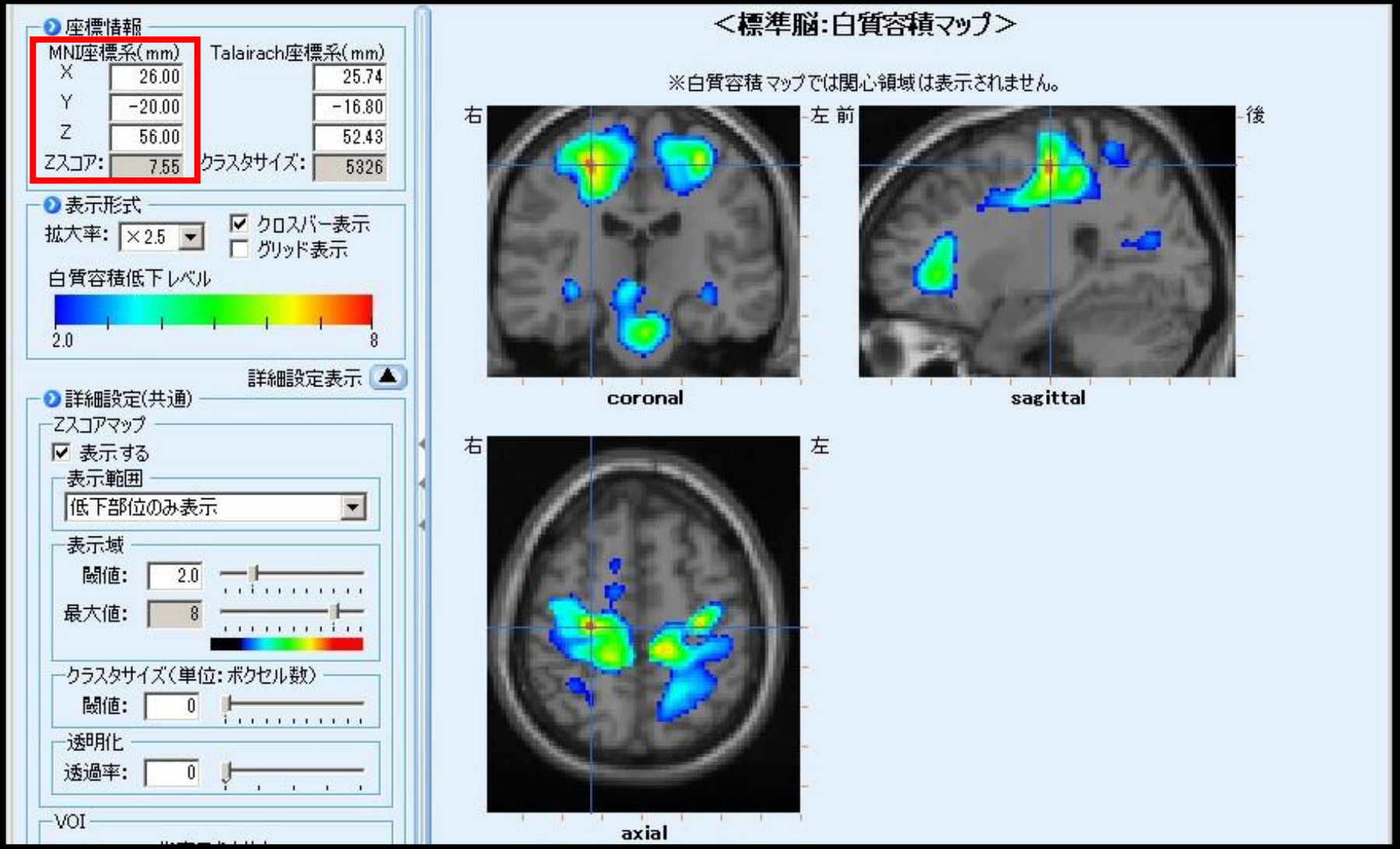
Gray matter



White matter

VSRAD advance (volume reduction)

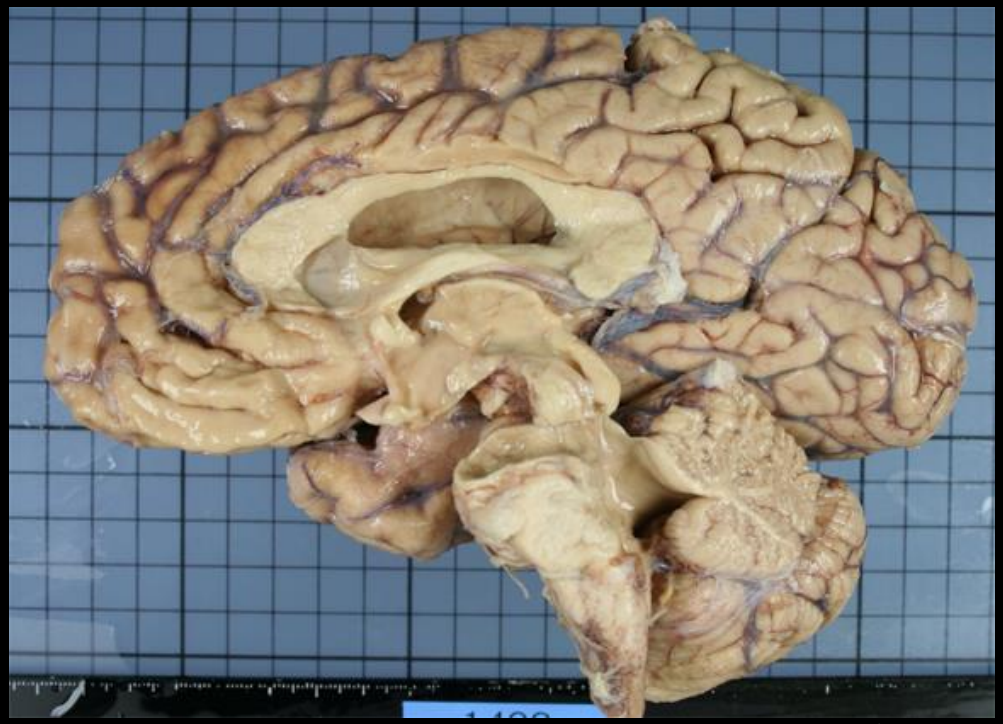
Gray matter: brain surface　White matter: axial

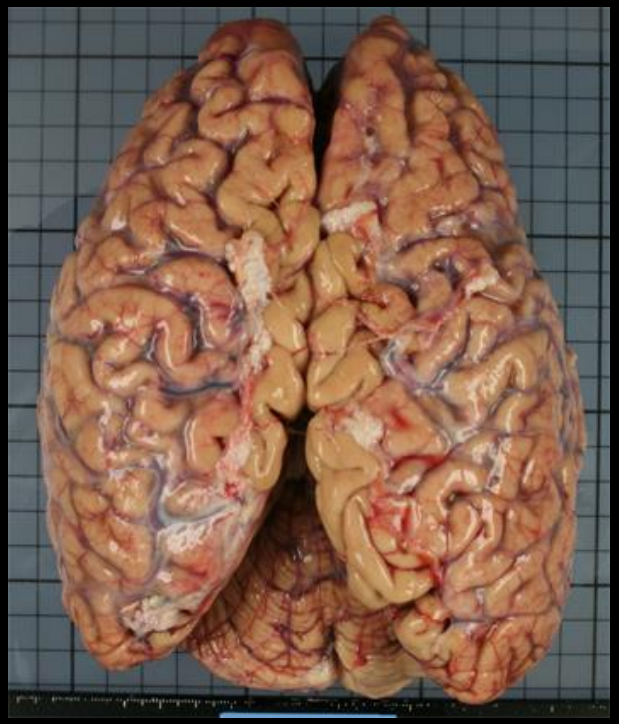


VSRAD advance white matter analysis

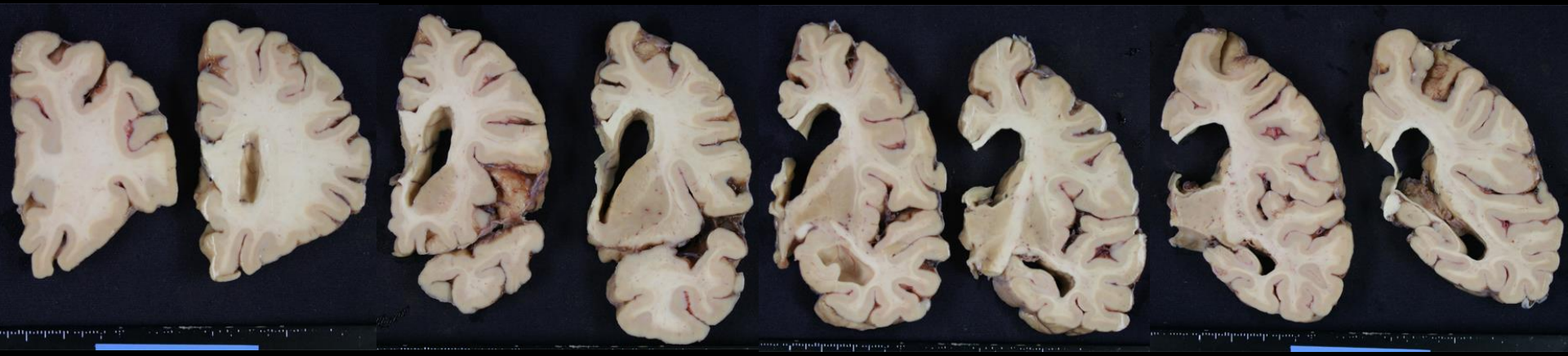
Most severe atrophy is found in the right precentral gyrus (Z score=7.55).

Thank you for your precise image interpretation !!

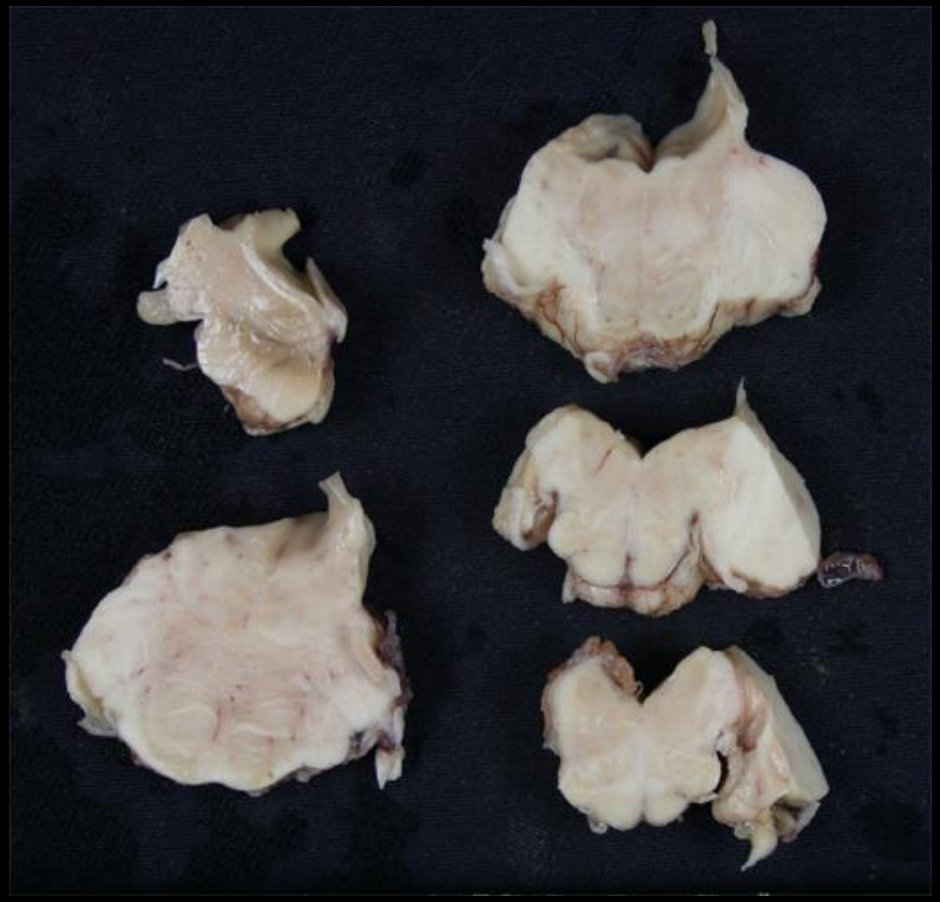


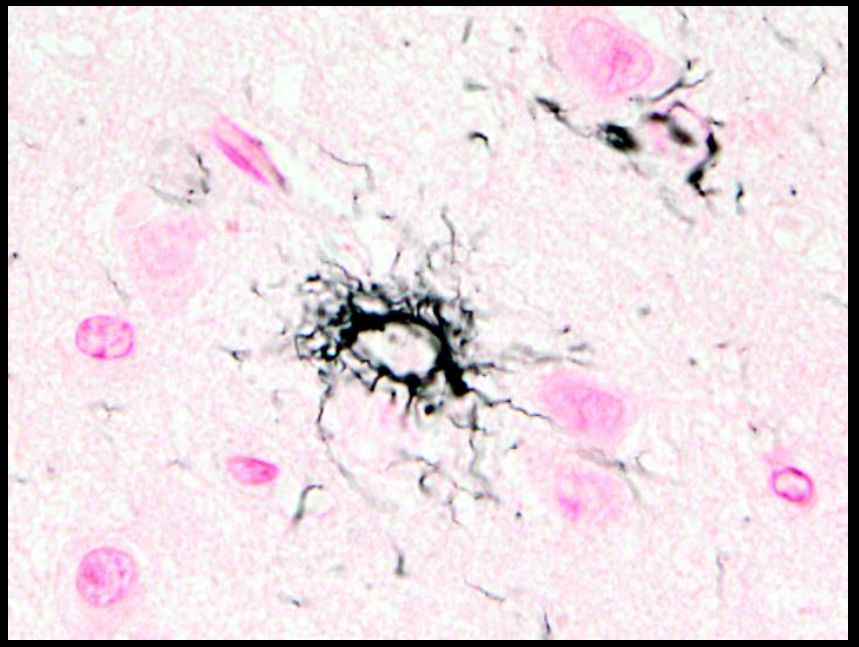


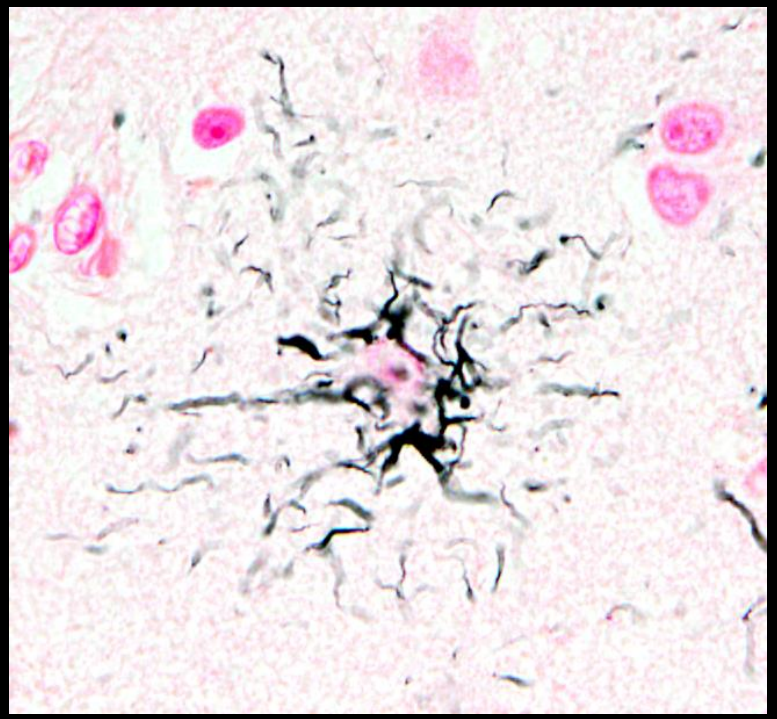
Brain weight 990g



Coronal section of the left brain







• In addition to the mild brainstem atrophy, depigmentation of the substantia nigra is evident.

• Tufted-shaped astrocytes suggestive of PSP are found in the left frontal cortices (superior frontal gyrus).

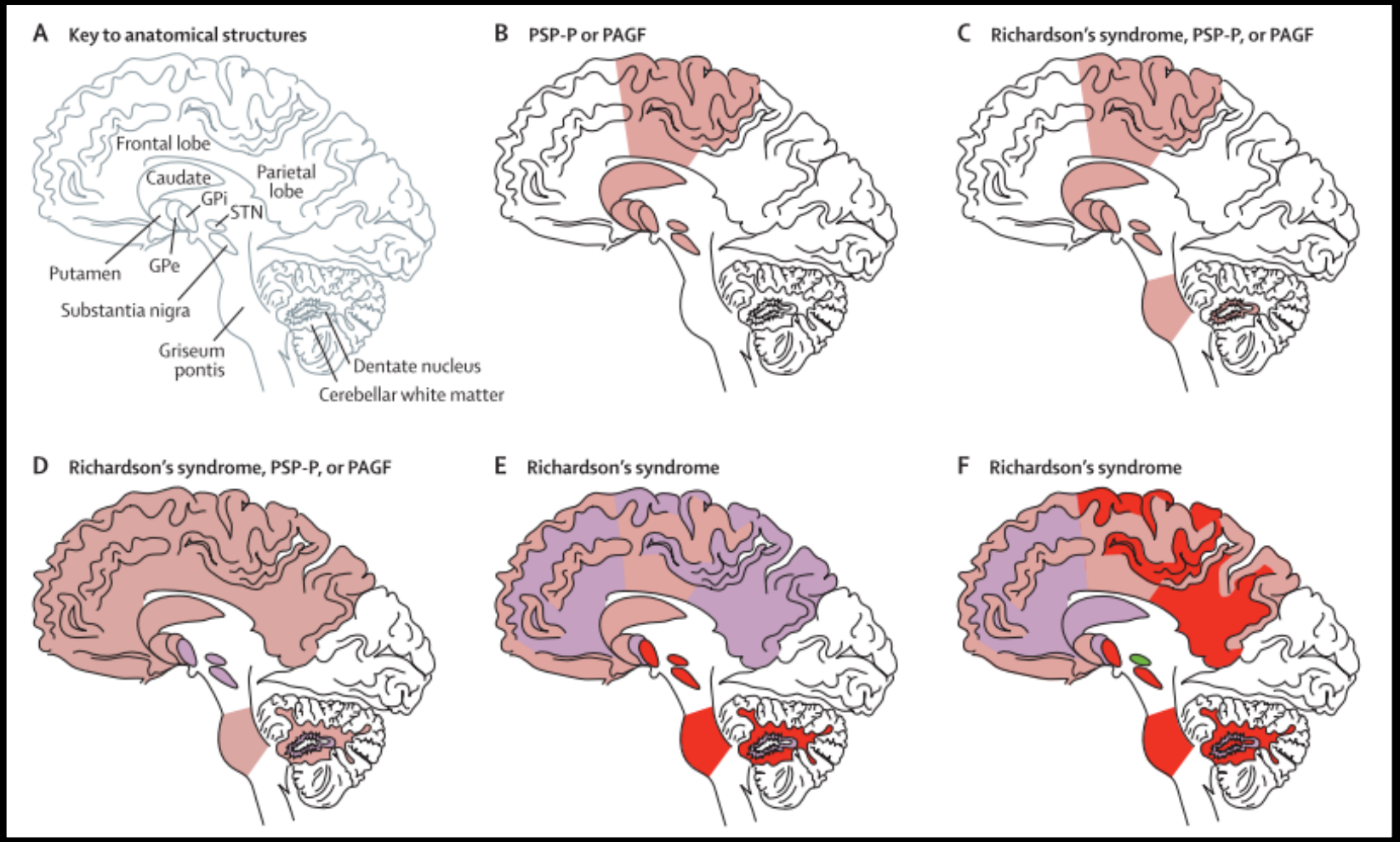
解答

○ Progressive supranuclear palsy with corticobasal syndrome presentation (PSP-CBS)

In addition to classic PSP syndrome (i.e., Richardson syndrome), several variants with different clinical symptoms have recently been identified by the clinicopathological studies.

Main clinical subtypes are as described below.

- PSP-parkinsonism (PSP-P)
- PSP-pure akinesia with gait freezing (PSP-PAGF)
- PSP-corticobasal syndrome (PSP-CBS)
- PSP-progressive nonfluent aphasia (PSP-PNFA)
- PSP with predominant cerebellar ataxia (PSP-C)



Relation between severity of tau pathology and PSP clinical subtypes

PSP-tau score is a reasonable surrogate marker for pathological disease severity with significant clinical correlations (excerpt from Lancet Neurol 2009; 8: 270-9).

Wide clinical spectrum of PSP [1)]

1) Richardson syndrome (RS):

Typical subtype presents with impairment of postural reflex, tendency to fall, and vertical supranuclear gaze palsy.

2) PSP-parkinsonism (PSP-P):

Subtype presents with asymmetric limb signs including rigidity and tremor. Initial response to levodopa may mislead to the diagnosis of Parkinson disease.

3) PSP-pure akinesia with gait freezing (PSP-PAGF):

Subtype presents with progressive freezing of gait, speech, or writing without other symptoms.

4) PSP-progressive nonfluent aphasia (PSP-PNFA):

Subtype presents with progressive nonfluent aphasia including apraxia of speech.

1) Lancet Neurol 2009; 8: 270-9.

5) PSP with corticobasal syndrome presentation (PSP-CBS) [1]

- 進行性，非対称性の統合運動障害，皮質性感覚障害，他人の手徴候，固縮を伴う四肢のジストニアなど**皮質基底核変性症と類似した症状を呈する亜型**．失語を伴うこともある．
- 典型的 PSP と比較して，**眼球運動障害，姿勢反射障害，易転倒性，体幹部の固縮などの症状発現が遅い**．[2]
- PSP 160症例の病理学的検討では，5症例に同様の非対称性のジストニア，失行，他人の手徴候を呈する症例が報告．[2]
- **皮質基底核症候群において，皮質基底核変性症（CBD）の病理を呈する症例は24～35%に過ぎず**，その他はアルツハイマー病（AD），PSP，TDP-43 proteinopathy などと判明．[3, 4]

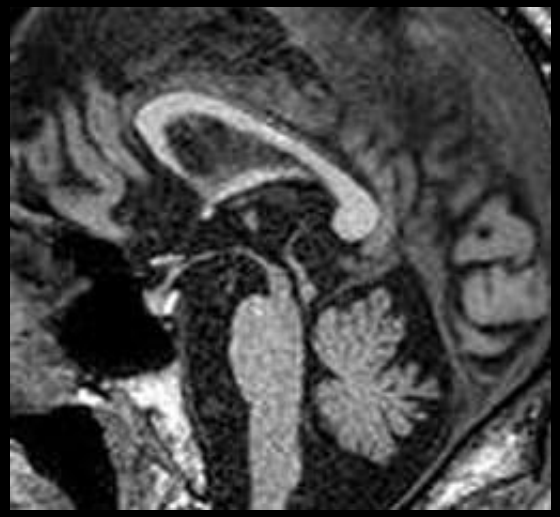
1) Lancet Neurol 2009; 8: 270-9.
2) Mov Disord 2005; 20: 982-8.
3) Brain 2010; 133: 2045-57.
4) Ann Neurol 2011; 70: 327-40.

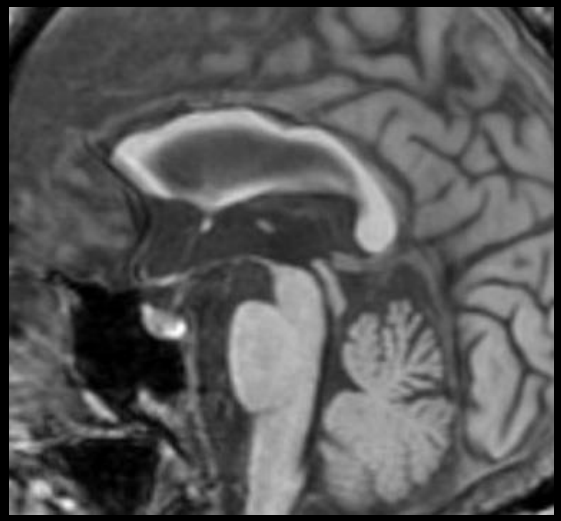
【Atrophic pattern depends on clinical subtypes】

It has been reported that various factors including disease subtypes and stage affect the severity of brainstem atrophy. [1)]

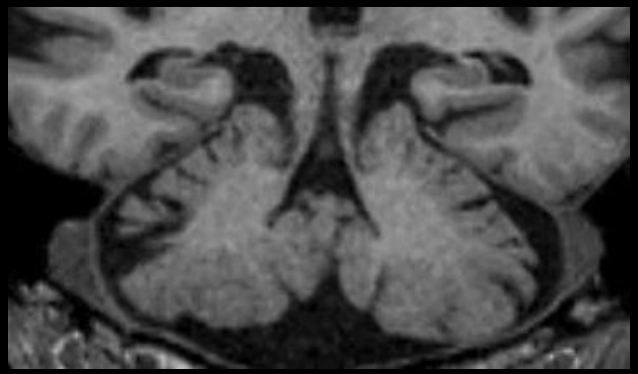
3D GRE T1WI

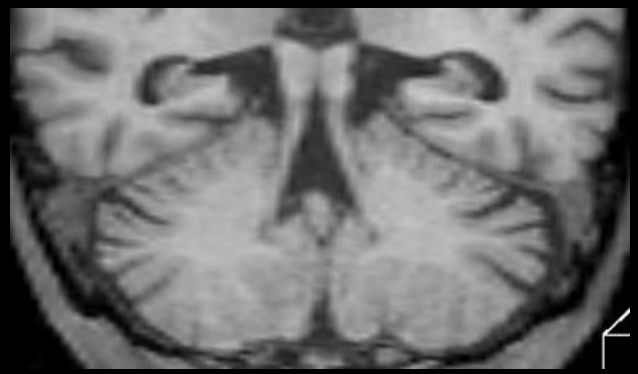
Typical case
RS
M = 50.2 mm^2
P = 420.8 mm^2
M/P = 0.12
MRPI = 24.3





Atypical case
PSP+LBD
M = 123 mm^2
P = 585 mm^2
M/P = 0.22
MRPI = 12.6

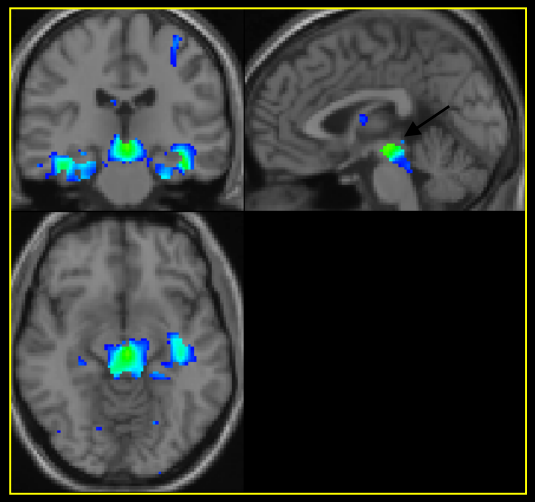




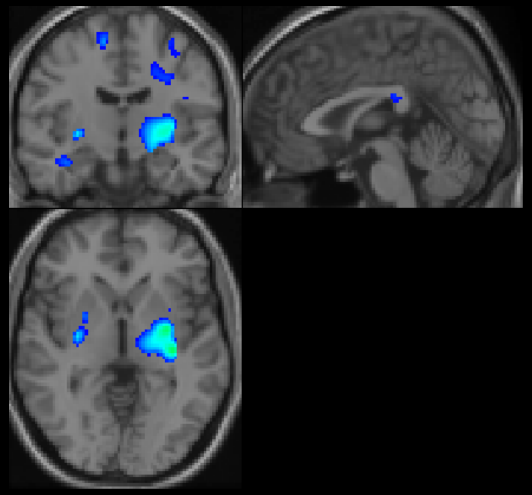
1) Mov Disord. 2011; 26: 247-55.

【VSRAD WM analysis of pathologically proven cases】

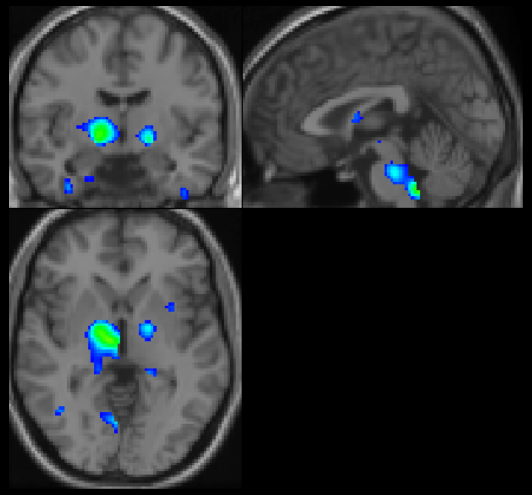
PSP-RS 77M



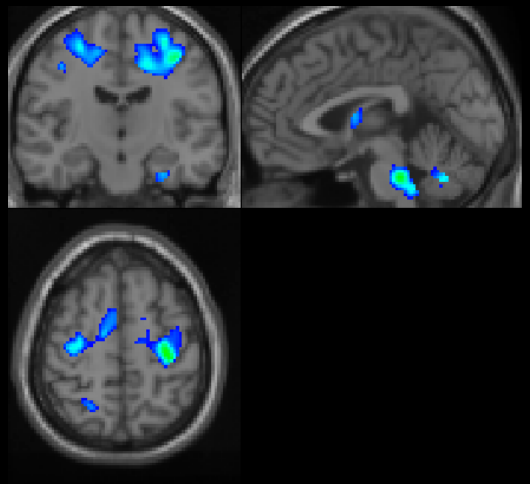
PSP+LBD 84F



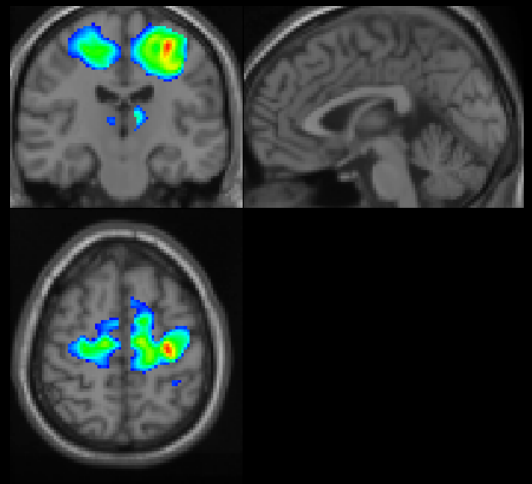
PSP-PAGF 83F



PSP-PNFA 86M



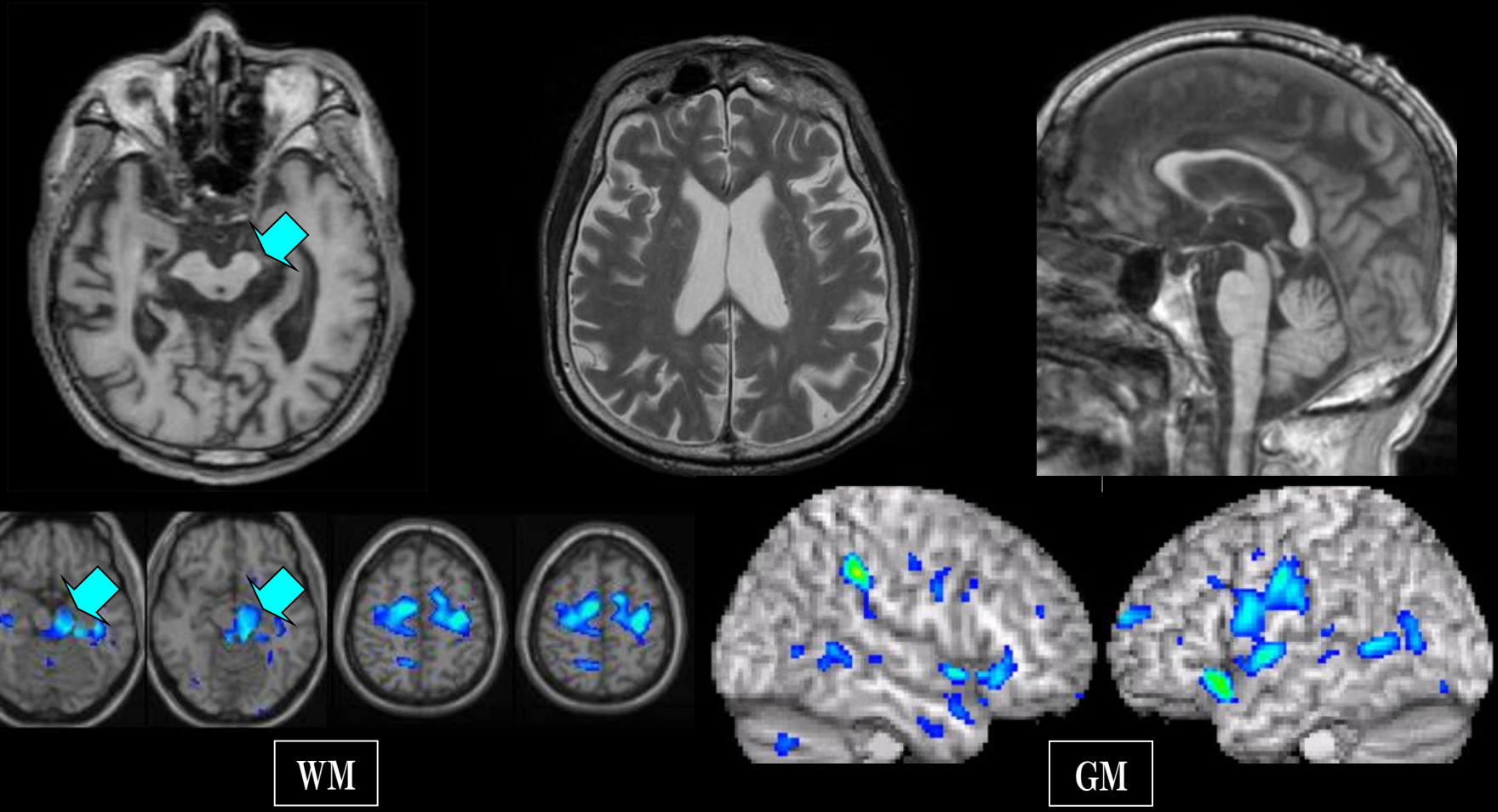
PSP-CBS? 76F



PSP-RS patient reveals the typical midbrain atrophy. However, this finding is not evident in patients with other PSP subtypes.

○ PSP-PNFA (with pathological proof)

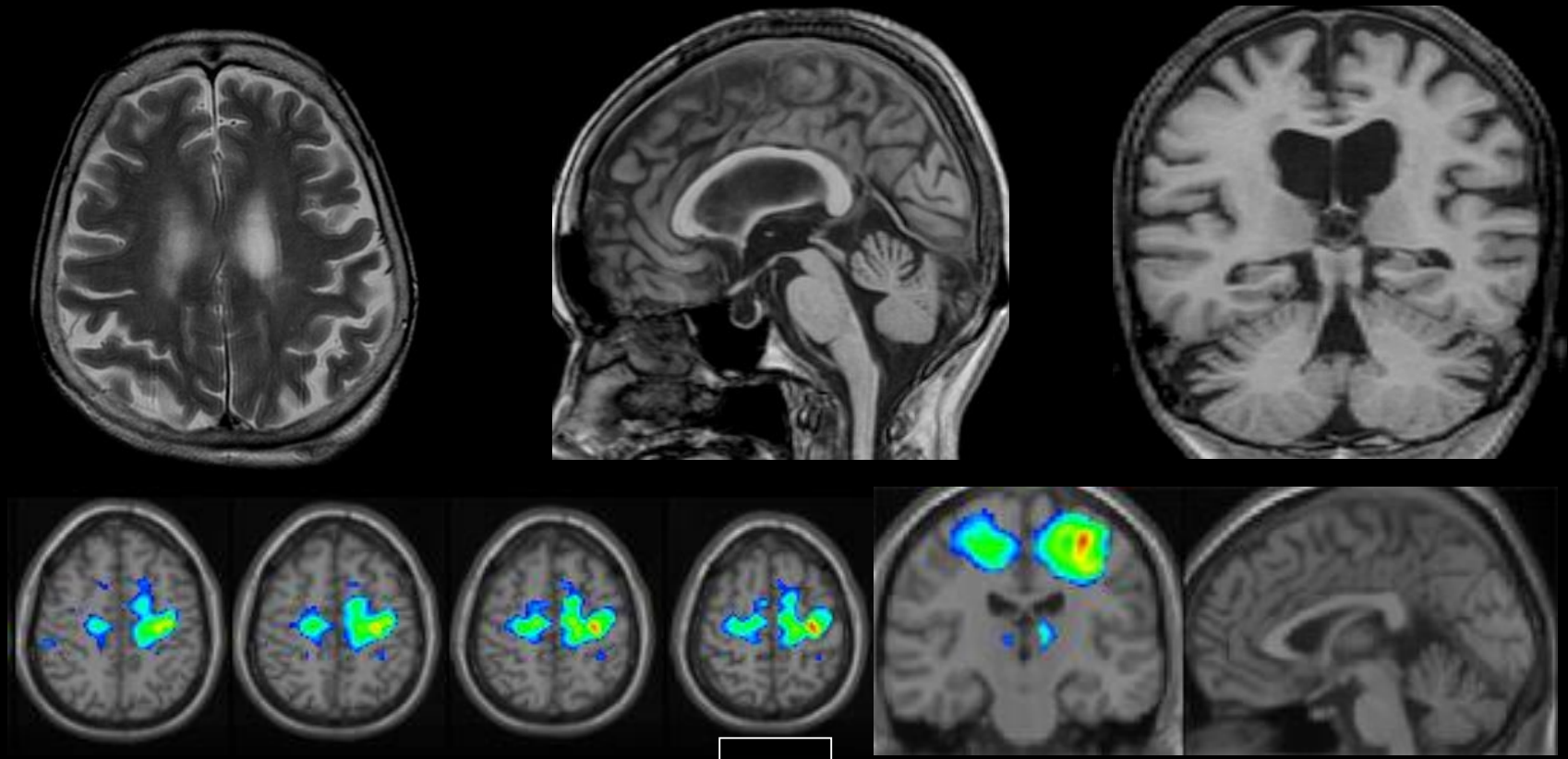
80's-year-old male suffered from progressive apraxia of speech. Additionally, oculomotor dysfunction appeared later.



This case showed mistakable asymmetric atrophy of the frontal WM and cerebral peduncle similar to that of CBD.

○ PSP-CBS (with pathological proof)

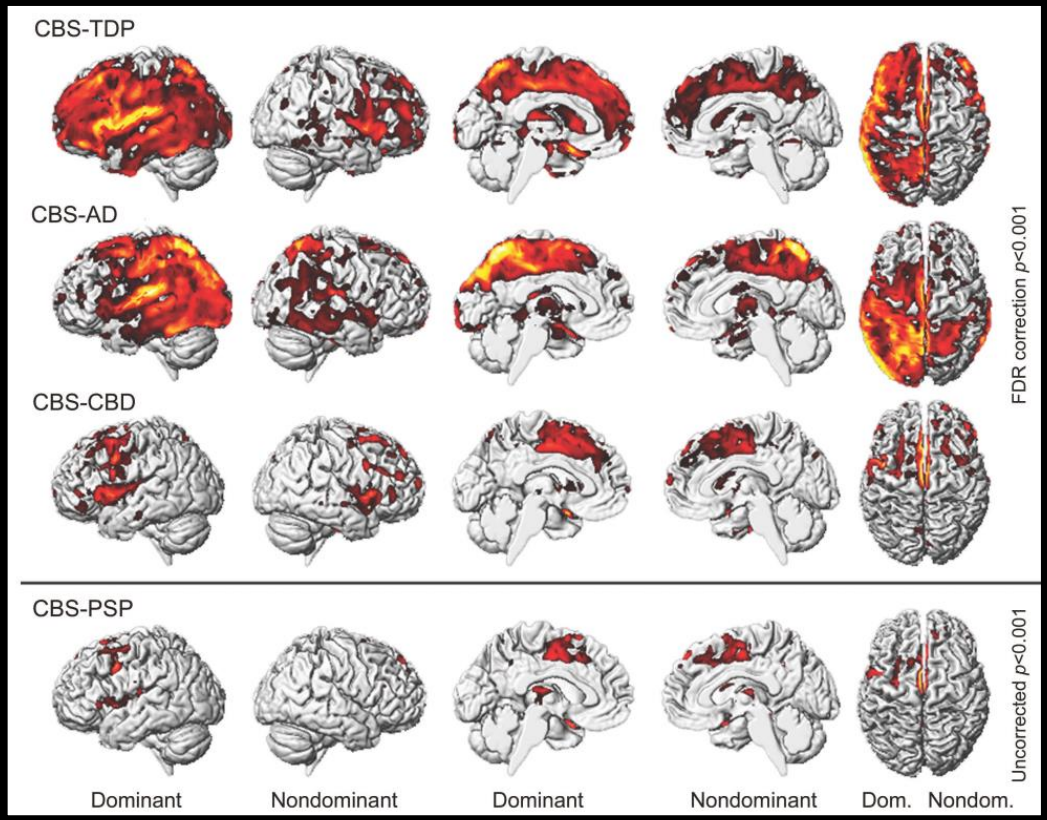
80's-year-old female suffered from gait disturbance, tendency to fall and right dominant extrapyramidal symptoms. Of special note was the lack of oculomotor disturbance.



WM

Asymmetric frontal WM atrophy was confusingly similar to that of CBD.

【Corticobasal syndrome】

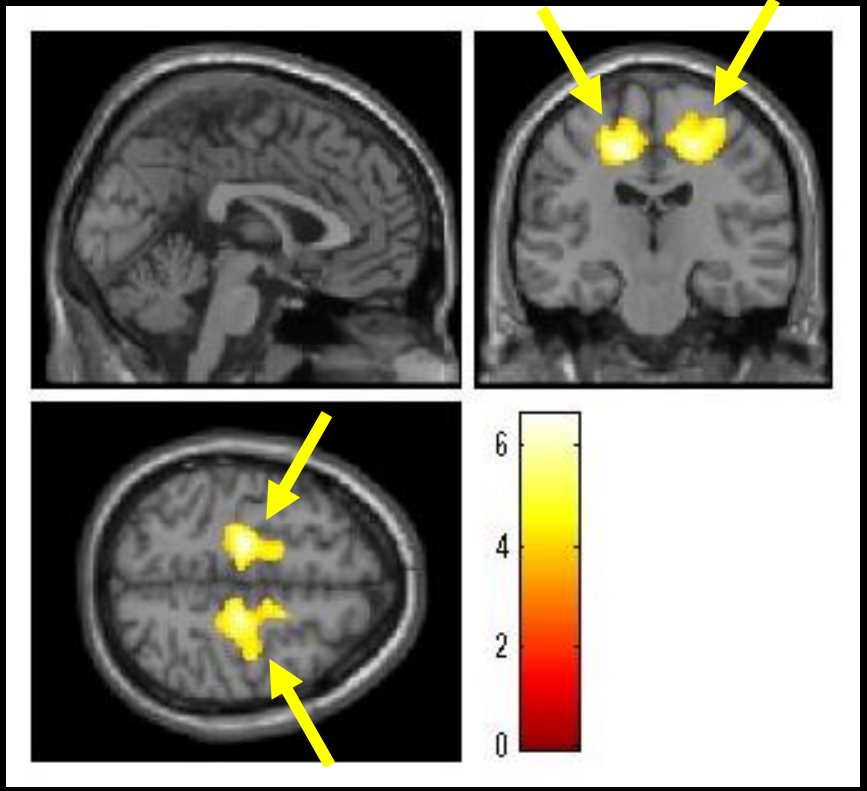


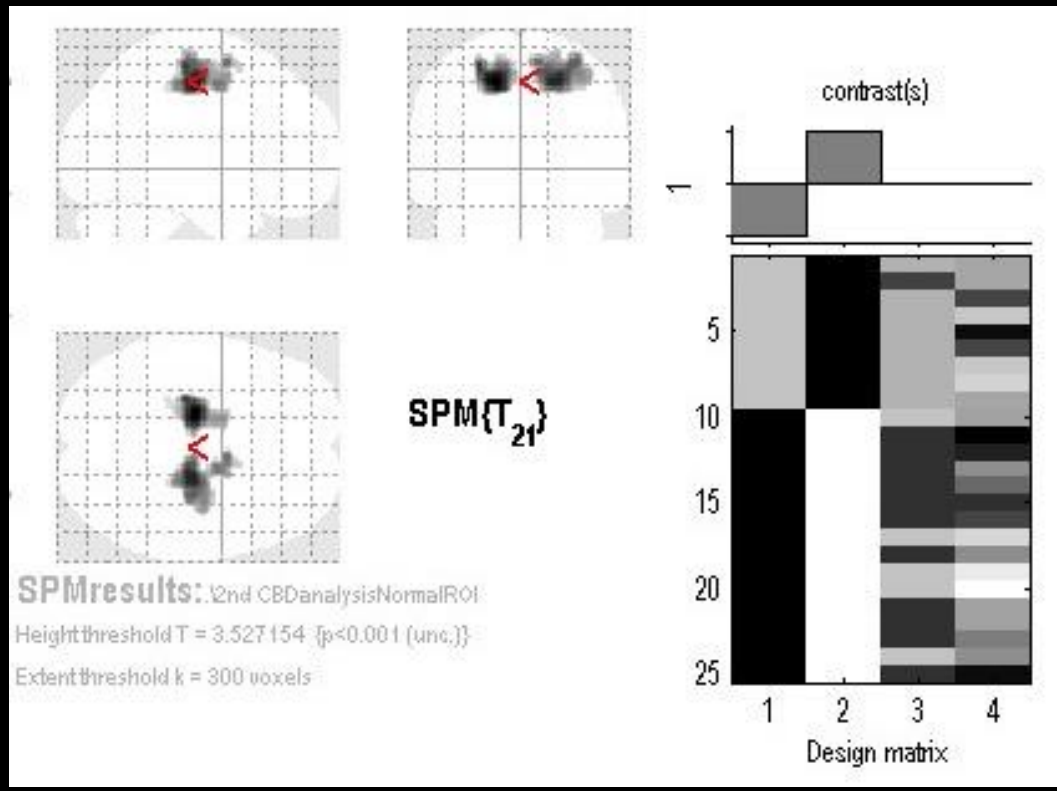
Neurology 2010; 75: 1879–87.

CBS is a general term for the pathologic condition with asymmetric symptoms similar to those of CBD. It is reported that Alzheimer's disease, frontotemporal lobar degeneration, and PSP can display symptoms of CBS.

【White matter atrophy of CBS】

SPM analysis of clinically diagnosed CBS patients





The most significant areas of atrophy observed in CBS patients compared to controls are the bilateral frontal subcortical WM including the left dominant bilateral precentral and right cingulate gyrus.

Neuroimage: Clinical, in press

Key points of this case

- PSP patient can reveal not only neurological symptoms but also imaging abnormalities, similar to those of CBD patients.
- PSP and its variants reveal various clinical symptoms and imaging abnormalities specific to their pathological variations.
- Atrophy of MRI reflects clinical presentation rather than specific pathological markers.