# Taupathies including:
- Progressive Supranuclear Palsy
- Corticobasal syndrome
- Frontotemporal dementia

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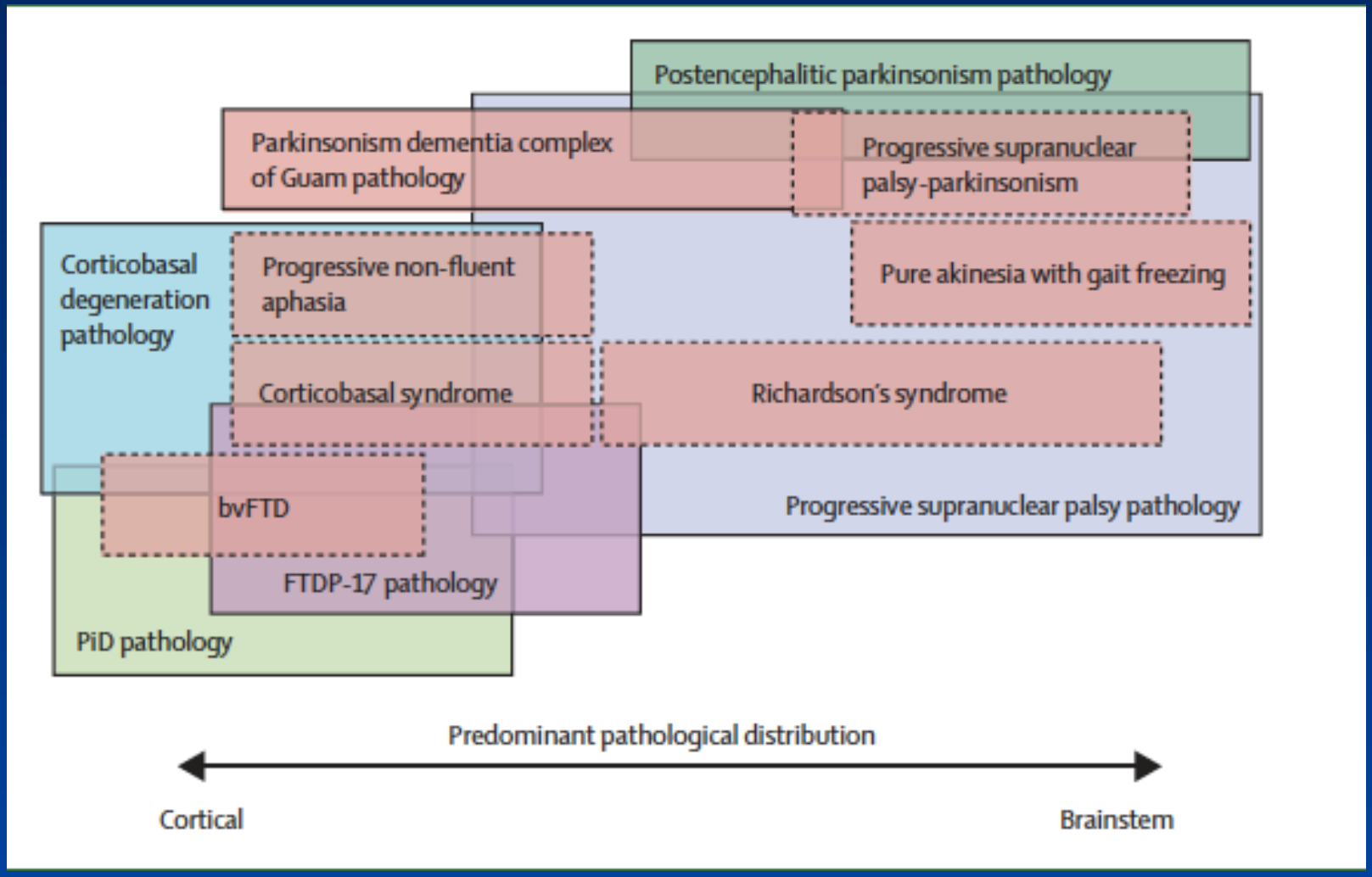
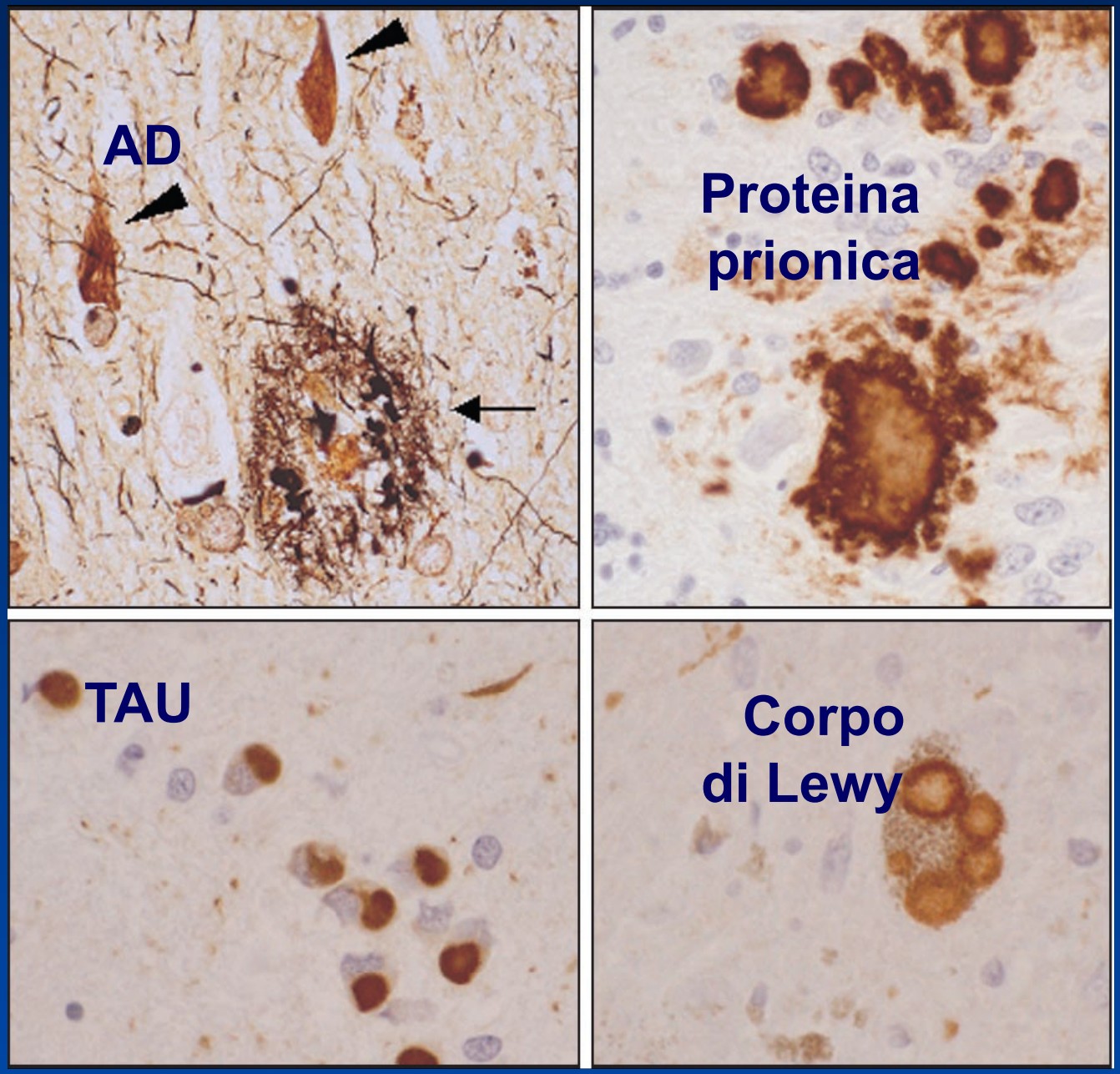
# Distribution of tau pathology in clinical and pathological nosological syndromes of progressive supranuclear palsy




Dashed boxes=clinical syndromes. Solid boxes=pathologically defined diseases. PiD=Pick's disease. FTDP-17=frontotemporal dementia with parkinsonism-17. bvFTD=behavioural variant of frontotemporal dementia.[3,64,65,65]

*Williams & Lees Lancet Neurology 2009*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# NINDS-SPSP Consensus Conference:

## Diagnostic categories for Progressive Supranucler Palsy

I. Possible PSP: gradually progressive disorder; onset after age 40; vertical SNGP OR slowing of vertical saccades AND postural instability with falls in the first year of symptom onset; no evidence of other diseases

II. Probable PSP: gradually progressive disorder; onset after age 40; vertical SNGP; postural instability with falls in the first year of symptom onset; no evidence of other diseases

III. Definite PSP: pathologically confirmed

There is a significant overlap between different taupathies and in particular between PSP and CBD/CBS

- **Progressive supranuclear palsy (PSP)**
  - Supranuclear vertical gaze palsy
  - Upright posture/frequent falls
  - Pseudobulbar emotionality
  - Furrowed brow/stare
  - Fronto-limbic dementia
- **Corticobasal degeneration (CBD)**
  - Unilateral, coarse tremor
  - Limb apraxia/limb dystonia/alien hand

## Exclusion criteria

**For possible and probable:**

- Recent history of encephalitis
- Alien limb
- Focal frontal and temporoparietal atrophy
- Hallucinations or delusions unrelated to dopaminergic therapy
- Cortical dementia of Alzheimer type
- Prominent early cerebellar symptoms or unexplained dysautonomia
- Neuroradiological evidence of relevant structural anomaly
- Whipples disease confirmed by polymerase chain reaction
- Evidence of other diseases that could explain the clinical features

## Supportive criteria

- Symmetric akinesia or rigidity
- Proximal more than distal
- Abnormal neck posture, especially retrocollis
- Poor or absent reponse of parkinsonism to levodopa
- Early dysphagia, dyarthria
- Early onset of cognitive impairment including > 2 of: apathy, impairment in abstract thought, decreased verbal fluency, utilization or imitiation behavior or frontal release signs

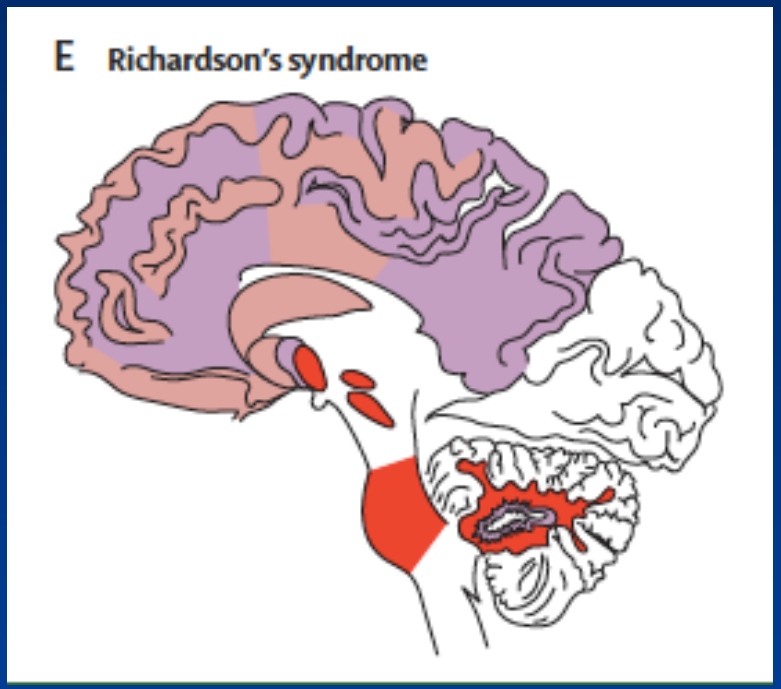
# Clinical and anatomical correlations of PSP-tau pathology

| | Clinical features |
|---|---|
| Frontal cortex | Dysexecutive syndrome; progressive non-fluent aphasia; perseveration; impulsivity |
| Parietal cortex | Alien limb |
| Substantia nigra | Rigidity; bradykinesia; postural instability; dystonia |
| Extranigral midbrain dopamine neurons | No response to levodopa |
| Periaqueductal grey and raphe nucleus | Sleep disturbances |
| Dentate nucleus | Gaze fixation (excess of square wave jerks) |
| Pontine and medullary nuclei | Dysarthria; dysphagia |
| riMLF (premotor burst neurons) | Slow saccades |
| Cholinergic neurons of the lower pontine reticular formation | No startle response; oculomotor dysfunction |

riMLF=rostral interstitial nuclei of the medial longitudinal fasciculus.

*Williams & Lees Lancet Neurology 2009*

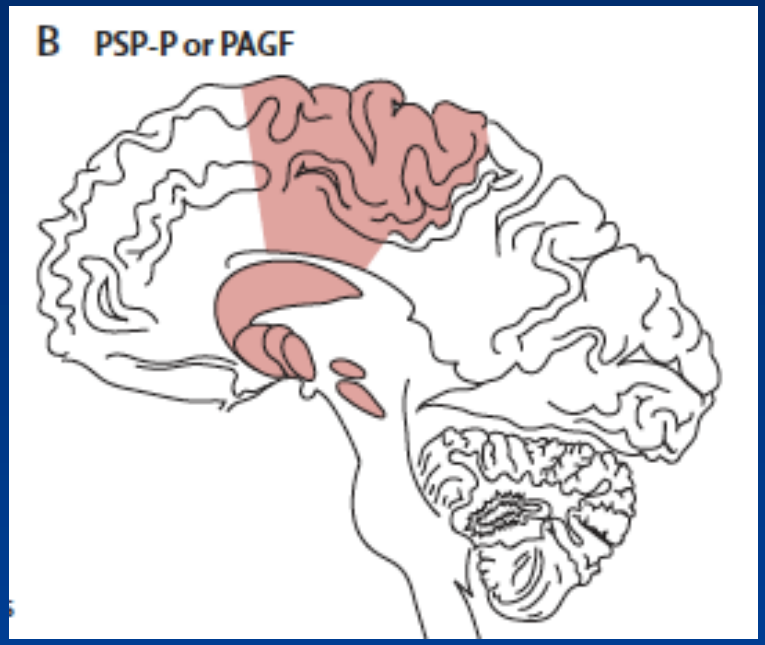
# Richardson's syndrome




- Lurching gait
- Unexplained falls backwards without loss of consciousness
- Personality change or cognitive slowing within the first 2 years
- Slowing of saccadic eye movements (with later vertical gaze palsy)
- Absence of limb rigidity and bradykinesia but presence of axial rigidity

*Williams & Lees 2009*

# PSP-Parkinson type

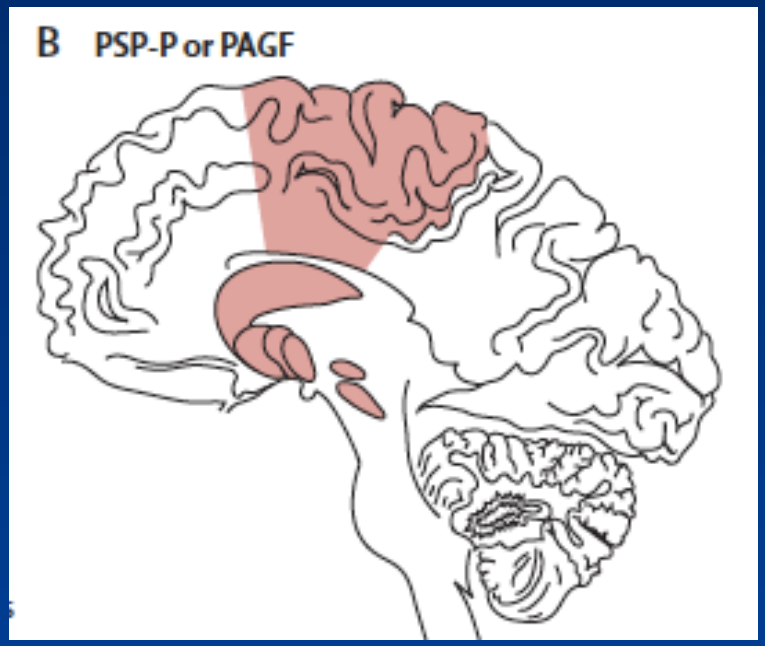



- Limb bradykinesia, rigidity although with significant axial involvement
- Presence of jerky postural tremor and even 4–6 Hz rest tremor
- Falls and cognitive dysfunction occur later in PSP-P than in the Richardson type
- Moderate effect of levodopa especially in the first years

*Williams & Lees Lancet Neurology 2009*

# PSP-PAFG

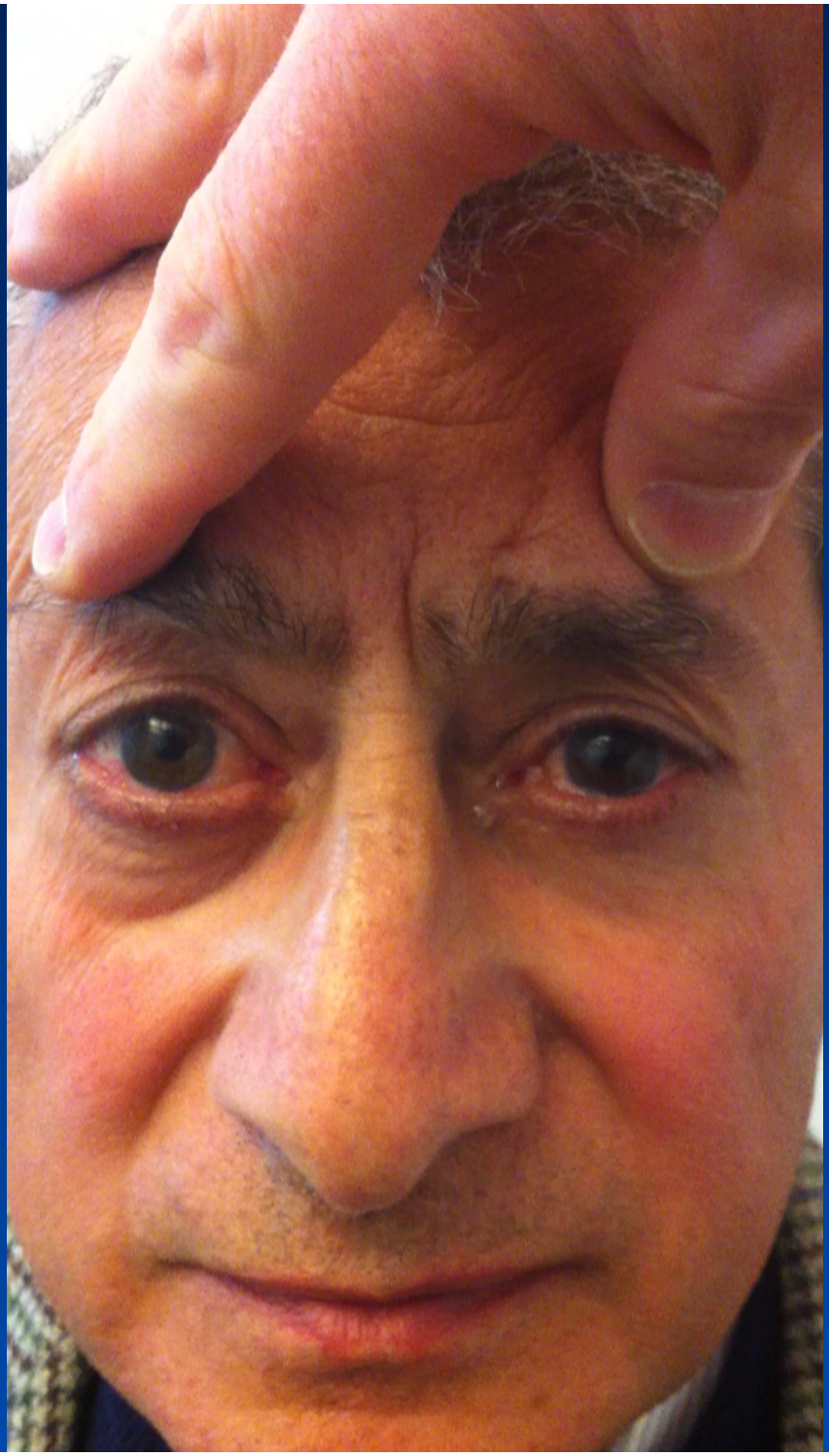
## (pure akinesia and freezing of gate)




- Progressive onset of gait disturbance with start hesitation and subsequent freezing of gait, speech, or writing
- Long disease duration without development of other parkinsonian features for many years

*Williams & Lees Lancet Neurology 2009*

- His age is now 76
- 12 years disease duration
- Started in 2002 with gait problems
-He would not tolerate any dopaminergic  agent because worsened his walking



# Clinical Characteristics of the various PSP phenotypes

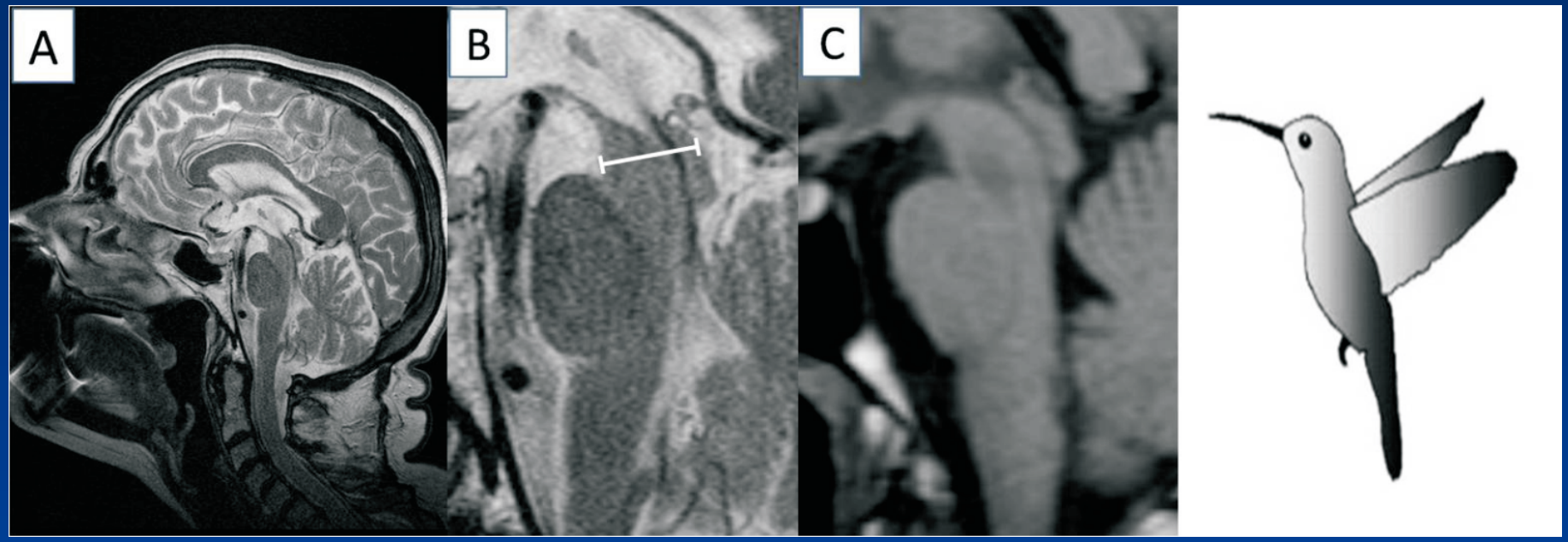
| | Richardson's syndrome | PSP-P | PSP-PAGF | PSP-CBS | PSP-PNFA | Parkinson's disease |
|---|---|---|---|---|---|---|
| Rigidity | Axial much more than limb | Axial less than or the same as limb | Axial | Yes | Sometimes | Limb much more than axial |
| Bradykinesia | Mild | Moderate | Moderate | Yes | Mild | Moderate |
| Tremor | No | Yes/no (rest or jerky postural) | No | No | No | Yes (at rest) |
| Early falls | Yes | No | No | Sometimes | Sometimes | No |
| Early postural instability | Yes | No | Yes | .. | .. | No |
| Early cognitive decline | Often | No | No | No | Yes | No |
| Early abnormalities of eye movement | Yes | No | No | No | Sometimes | No |
| Response to levodopa | No | Often | No | No | No | Usually |
| Hyposmia | No | No | .. | .. | .. | Yes |
| Cardiac MIBG | Normal | Normal* | Normal* | .. | .. | Abnormal |

PSP=progressive supranuclear palsy. CBS=corticobasal syndrome. PAGF=pure akinesia with gait freezing. PNFA=progressive non-fluent aphasia. MIGB=$^{131}$I-labelled meta-iodobenzylguanidine. ..=unknown. *Author's unpublished data.

*Williams & Lees 2009*

# MRI in Progressive Supranuclear Palsy

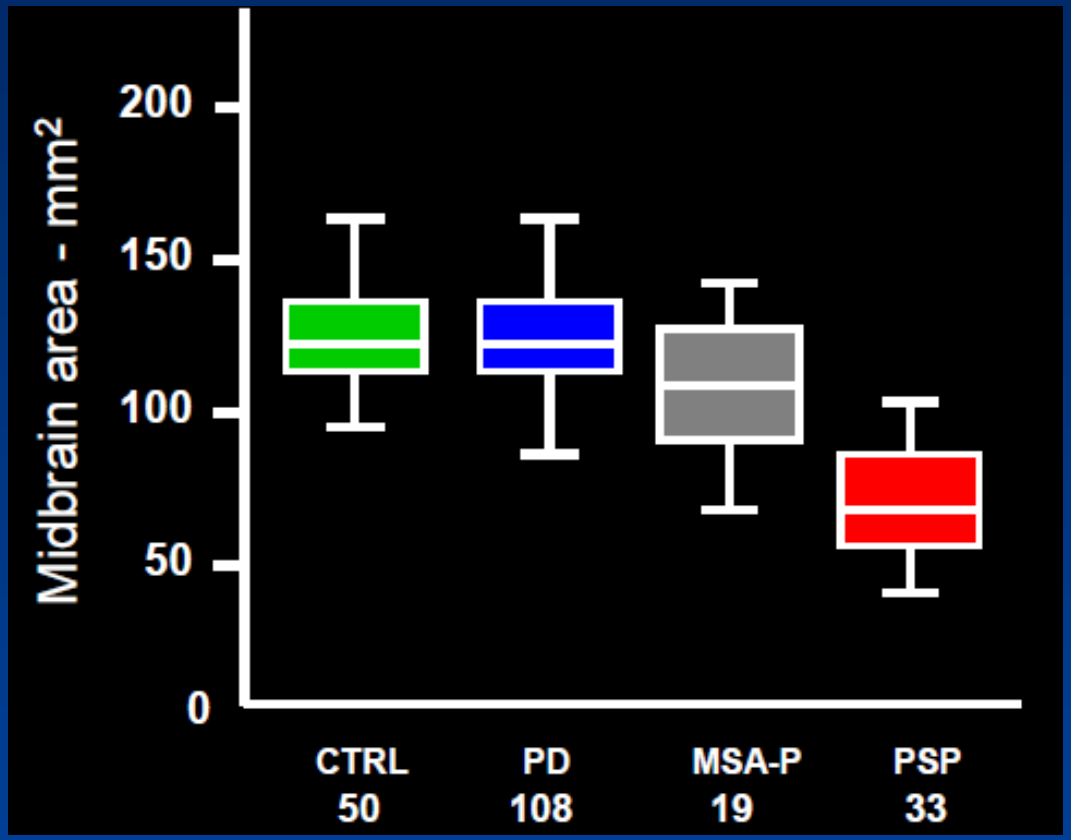
## Midbrain atrophy and 'humming bird sign' in PSP

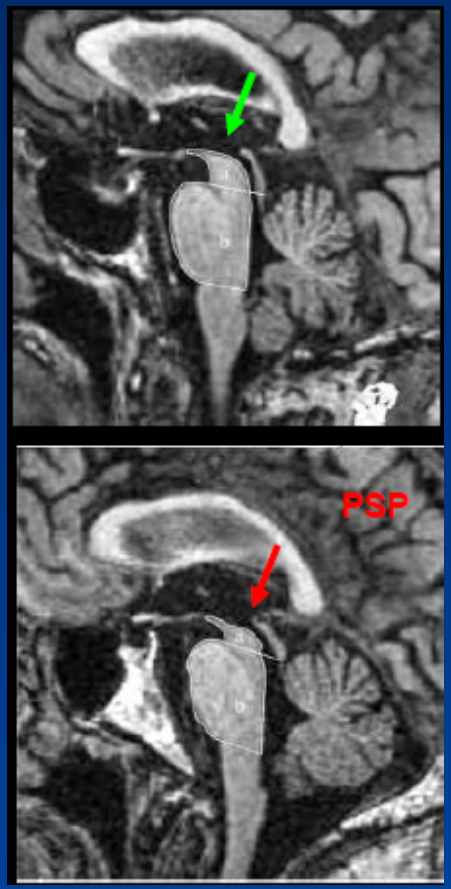



A: T2 MRI in a patient with PSP
B: Detailed picture of the brainstem in the same patient showing midbrain atrophy (diameter of 13.3 mm = white line) resulting in the so-called 'humming bird sign'
C: detailed picture of a normal brainstem

*Righini, et al., AJNR 2004*

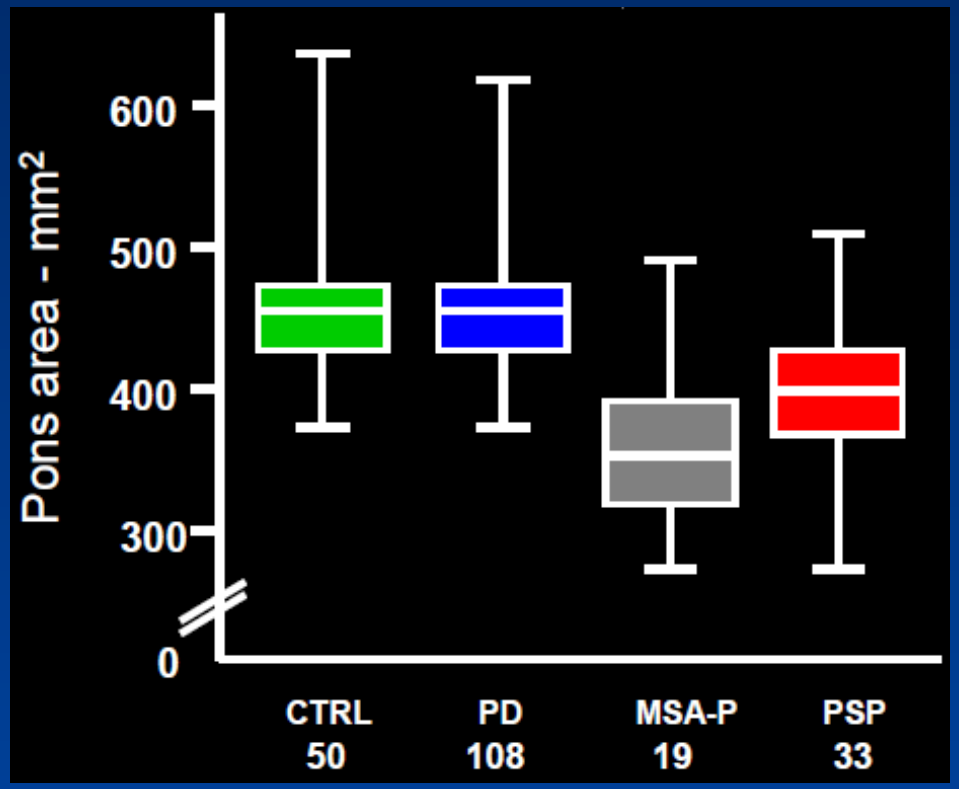
# Midbrain area in PSP, MSA-P, PD and Controls

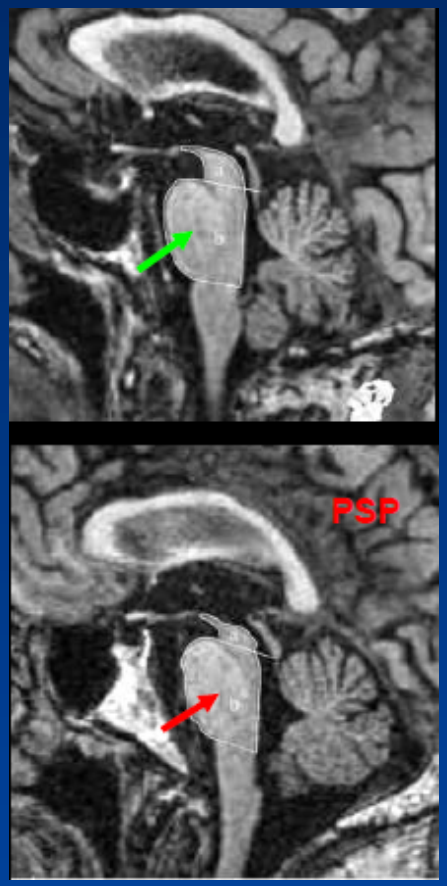



*Quattrone et al., 2008*

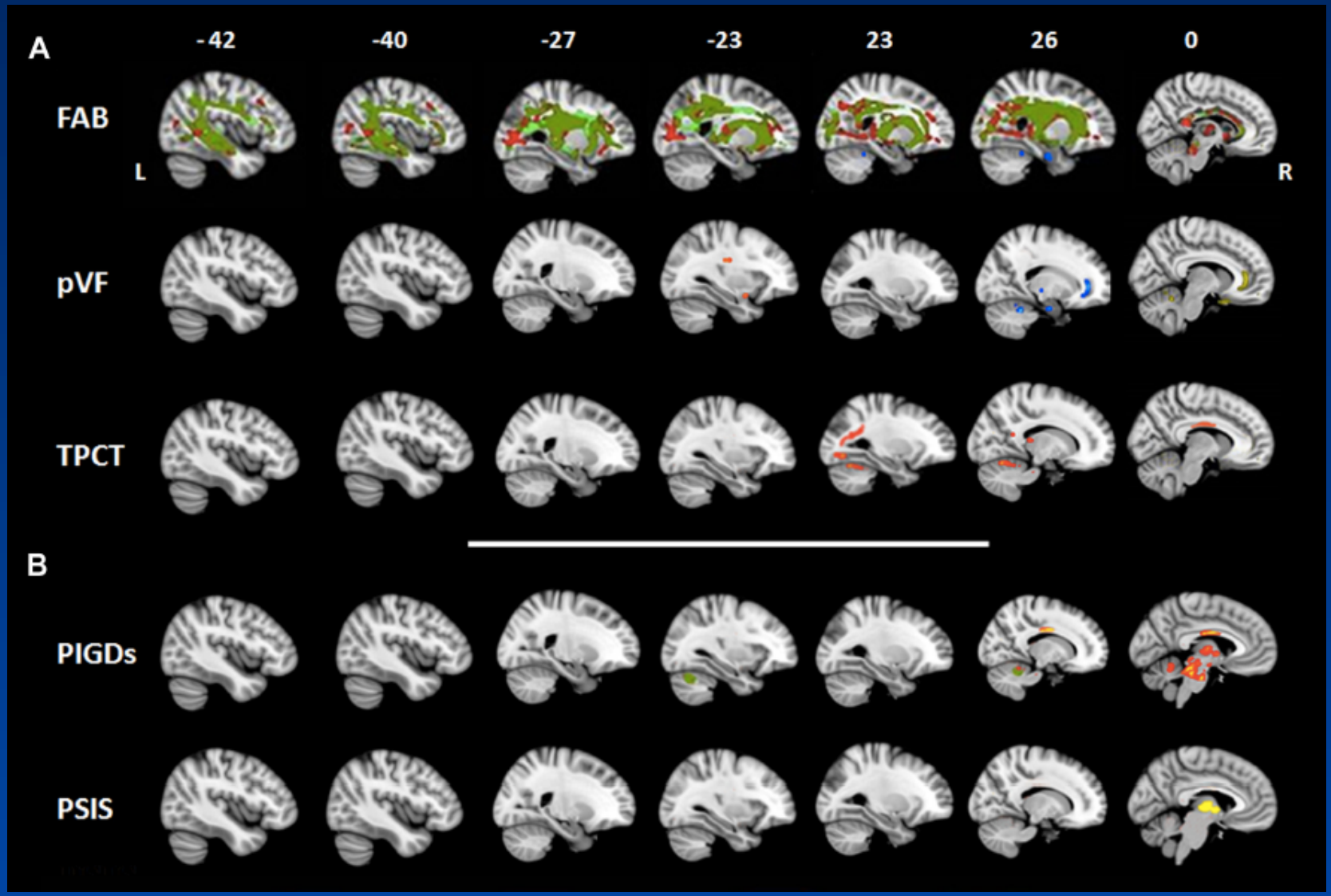
# Pons area in PSP, MSA-P, PD and Controls




*Quattrone et al., 2008*

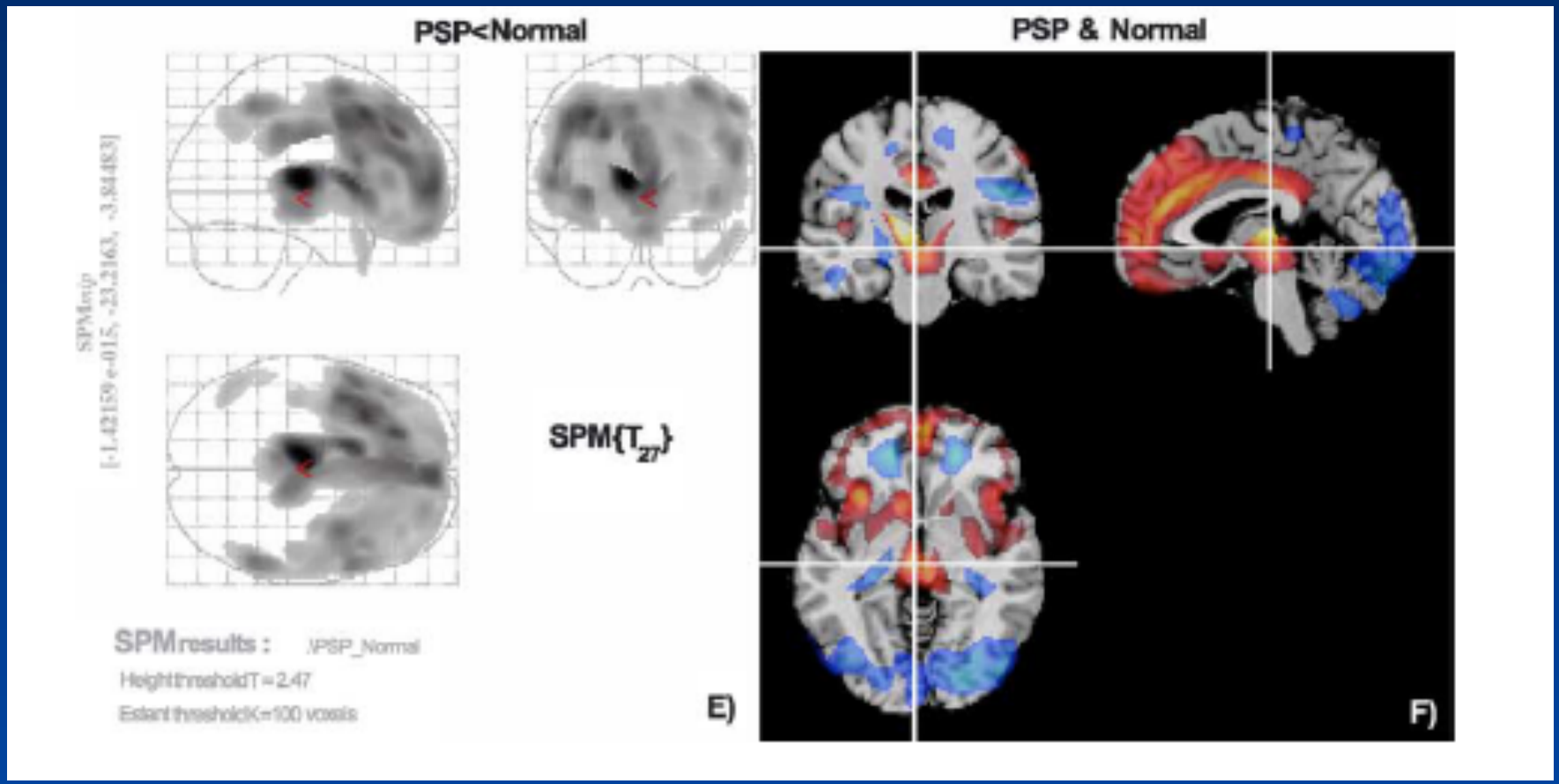
# Correlations between WM loss and clinical-cognitive features




TPCT: ten-point clock test; PSIS: PSP saccadic impairment scale; pVF: phonological verbal fluency

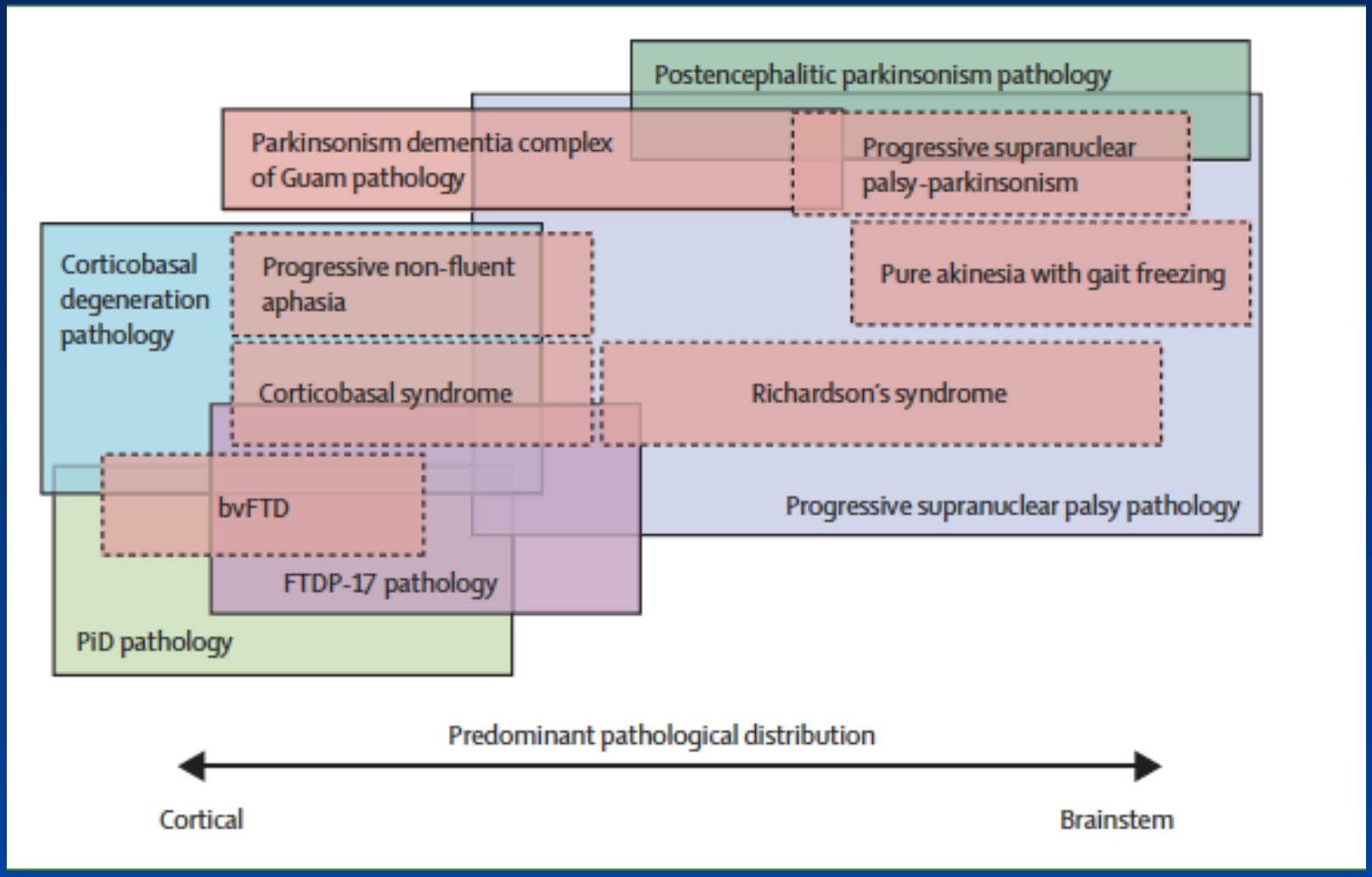
*Tessitore et al, Neurobiology of aging 2014*

# Areas of reduced metabolism in PSP vs. controls (18F-FDG PET)
# Areas in red show the largest decrement




*Joh R et al. European Journal of Radiology 2004*

# Corticobasal syndrome

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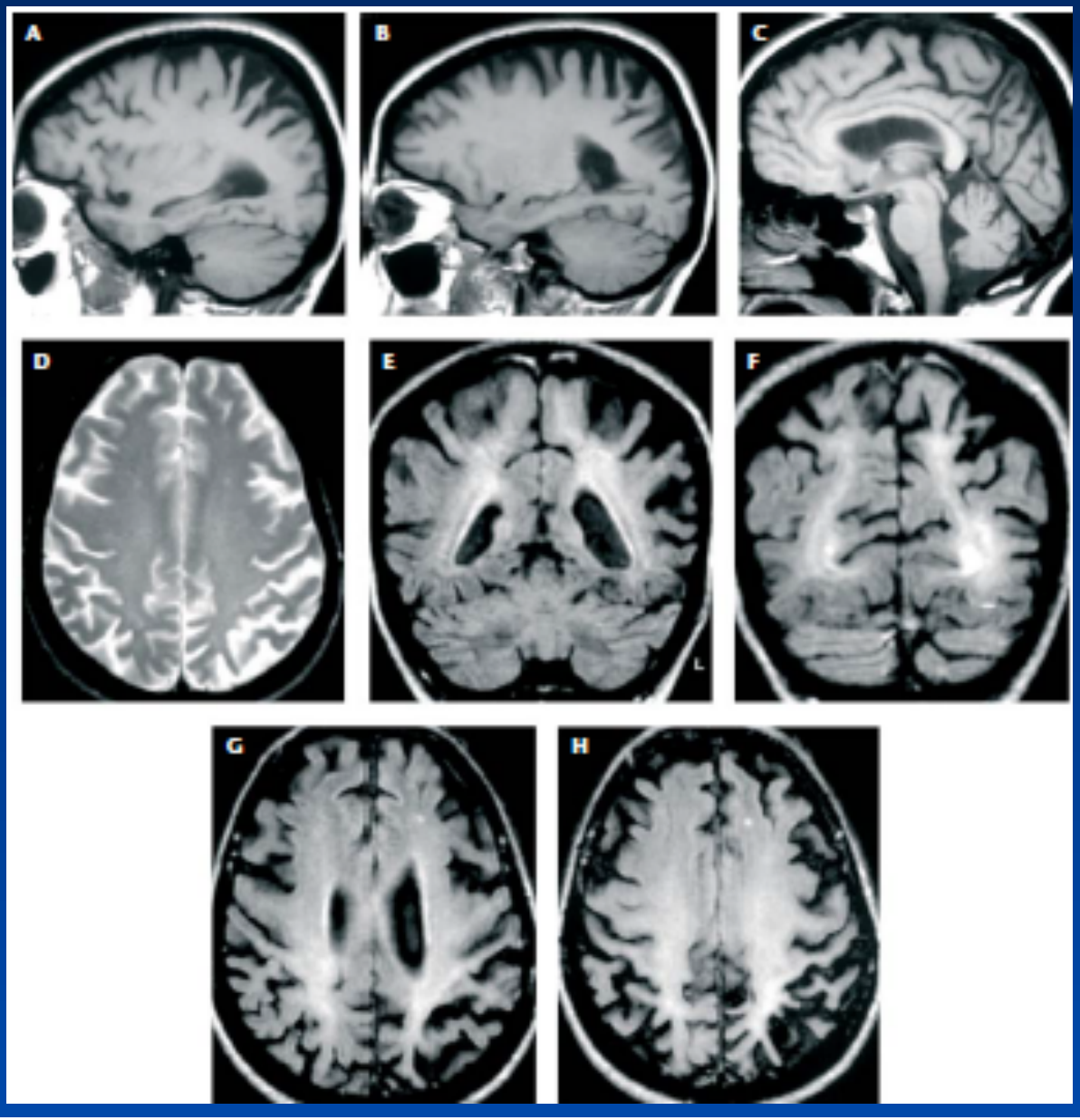
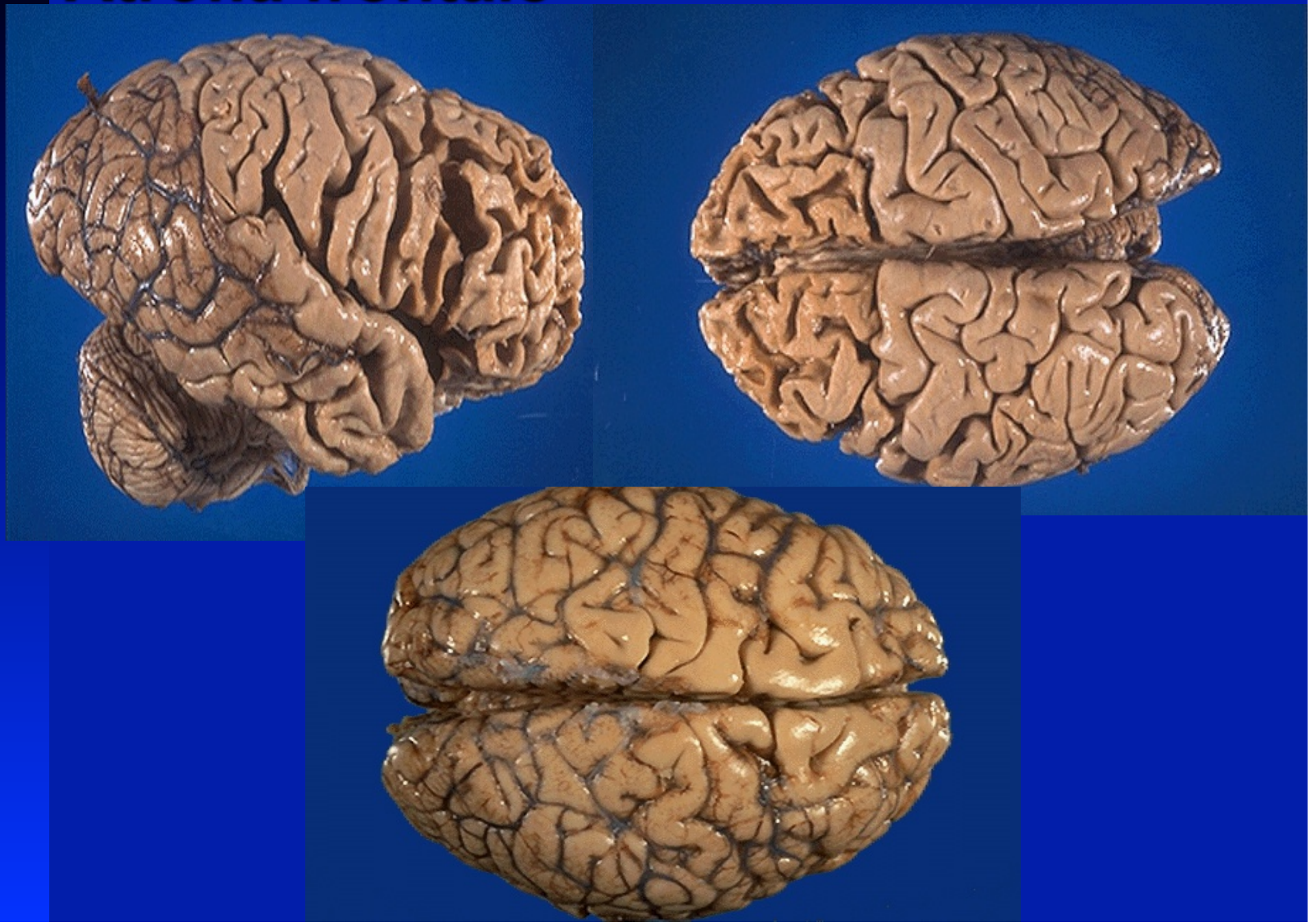
# Cortical Basal Degeneration/Syndrome

## Asymmetric atrophy in the parietal-occipital region




PAZIENTE N° 2

# Atrofia frontale



# Demenze frontali: disturbi comportamentali

- Vanno considerati l'età, il gruppo sociale, la personalità premorbosa
- Comportamento socialmente inappropriato
- Mancanza di adeguamento alle regole e restrizioni sociali
- Impulsivi, disinibiti, periodi di rabbia ed aggressività

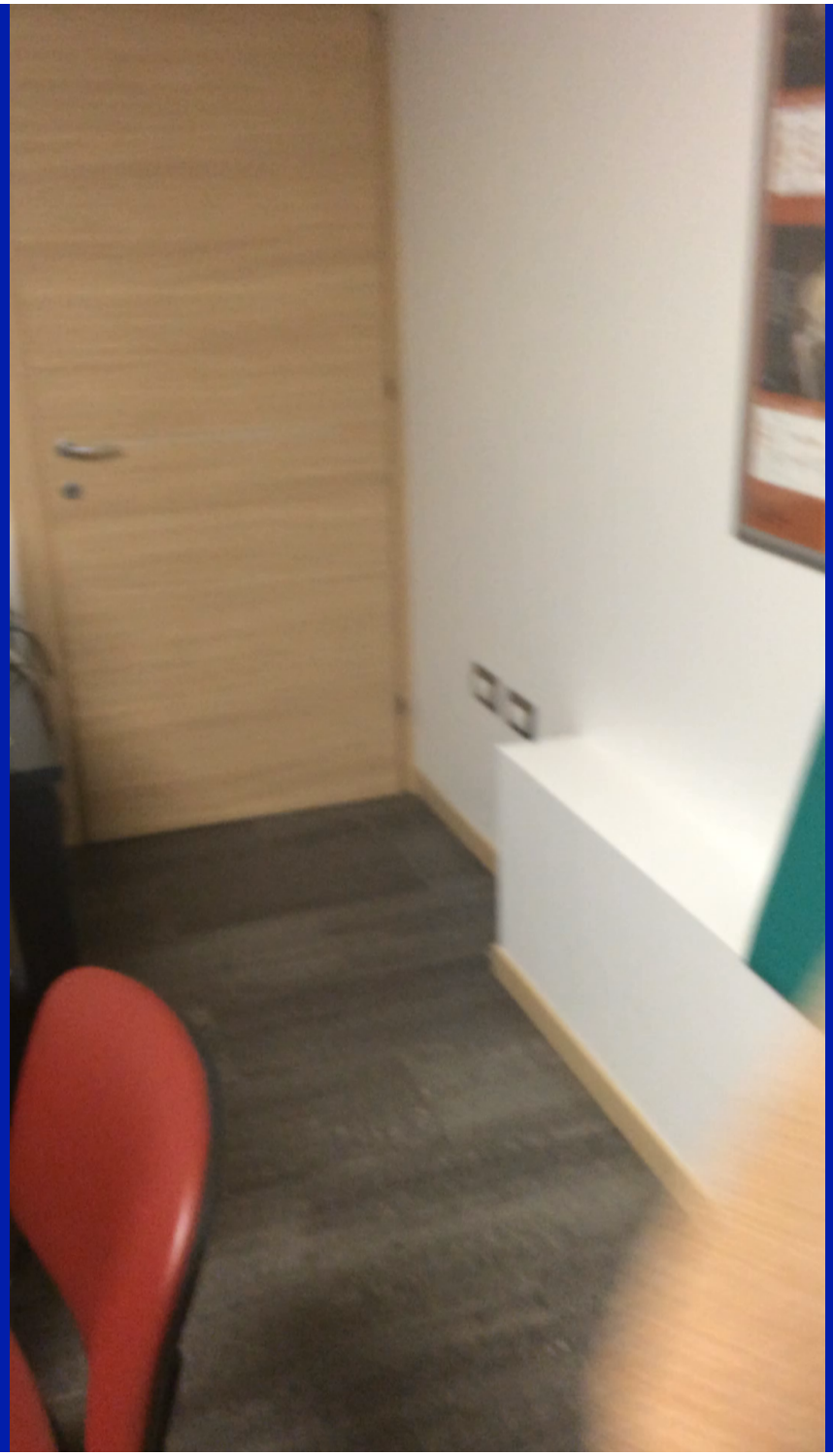
# Demenze frontali: disturbi comportamentali

- Risposta emotiva appiattita
- Riduzione della volontà, apatia
- Mancanza del senso di sè

# Esempi clinici

**“Prima era un uomo religioso, attaccato alla famiglia, onesto e lavoratore. Dopo diventò instabile, irriverente, dedito alle peggiori profanità, intollerante verso le restrizioni, ostinato, inizia ed abbandona continuamente progetti”.**

**“Era tranquillo, non iniziava la conversazione e sembrava lontano ed assente. Aveva incontinenza, ma non se ne preoccupava e non faceva nulla per porvi rimedio”.**



CABBIA ERASTO 1.12.2014