# Le demenze
# a presentazione atipica

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# Cosa è «atipico»?

- Sintomi di esordio
- Rapidità di evoluzione
- Età

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# Fenotipi clinici: una classificazione sindromica

- **Prevalenti disturbi visuopercettivi**
- **Prevalenti disturbi del linguaggio**
- **Prevalenti disturbi comportamentali e/o disesecutivi**
- **Associazione con disturbi del movimento**

# Fenotipi clinici: una classificazione sindromica

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- **Prevalenti disturbi del linguaggio**
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# Può essere lo stesso Alzheimer: presentazioni «atipiche»

- Atrofia Corticale Posteriore
- Afasia progressiva (variante logopenica)
- Variante «frontale»

# Criteri per la PCA (Mendez et al., 2001)

- Inizio insidioso e progressione graduale
- Presentazione con disturbi visivi ma acuità conservata
- Evidenza di disturbi visivi complessi
- Disturbo relativamente minore della memoria e del linguaggio
- Consapevolezza conservata con o senza depressione

# Table 1

***Table 1*** *Clinical features of 27 cases of primary posterior cortical dysfunction (PPCD) by pathologic diagnoses*

| Subject no. | Onset age, y | T1 age, y | Age at death, y | Sex | CDR at entry | Visuoperceptual: Balint syndrome: Environmental agnosia | Visuoperceptual: Balint syndrome: Oculomotor apraxia | Visuoperceptual: Balint syndrome: Optic ataxia | Visuoperceptual: Balint syndrome: Simultan-agnosia | Visuoperceptual: Prosop-agnosia | Visuospatial neglect |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Alzheimer disease | | | | | | | | | | | |
| 1 | 52 | 55 | 65 | M | 1 | − | + | + | + | − | + |
| 2 | 52 | 62 | 67 | M | 1 | + | − | − | − | − | + |
| 3 | 62 | 64 | 69 | F | 1 | − | − | + | + | + | − |
| 4 | 68 | 70 | 78 | F | 0.5 | − | − | − | − | − | + |
| 5 | 84 | 86 | 86 | F | 2 | − | − | − | − | − | + |
| 6 | 63 | 67 | 69 | M | 2 | + | − | + | + | − | + |
| 7 | 61 | 63 | 72 | M | 0.5 | − | + | + | + | + | + |
| 8* | 55 | 65 | N/A | F | 0 | + | − | + | + | − | − |
| 9* | 50 | 57 | 59 | F | 3 | − | − | − | − | − | − |
| 10* | 49 | 57 | 58 | M | 1 | − | − | − | + | + | + |
| 11* | 54 | 60 | 64 | M | 0.5 | + | − | − | − | − | + |
| Mixed Alzheimer disease/Parkinson disease/dementia with Lewy bodies | | | | | | | | | | | |
| 12 | 77 | 78 | 82 | F | 2 | − | − | + | + | − | + |
| 13 | 62 | 65 | 69 | M | 2 | + | − | + | + | + | − |
| 14 | 54 | 57 | 63 | F | 1 | + | + | + | + | − | − |
| 15* | 65 | 68 | 68 | M | 1 | − | − | − | + | − | + |
| 16* | 69 | 69 | 73 | M | 1 | + | − | − | − | − | + |
| Corticobasal degeneration | | | | | | | | | | | |
| 17 | 52 | 53 | 59 | M | 1 | − | + | + | − | − | + |
| 18 | 58 | 61 | 66 | M | 1 | + | − | − | − | − | − |
| Prion disease | | | | | | | | | | | |
| 19* | 68 | 68 | 69 | M | 3 | + | − | + | + | + | − |
| 20* | 63 | 67 | 69 | M | 2 | + | − | − | − | − | − |
| Subcortical gliosis | | | | | | | | | | | |
| 21 | 61 | 66 | 76 | F | 1 | − | − | − | − | + | − |
| No pathologic diagnosis | | | | | | | | | | | |
| 22 | 71 | 73 | — | M | 2 | − | + | + | − | + | − |
| 23 | 76 | 79 | — | F | 1 | − | + | + | − | − | − |
| 24 | 55 | 60 | — | F | 2 | − | − | + | + | − | − |
| 25 | 52 | 56 | — | F | 1 | − | − | + | + | − | − |
| 26 | 63 | 65 | — | F | 0.5 | − | − | − | − | + | − |
| 27* | 69 | 71 | — | F | 2 | − | − | + | + | − | − |
| Totals | | | | | | 10 | 6 | 15 | 14 | 8 | 12 |

Clinical features were considered present (+) if documented by physical examination or history at any point in the clinical course.

* PPCD only cases; all others PPCD with concomitant diagnosis of dementia of the Alzheimer type.

CDR = Clinical Dementia Rating.

**Progressive posterior cortical dysfunction: A clinicopathologic series.**
Renner, J; Burns, J; Hou, C; McKeel, D; Storandt, M; Morris, J

Neurology. 63(7):1175-1180, October 12, 2004.

Table 1 Clinical features of 27 cases of primary posterior cortical dysfunction (PPCD) by pathologic diagnoses

Wolters Kluwer Health | OvidSP

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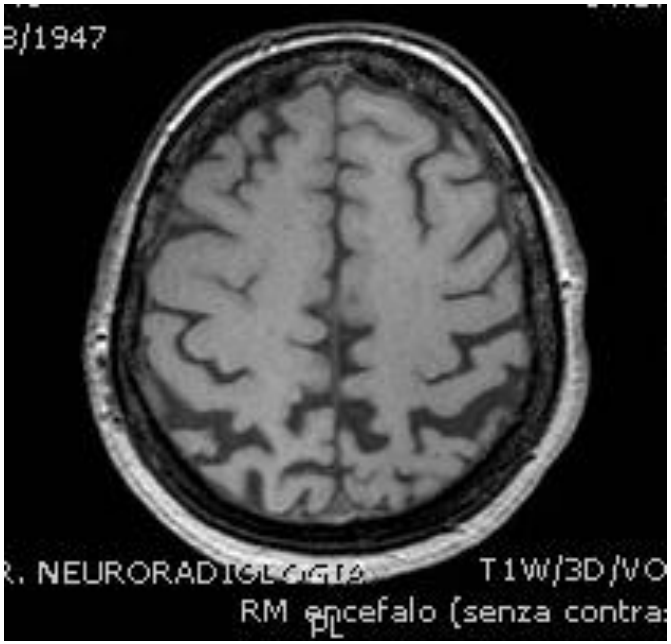
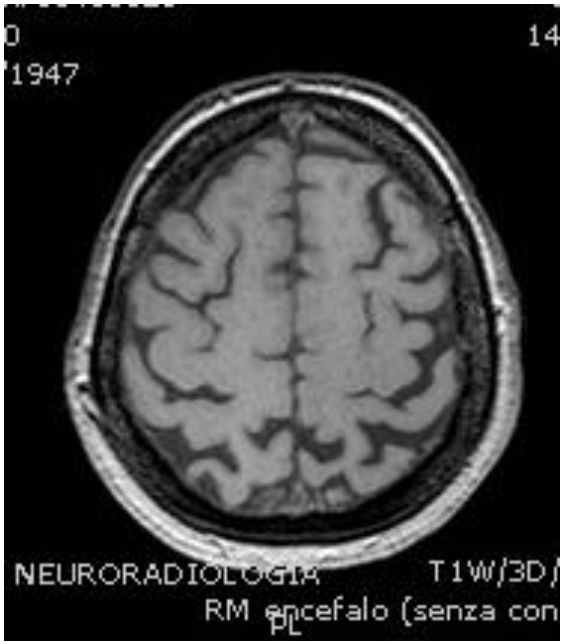
# MR: atrofia parietale focale



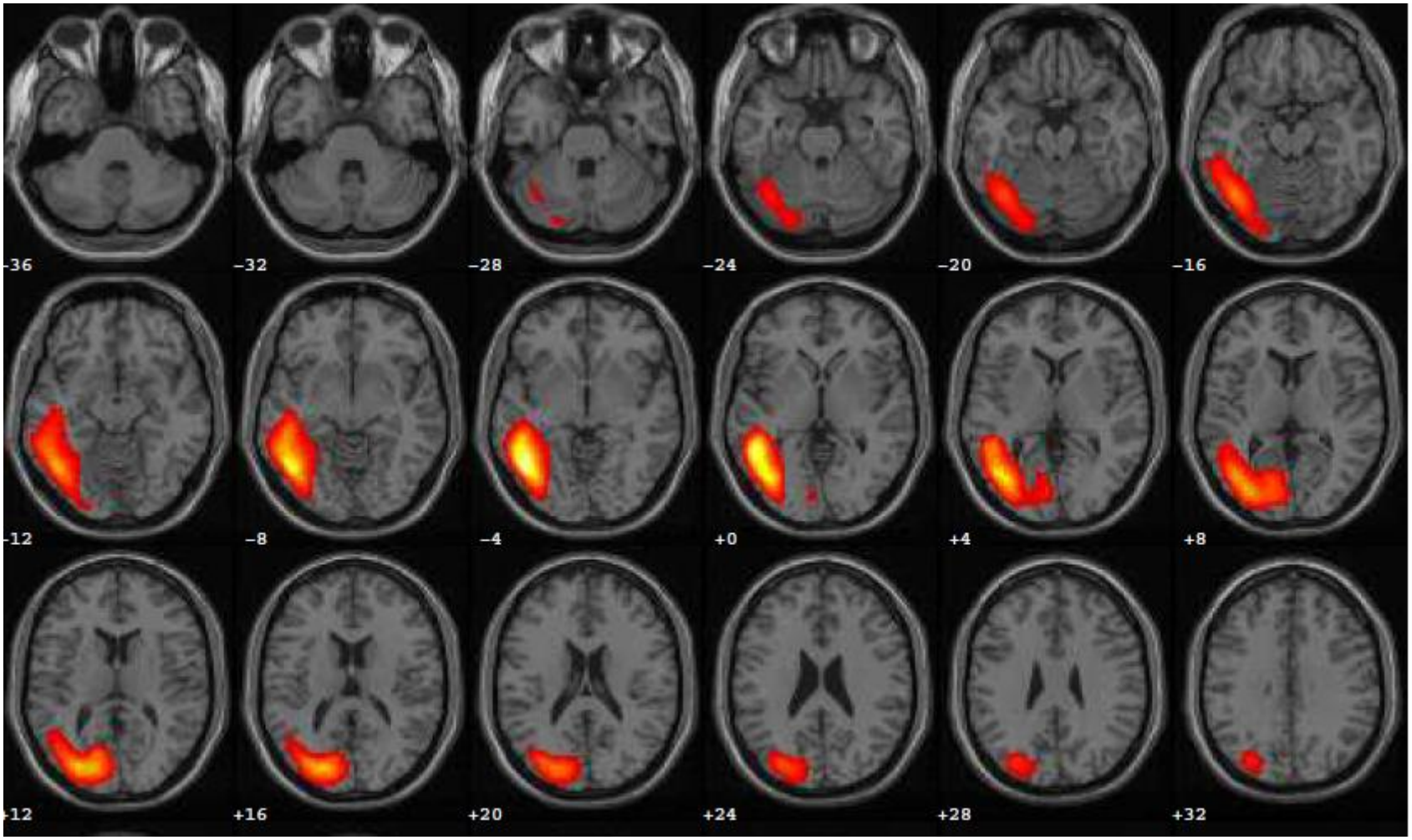
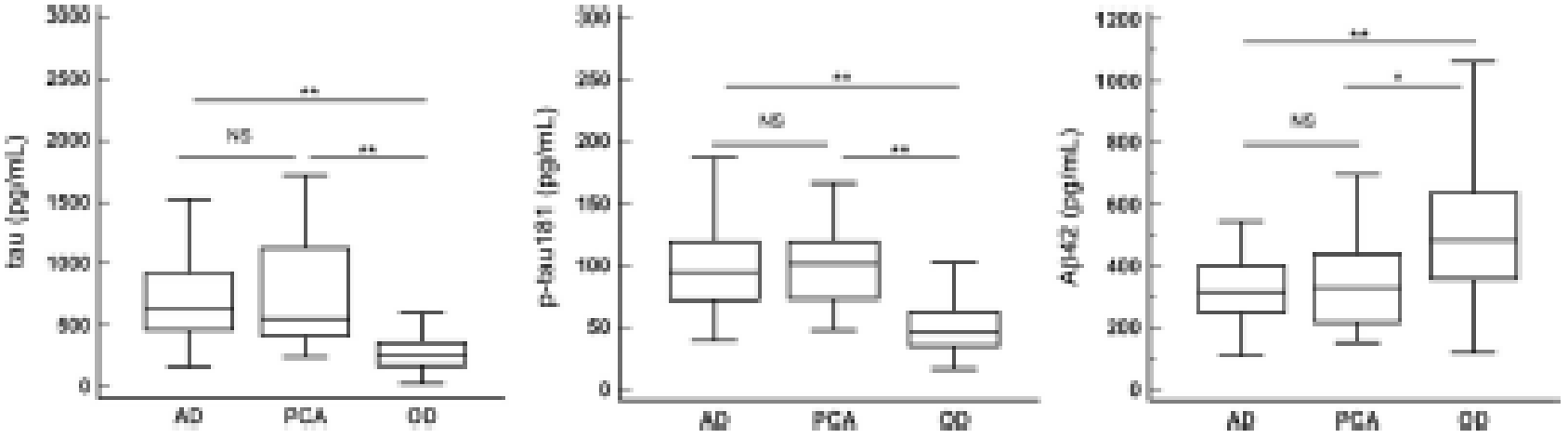

-36
-32
-28
-24
-20
-16
-12
-8
-4
+0
+4
+8
+12
+16
+20
+24
+28
+32

**Figure 1** Comparison of total tau proteins (t-tau), phosphorylated tau on amino acid 181 (p-tau181), and amyloid β peptide (Aβ42) CSF patterns among patients with Alzheimer disease (AD), patients with posterior cortical atrophy (PCA), and patients with other dementias (OD)




Box plot showing median CSF levels of t-tau, p-tau181, and Aβ42 in AD, PCA, and OD subgroups (**$p < 0.0001$; *$p < 0.0016$; NS = nonsignificant).

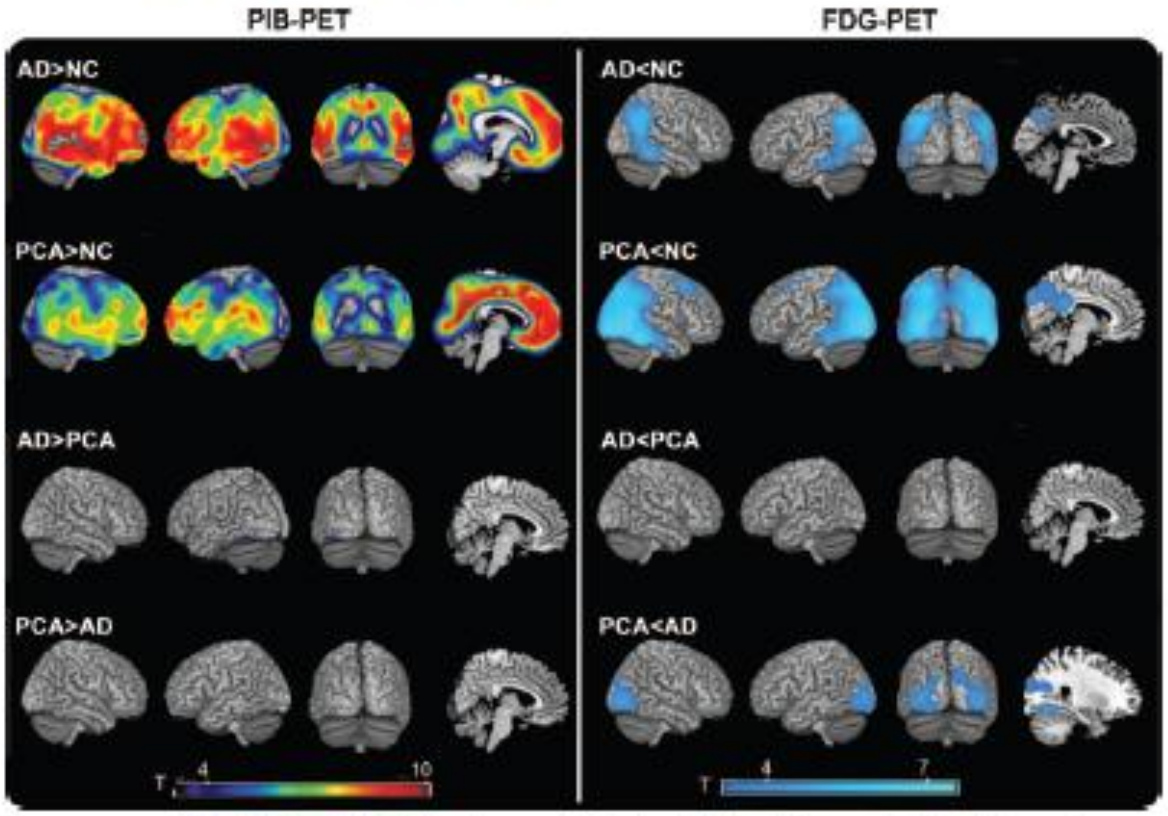
NEUROLOGY

# Distinct clinical and metabolic deficits in PCA and AD are not related to amyloid distribution

M.H. Rosenbloom, A. Alkalay, N. Agarwal, et al.

*Neurology*; Prepublished online April 27, 2011;
DOI 10.1212/WNL.0b013e31821cccad

Figure 1 Patterns of Pittsburgh compound B (PiB) and FDG binding in Alzheimer disease (AD) and posterior cortical atrophy (PCA) compared to normal controls (NC) and to each other




T-score maps are rendered on the *ch2* template brain. All results are presented at a threshold of $p < 0.001$, uncorrected for multiple comparisons.

# Fenotipi clinici: una classificazione sindromica

- Prevalenti disturbi visuopercettivi
- **Prevalenti disturbi del linguaggio**
- Prevalenti disturbi comportamentali e/o disesecutivi
- Associazione con disturbi del movimento

**Table 1. Diagnostic Criteria for Primary Progressive Aphasia.***

There is an insidious onset and gradual but progressive impairment of word finding, object naming, syntax, or word comprehension manifested during conversation or assessed with the use of standard neuropsychological tests of language.

All major limitations in activities of daily living can be attributed to the language impairment for at least two years after onset.

Premorbid language function (except for developmental dyslexia) is known to be intact.

Prominent apathy, disinhibition, loss of memory of recent events, visuospatial impairment, visual-recognition deficits, and sensory-motor dysfunction are absent during the initial two years of illness, as indicated by the history, evaluation of activities of daily living, or neuropsychological testing, so that the patient would not fulfill diagnostic criteria for any other dementia syndrome.

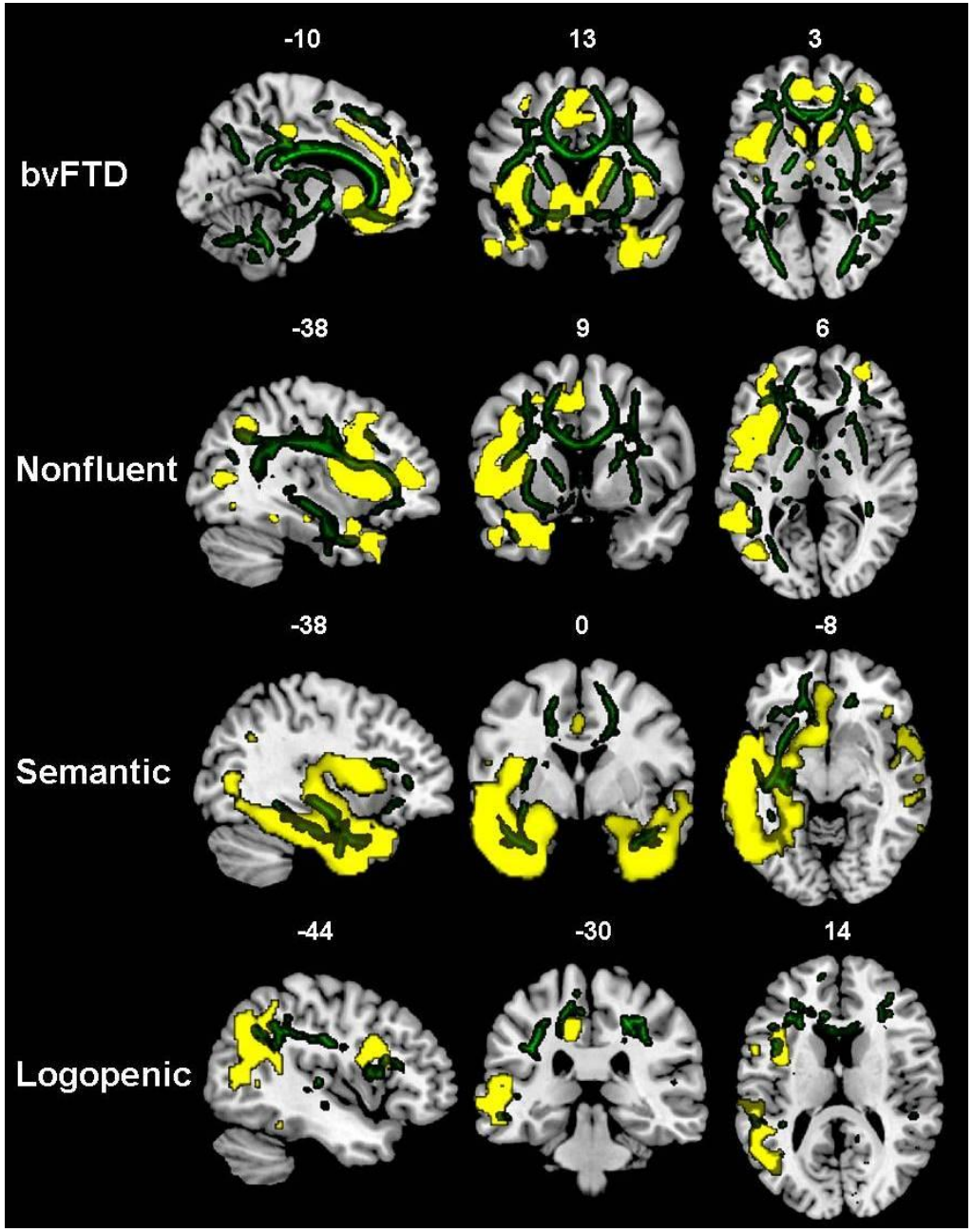
Acalculia (inability to perform simple mathematical calculations) and ideomotor apraxia (inability to pantomime movement as instructed by an examiner) can be present even in the first two years of illness, and deficits in copying simple drawings and perseveration may also be noted, but neither visuospatial deficits nor behavioral disinhibition substantially limits activities of daily living.

Other cognitive functions may be affected after the first two years of illness, but language remains the most impaired function throughout the course of the illness and deteriorates faster than other affected functions.

Specific causes of aphasia, such as stroke or tumor, as ascertained by neuroimaging, are absent.

# Le afasie primarie progressive: fenotipi clinici

- **Variante logopenico/fonologica**
- **Variante non fluente/agrammatica**
- **Variante semantica**




**Agosta et al., submitted**

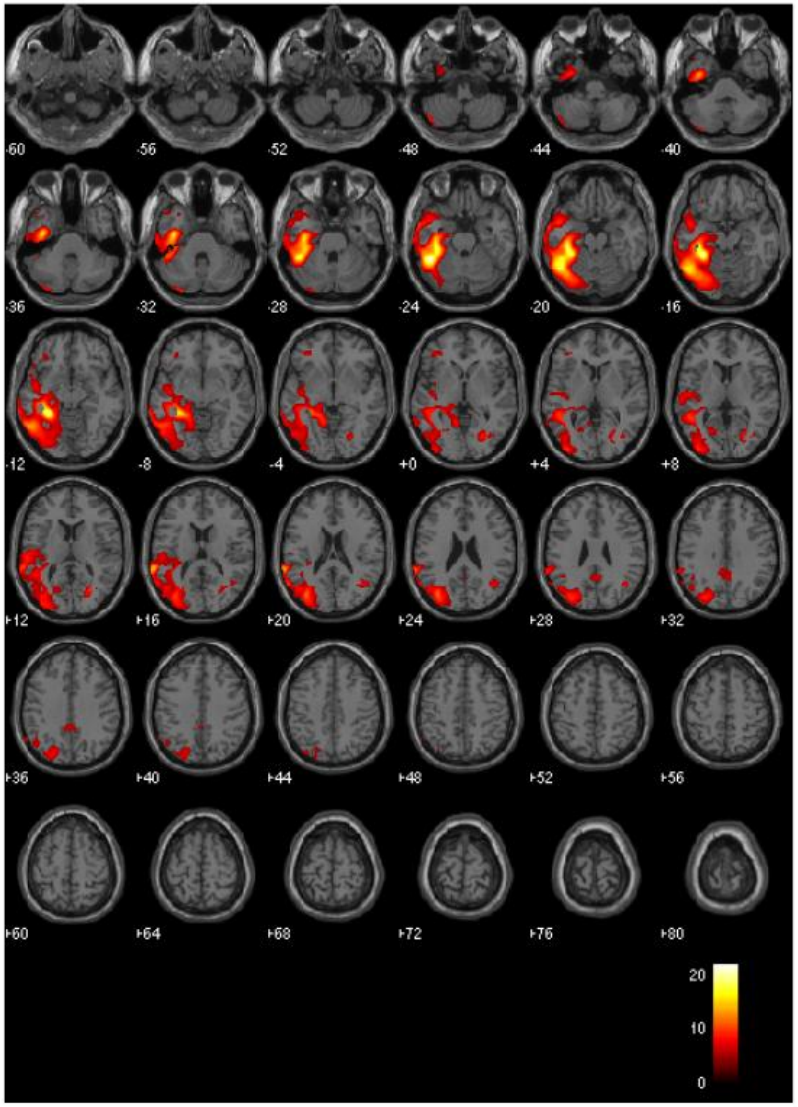
# Può essere lo stesso Alzheimer: presentazioni «atipiche»

- Atrofia Corticale Posteriore
- Afasia progressiva (variante logopenica)
- Variante «frontale»

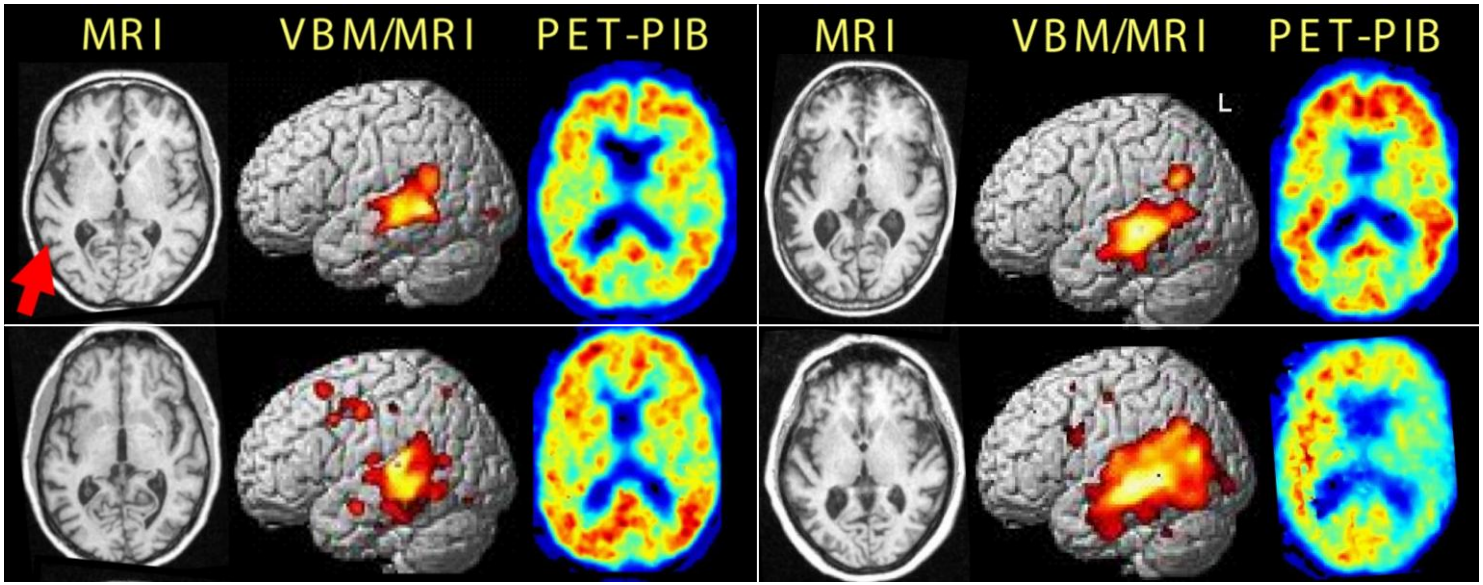
## CSF Aβ42 and Tau measures

| | | | |
|---|---|---|---|
| LCR-BETA AMILOIDE (I-42) | 269 | ng/L | > 500 |
| LCR-PROTEINA TAU | 322 | ng/L | 0.0 - 500.0 |
| LCR-PROTEINA TAU FOSFORILATA | 74 | ng/L | 0.00 - 61.00 |

## SPM-T map of hypometabolism of the single patient [$^{18}$F]FDG-PET scan compared to 112 HC (FWE)



**Structural MRI VBM versus 20 controls and PIB scans in four LPA patients.**




**Courtesy of M.L. Gorno-Tempini**

# Case S.P. ♂ 63 years old, 13 years of education, svPPA (GRN +)

**Figure 2.** Axial T1-weighted MRI images at the diagnosis (A) and at a 18-month follow up (B)

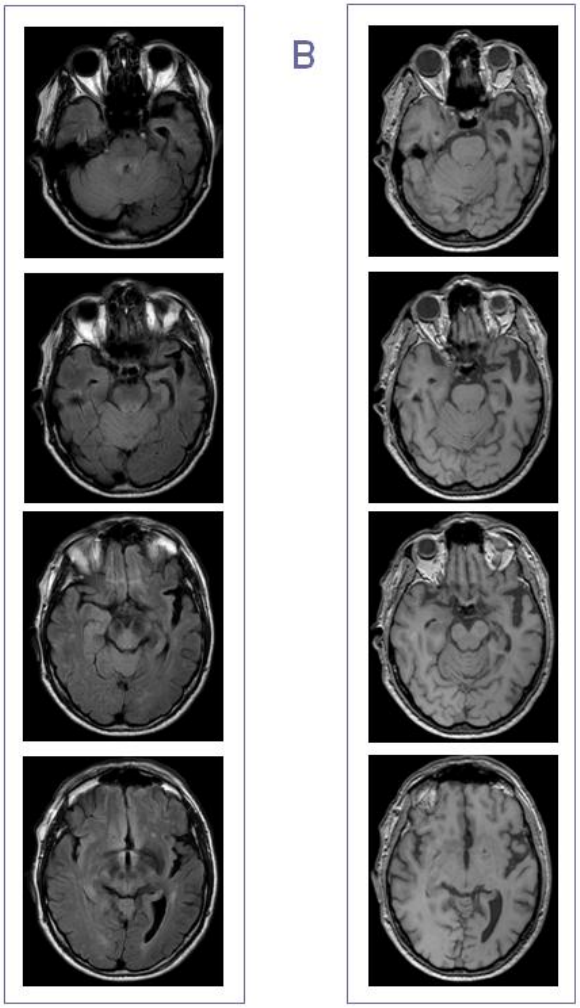
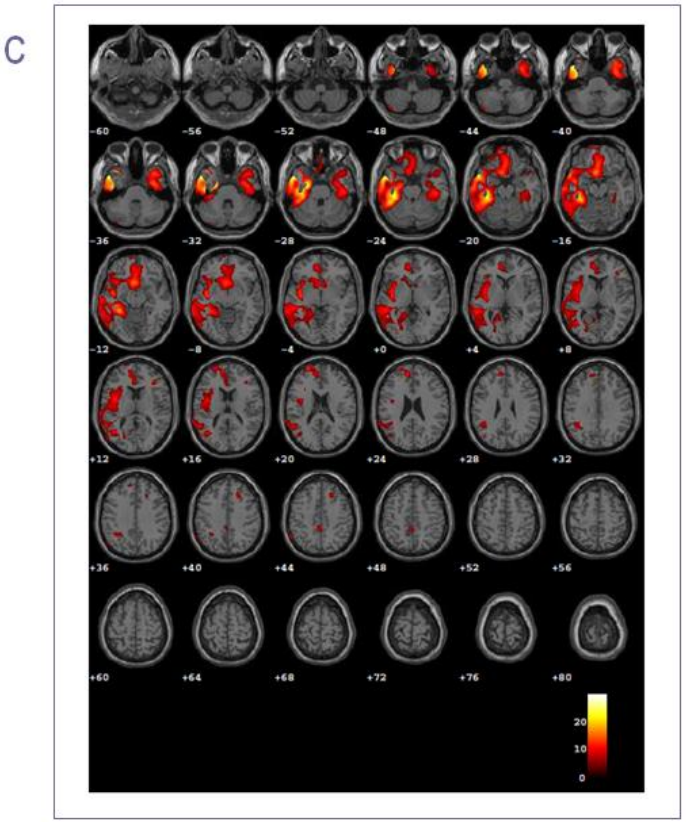
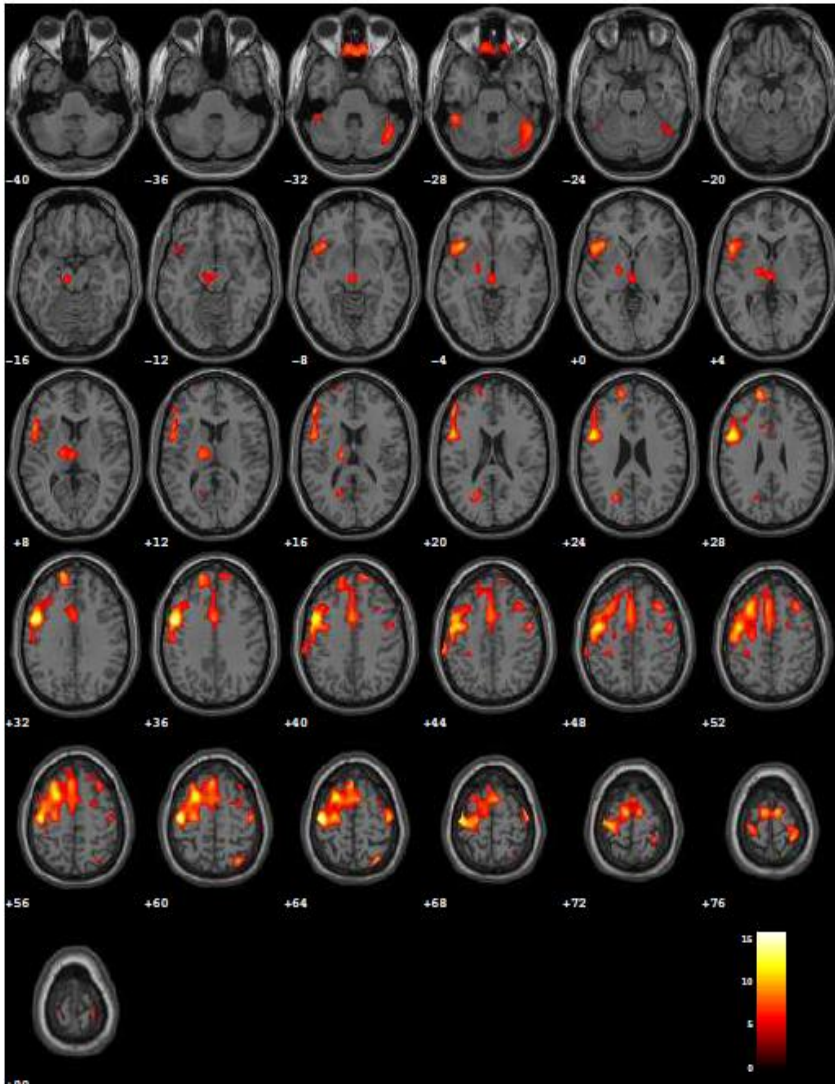



**Figure 3.** SPM-T map of hypometabolism (SPM5; http://www.fil.ion.ucl.ac.uk/spm/software/spm5/) of the single-patient [$^{18}$F]FDG-PET scan compared to 112 normal scans and displayed at a voxel-wise corrected threshold (p=0.05, FWE) with a minimum cluster size of 100 voxels



# Case M.G. ♀ 62 years old, 17 years education

## SPM-T map of hypometabolism of the single patient [$^{18}$F]FDG-PET scan compared to 112 HC (FWE)




## ❑ Neuropsychological Evaluation Language assessment

| AREA INDAGATA | TEST | P. GREZZO | P. CORRETTO | P. EQUIVALENTE |
|---|---|---|---|---|
| **LINGUAGGIO:** | | | | |
| **denominazione orale nomi** | CAGI: | 48/48 | 48 | 4 |
| **comprensione nomi** (*word picture matching test*)…… | | 48/48 | 48 | 4 |
| **comprensione di ordini complessi**…… | Token Test…… | 33/36 | 30.50 | 2 |
| **Comprensione grammaticale uditiva**…… | BADA: | 58/60 | Cut off: 58 | Al limite |
| **Comprensione grammaticale visiva**…… | | 42/45 | Cut off: 43 | Deficitario |
| **Accesso al lessico**…… | Fluenza semantica…… | 24 | 22 | 0 |
| | Fluenza fonemica…… | 10 | 5 | 0 |
| **Memoria semantica**…… | Test Palma Piramide | 48/52 | 45.77 | Nella norma |
| **Ripetizione** …… | AAT: | | | |
| | Suoni | 28/30 | | |
| | Parole | 30/30 | | |
| | Parole straniere | 30/30 | | |
| | Parole composte e sintagmi | 29/30 | | |
| | Frasi | 30/30 | | |
| | TOTALE | 147/150 | - | Nessun deficit |
| **Lettura**…… | AAT: | 30/30 | - | Nessun deficit |
| **Scrittura sotto dettato**…… | | 30/30 | - | Nessun deficit |

| | Articulation | Naming | Word comprehension | Repetition | Syntactic comprehension |
|---|---|---|---|---|---|
| NFPA | impaired | impaired-PP | preserved | impaired | impaired |
| SD | preserved | impaired-SP | impaired | preserved | rel. preserved |
| LPA | preserved (slow-hesitant) | impaired-PP | preserved | impaired | impaired |

# Classification and pathology of primary progressive aphasia

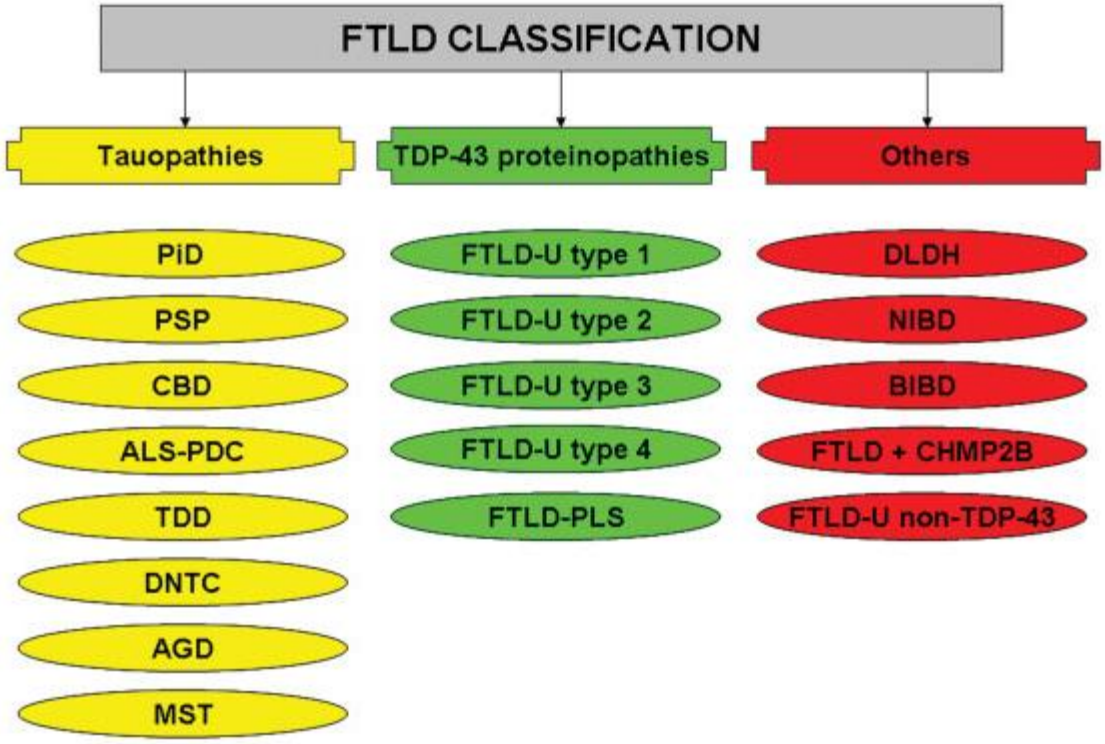
Jennifer M. Harris, BSc
Claire Gall, MB, ChB
Jennifer C. Thompson, PhD
Anna M.T. Richardson, MB, ChB
David Neary, MD
Daniel du Plessis, MB, ChB
Piyali Pal, MD
David M.A. Mann, PhD
Julie S. Snowden, PhD
Matthew Jones, MD

**Table 2** Pathologic relationships in PPA variants

| PPA subtype | Total no. of patients | No. of patients in each pathologic group |
|---|---|---|
| Nonfluent | 8 | 6 FTLD (2 TDP-43 type A—1 *GRN* mutation, 1 Pick disease, 3 corticobasal degeneration) |
| | | 1 CJD |
| | | 1 mixed DLB, AD, and vasculitis |
| Semantic | 4 | 4 FTLD (TDP-43 type C) |
| Logopenic | 13 | 3 FTLD (TDP-43 type A—1 *GRN* mutation, other 2 genetic information not available) |
| | | 7 AD (including 1 mixed AD and DLB) |
| | | 1 DLB |
| | | 1 CJD |
| | | 1 cerebrovascular disease |
| Unclassified | 5 | 3 FTLD (TDP-43 type A—2 *GRN* mutation) |
| | | 2 AD (including 1 mixed AD and cerebrovascular disease) |

Abbreviations: AD = Alzheimer disease; CJD = Creutzfeldt-Jakob disease; DLB = dementia with Lewy bodies; FTLD = frontotemporal lobar degeneration; *GRN* = progranulin; PPA = primary progressive aphasia; TDP-43 = transactive response DNA-binding protein 43. FTLD pathologic classification according to Mackenzie et al[13,14]; TDP-43 subtyping according to Mackenzie et al.[15]

# Le demenze fronto-temporali

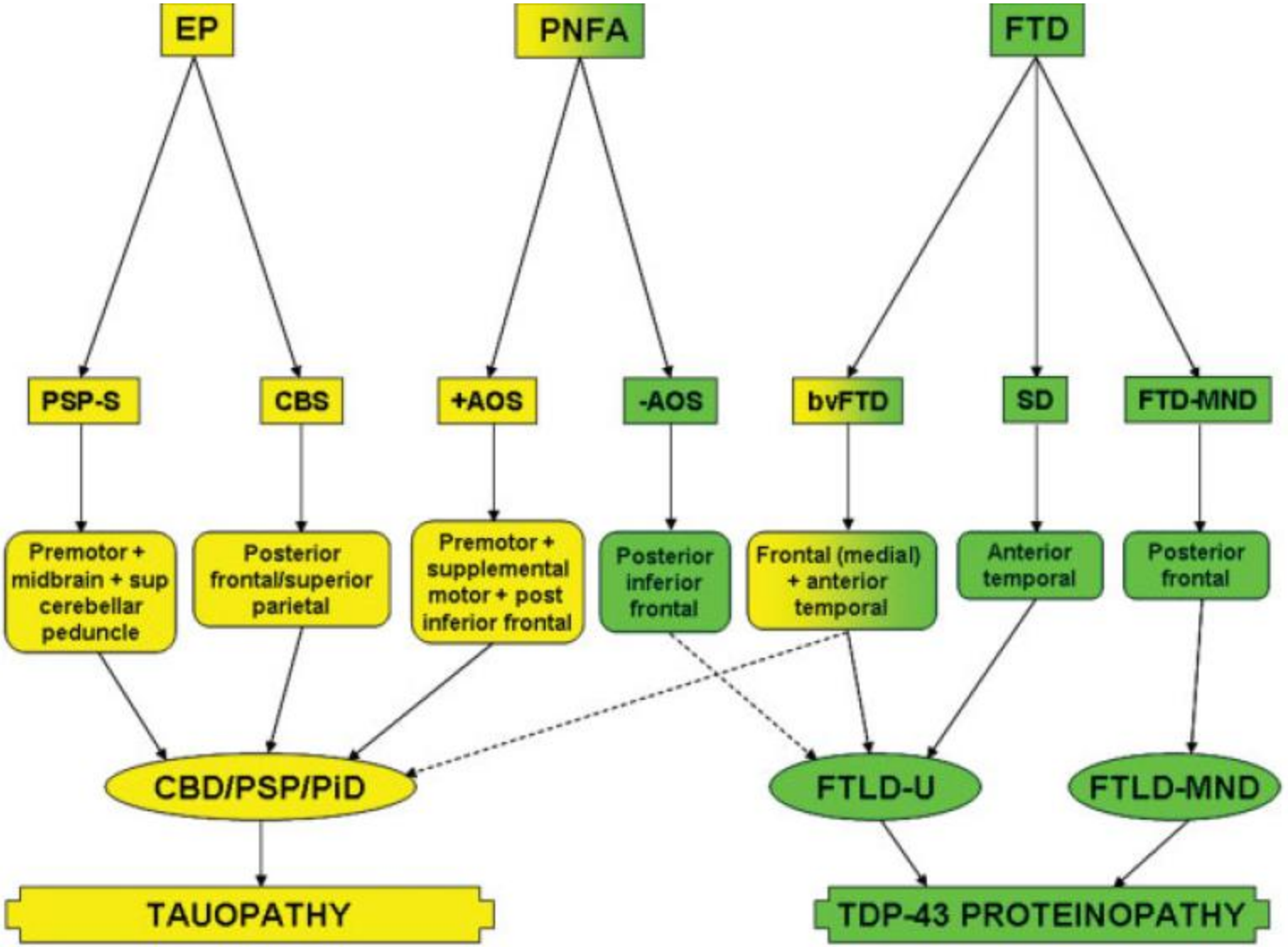



NEUROLOGICAL PROGRESS

Frontotemporal Dementia and Related Disorders: Deciphering the Enigma

Keith A. Josephs, MST, MD

# Correlazioni cliniche



# Fenotipi clinici: una classificazione sindromica

- Prevalenti disturbi visuopercettivi
- Prevalenti disturbi del linguaggio
- **Prevalenti disturbi comportamentali e/o disesecutivi**
- Associazione con disturbi del movimento

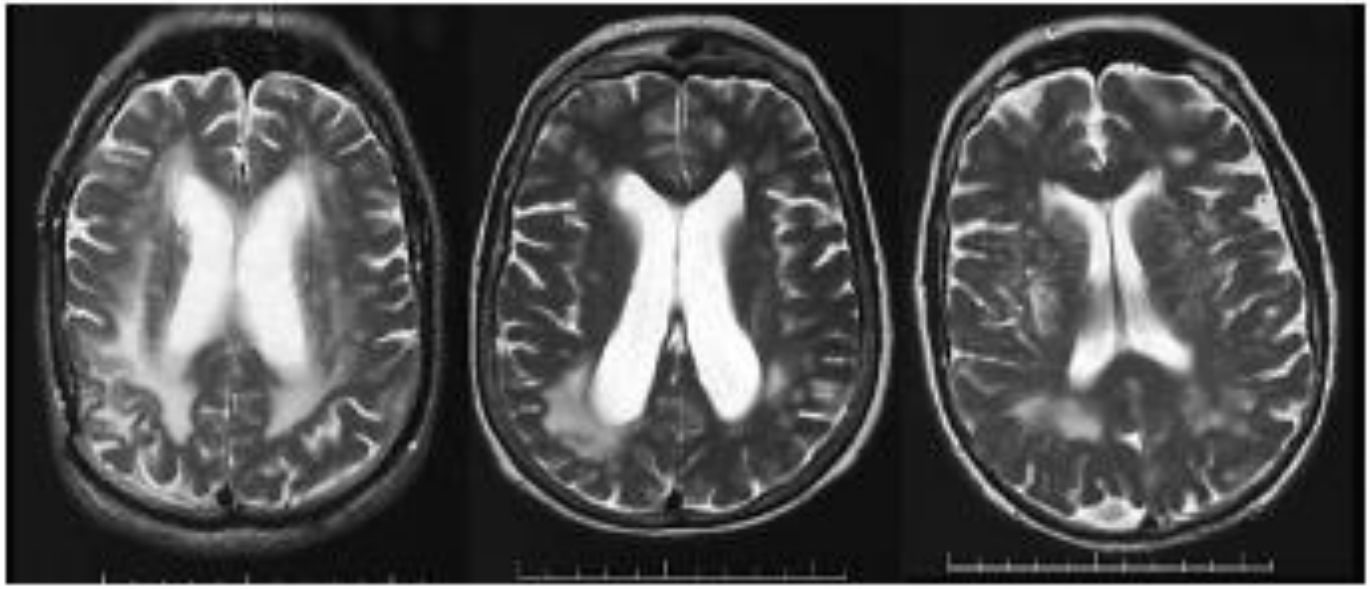
# Sindrome comportamentale e/o disesecutiva

- Modificazioni della personalità
- Alterazioni delle condotte sociali

- Deficit di ragionamento, pianificazione, monitoraggio
- Deficit della memoria di lavoro
- Deficit attenzionali

# Presentazione comportamentale/esecutiva

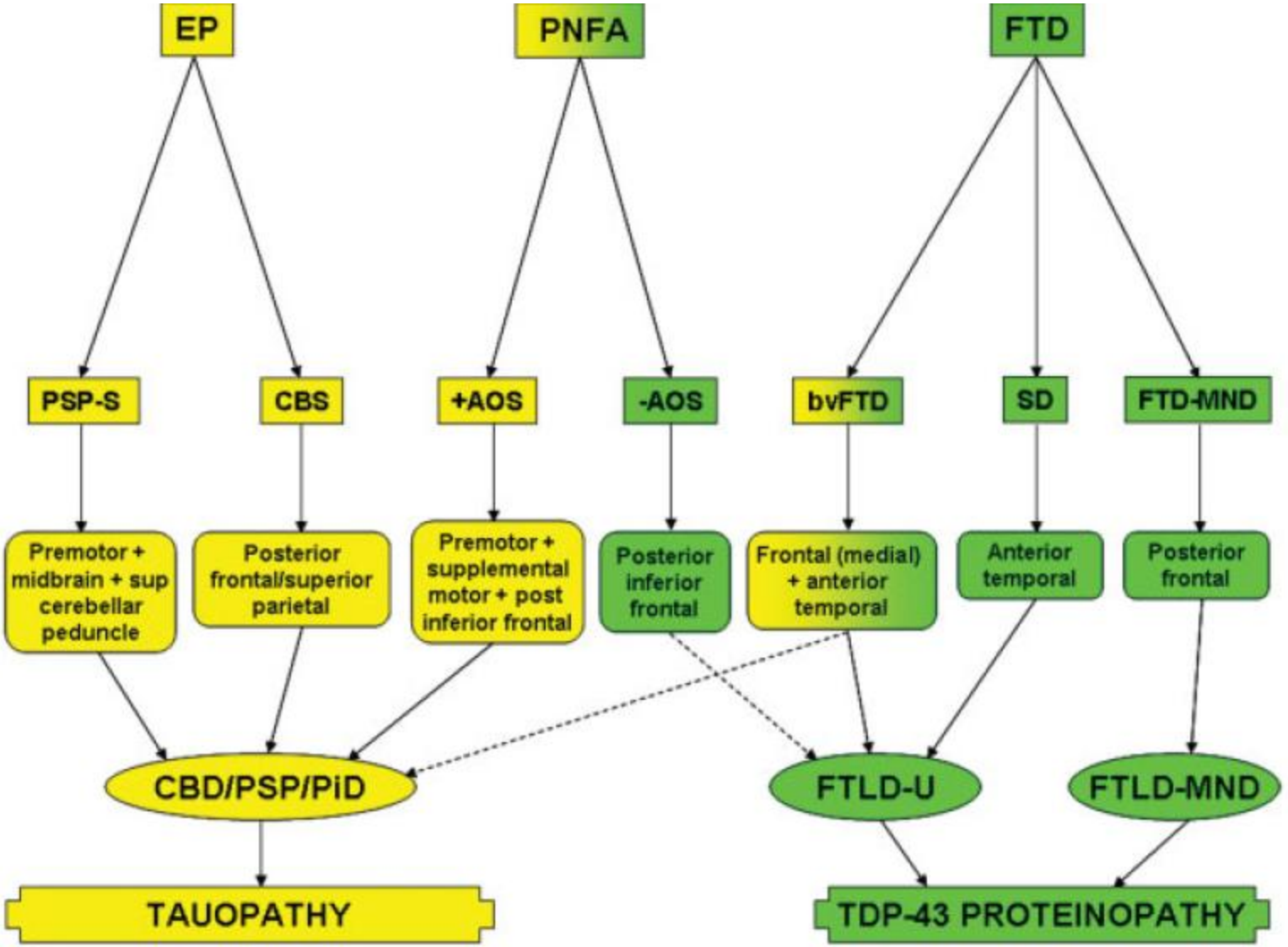
- Demenza vascolare
- AD ad esordio frontale
- Variante comportamentale della demenza fronto-temporale



# Caratteristiche distintive

- Meno deficit di memoria episodica
- Più deficit psicologici/comportamentali, esecutivi (es. memorai di lavoro, trail making), linguaggio (fluenze) e visuospaziali (copia disegni)

# Correlazioni cliniche



# International Consensus Criteria for bvFTD

A. Early behavioral dishinibition
B. Early apathy or inertia
C. Early loss of sympathy or empathy
D. Early perseverative, stereotyped or compulsive/ritualistic behavior
E. Hyperorality and dietary changes
F. Neuropsychological profile: executive/generation deficits with relative sparing of memory and visuospatial functions

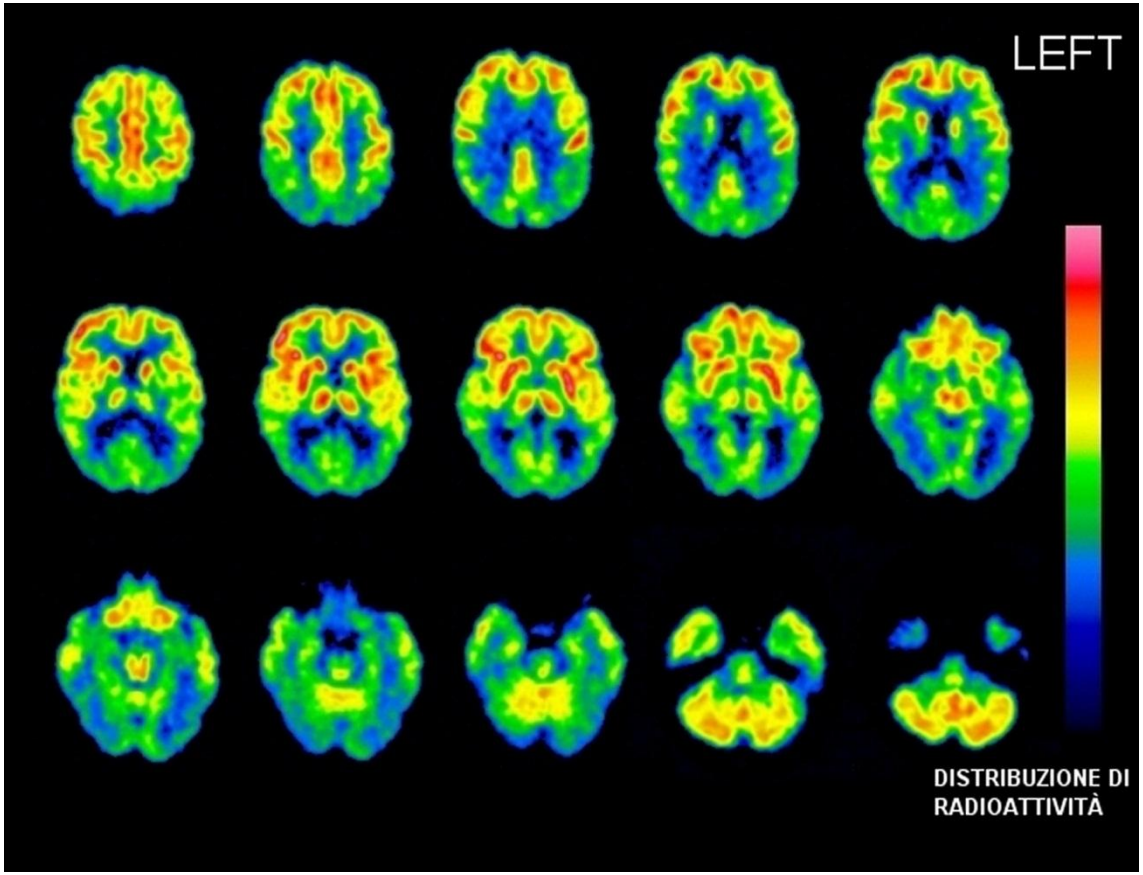
# Fenotipi clinici: una classificazione sindromica

- Prevalenti disturbi visuopercettivi
- Prevalenti disturbi del linguaggio
- Prevalenti disturbi comportamentali e/o disesecutivi
- **Associazione con disturbi del movimento**

# Criteri LBD (McKeith et al., 2005)

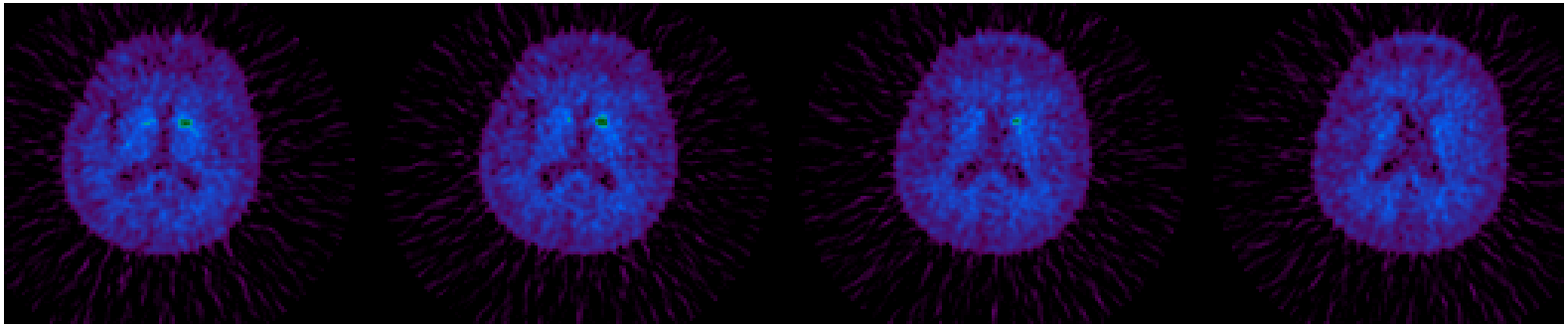
- **Central feature**
  - **Progressive dementia:** Deficits in attention and executive function are typical. Prominent memory impairment may not be evident in the early stages
- **Core features**
  - Fluctuating cognition with pronounced variations in attention and alertness.
  - Recurrent complex visual hallucinations, typically well formed and detailed.
  - Spontaneous features of parkinsonism
- **Suggestive features**
  - REM sleep behavior disorder (RBD), which can appear years before the onset of dementia and parkinsonism.
  - Severe sensitivity to neuroleptics occurs in up to 50% of LBD patients who take them.
  - Low dopamine transporter uptake in the brain's basal ganglia as seen on SPECT and PET imaging scans

# FDG PET

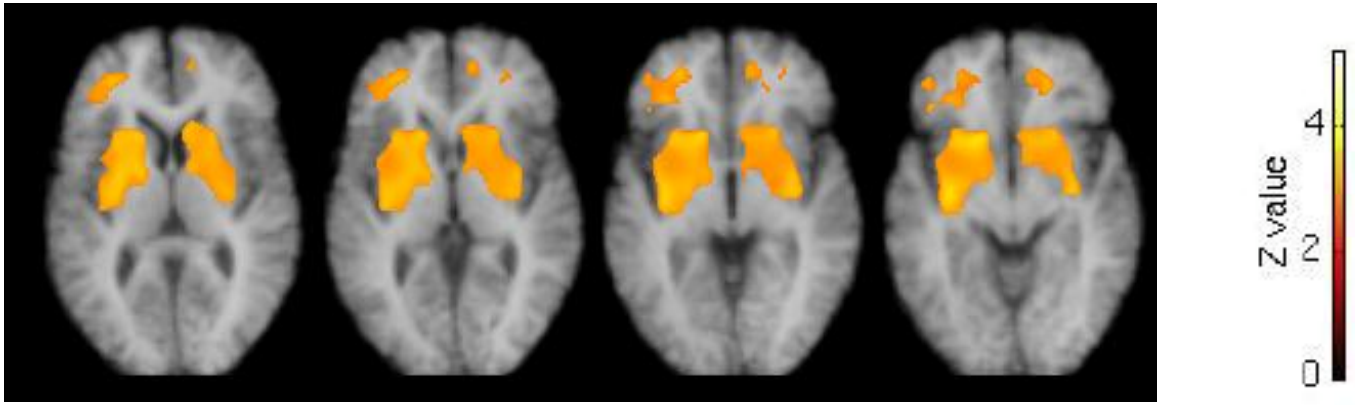


# [$^{11}$C]-b-CIT-FE PET

**PET images**



**SPM images**
**p<0.001**

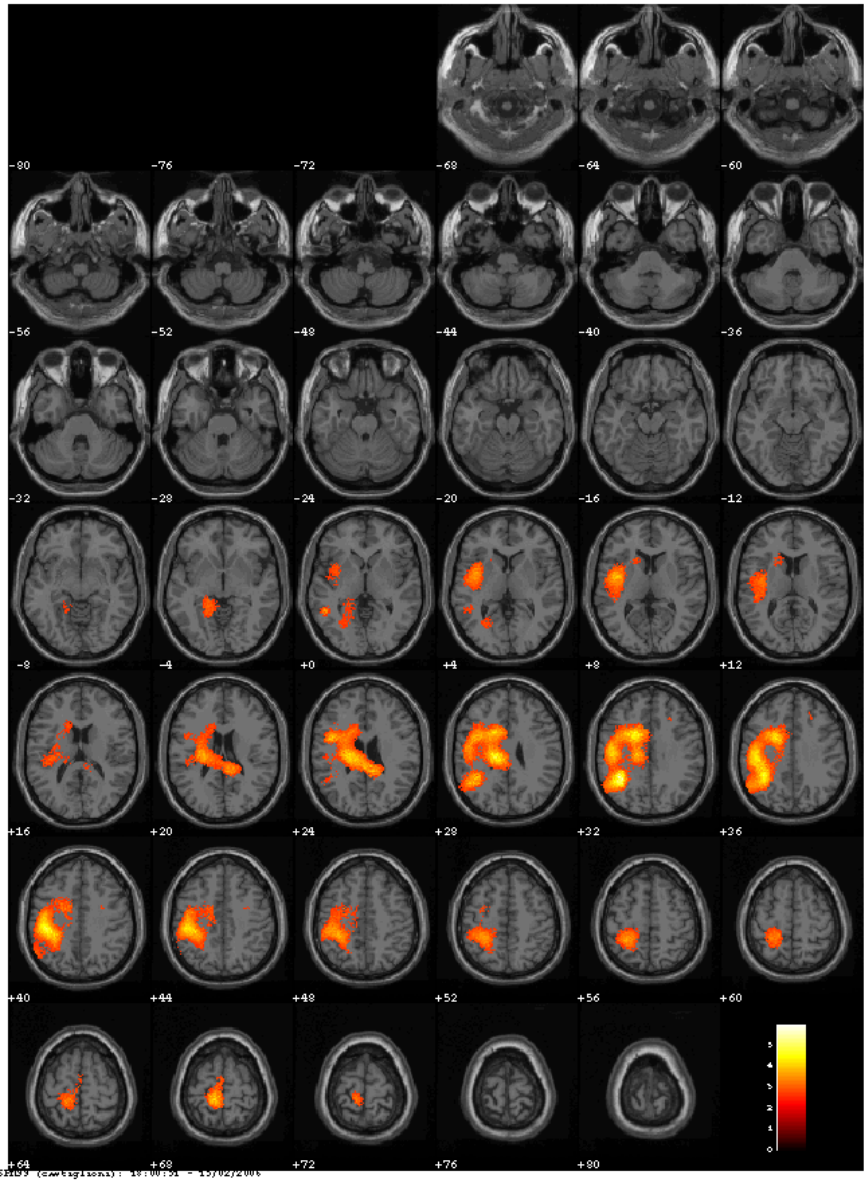



**HSR Milan**

# Criteri CBDS (Boeve et al., 2003)

- Disfunzione corticale indicata da almeno uno dei seguenti:
  - Aprassia ideomotoria focale o asimmetrica
  - Fenomeno dell'arto alieno
  - Emi-inattenzione
  - Aprassia costruttiva
  - Mioclono focale o asimmetrico
  - Aprassia dell'eloquio o afasia non fluente

- Disfunzione extrapiramidale indicata da almeno uno dei seguenti:
  - Rigidità artuale focale o asimmetrica che non risponde alla levodopa
  - Distonia artuale focale o asimmetrica


-80
-76
-72
-68
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-48
-44
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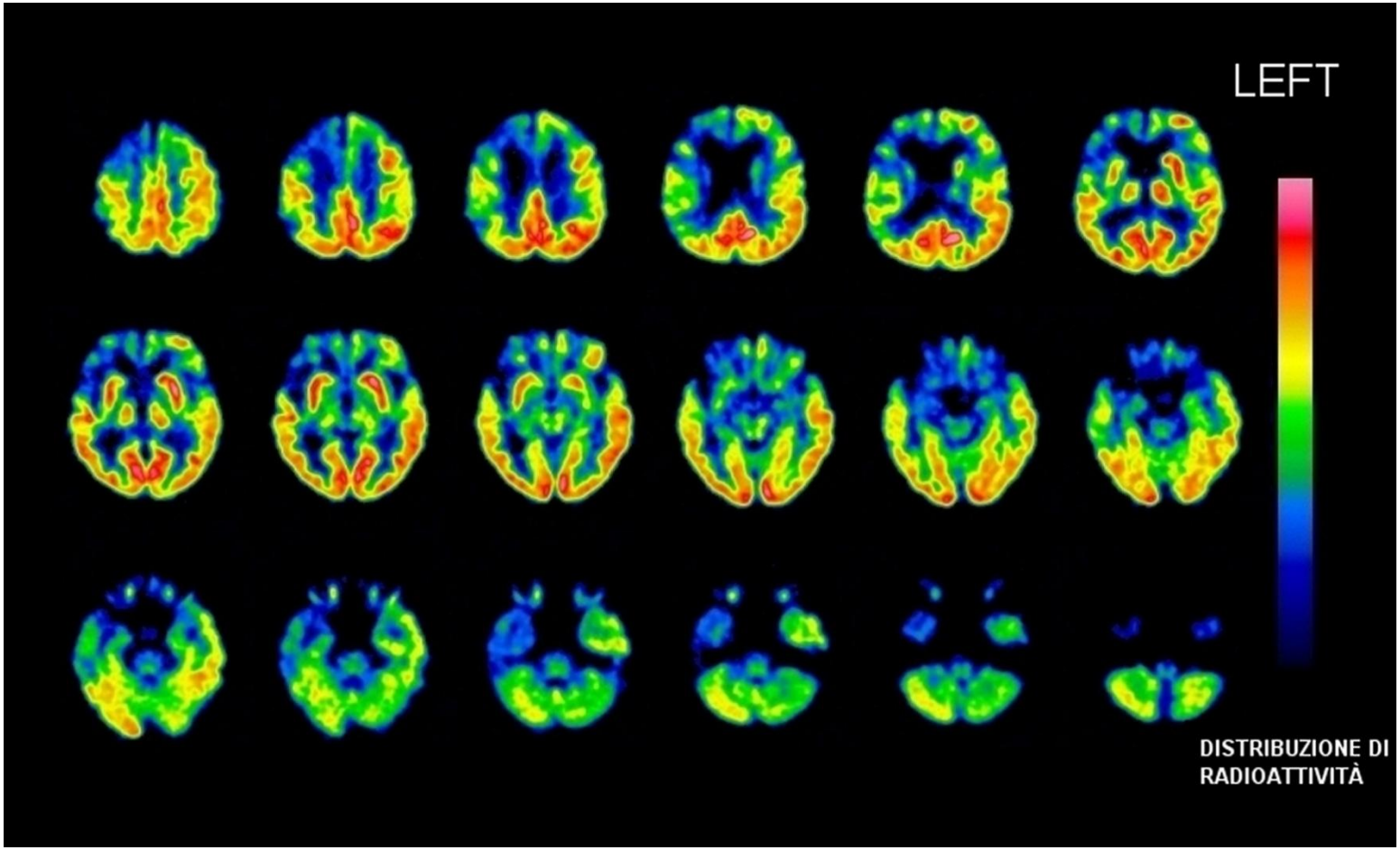
-20
-16
-12
-8
-4
+0
+4
+8
+12
+16
+20
+24
+28
+32
+36
+40
+44
+48
+52
+56
+60
+64
+68
+72
+76
+80

# Criteri diagnostici per PSP

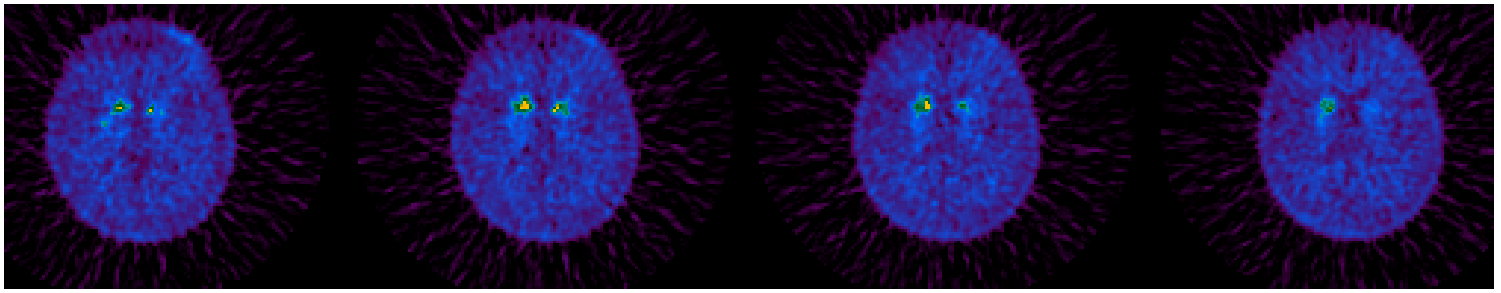
(Litvan et al, 1996)

- Possible PSP
  - 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
  - no evidence of other diseases that could explain these features.
- Probable PSP
  - vertical supranuclear gaze palsy
  - prominent postural instability
  - falls in the first year of onset
  - features of possible PSP.
- Definite PSP
  - a history of probable or possible PSP and histopathologic evidence of typical PSP

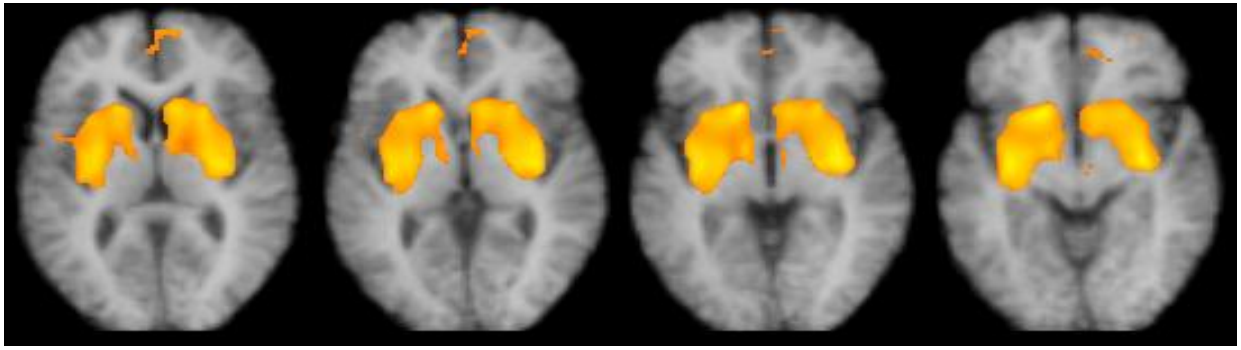

LEFT
DISTRIBUZIONE DI
RADIOATTIVITÀ

# Progressive supranuclear palsy

**[$^{11}$C]-β-CIT-FE**



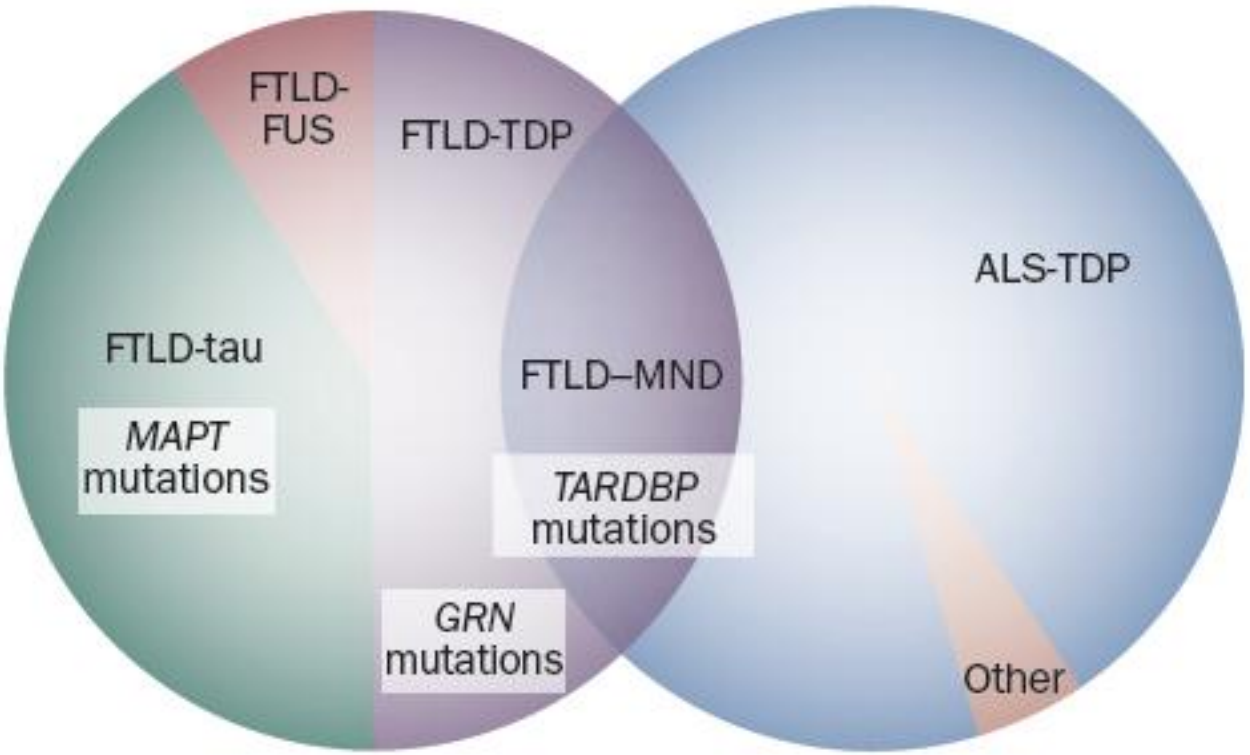
PET images




SPM images
p<0.001

HSR Milan

# The Bv-FTD-MND spectrum



# Cosa è «atipico»?

- Sintomi di esordio
- Rapidità di evoluzione
- Età

# Malattia prionica

# MRI-CJD Consortium criteria for sporadic Creutzfeldt–Jakob disease.

**I. clinical signs:**

1. dementia
2. cerebellar or visual
3. pyramidal or extrapyramidal
4. akinetic mutism

**II. tests:**

1. PSWCs in EEG
2. 14-3-3 detection in CSF (in patients with a disease duration of less than 2 year)
3. high signal abnormalities in caudate nucleus and putamen or at least two cortical regions (temporal-parietal-occipital) either in DWI or FLAIR

**Probable CJD**

two out of I and at least one out of II

**Possible CJD**

two out of I and duration less than 2 years

**Zerr I et al. Brain 2009;132:2659-2668**

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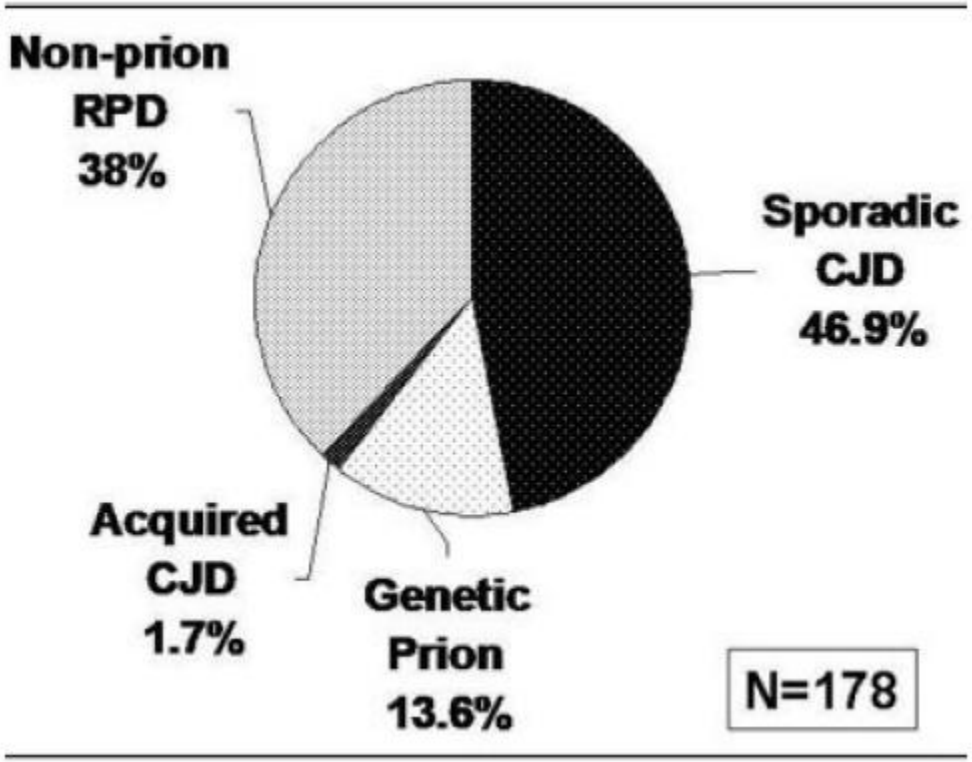


M. Geschwind et al., 2008

*Table 1.* **Nonprion Diagnoses of Patients in University of California, San Francisco Cohort Initially Suspected of Having Creutzfeldt–Jakob Disease**

| Condition | Cases (n) | Percentage of Nonprion RPDs |
|---|---|---|
| Neurodegenerative | | |
| Corticobasal degeneration | 8 | |
| Frontotemporal dementia[a] | 7 | |
| Dementia with Lewy bodies | 4 | |
| Alzheimer's disease[b] | 5 | |
| Progressive supranuclear palsy | 2 | |
| Subtotal | 26 | 39 |
| Autoimmune | | |
| Hashimoto's encephalopathy | 4 | |
| Multiple sclerosis | 1 | |
| Sarcoid | 1 | |
| Antibody mediated | | |
| VGKC | 2 | |
| Yo and Hu | 1 | |
| Ma[c] | 1 | |
| CV2[c] | 1 | |
| GAD65 | 1 | |
| Neuropil[c] | 1 | |
| Adenylate kinase 5 | 1 | |
| Glial | 1 | |
| Subtotal | 15 | 22 |
| Unknown causative factor[d] | 8 | 12 |
| Infectious[e] | 4 | 6 |
| Psychiatric | 4 | 6 |
| Malignancy[f] | | |
| PCNSL | 2 | |
| Non–antibody-mediated paraneoplastic | 2 | |
| Subtotal | 4 | 6 |
| Toxic/metabolic | | |
| Ethanol toxicity | 1 | |
| Methylmalonic acidemia | 1 | |
| Methotrexate toxicity | 1 | |
| Subtotal | 3 | 4 |
| Vascular | 3 | 4 |
| Total | 67 | 100 |

[a]Includes two frontotemporal dementia/acute lateral sclerosis and one progressive subcortical gliosis PSG patient. [b]Includes one familial subject. [c]Includes one paraneoplastic patient. [d]Includes one leukoencephalopathy, one pathology-proven astrogliosis, and one suspected cerebral amyloid angiopathy patient. [e]Includes two pathology-proved meningoencephalitis and two viral encephalitis patients (unknown agent; patients recovered). [f]Includes one thymoma and one systemic lymphoma with encephalopathy patient and two central nervous system lymphoma patients. RPD = rapidly progressive dementia; VGKC = voltage-gated potassium channel antibody; PCNSL = primary central nervous system lymphoma.

# Cosa è «atipico»?

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**Table 2** Causes of young onset dementia: sporadic and acquired (bold, treatable condition; * , often absent)

| Disease | Clues to diagnosis: Clinical features | Investigations |
|---|---|---|
| Primary neurodegenerations | | |
| Alzheimer's disease | History of becoming lost, biparietal signs | EEG: absent α rhythm<br>MRI: early hippocampal atrophy |
| Frontotemporal lobar degenerations: | | |
| Frontotemporal dementia | Early behavioural change, frontal features | EEG: preserved α rhythm |
| Semantic dementia[25] | Early circumscribed semantic impairment | MRI: selective anterior left temporal atrophy |
| Primary progressive non-fluent aphasia[28] | Progressive speech production impairment | MRI: circumscribed left perisylvian atrophy |
| Frontal dementia (motor neurone disease)[29] | Orofacial apraxia, bulbar features, fasciculations (especially deltoid), amyotrophy | EMG: changes of denervation* |
| Dementia with Lewy bodies[30] | Visual hallucinations, extrapyramidal syndrome, fluctuation | |
| Multiple system atrophy[31] | Dysautonomia, cerebellar, extrapyramidal features | MRI: midbrain atrophy, "hot cross bun sign"* (increased signal in cerebellum, middle cerebellar peduncles, pons) |
| Corticobasal degeneration[32] | Early asymmetric apraxia and rigidity, dystonia, cortical sensory deficit, alien limb | |
| Parkinson's disease[26] | Established typical parkinsonian syndrome predating cognitive decline | |
| Progressive supranuclear palsy (Steele-Richardson-Olszewski)[27] | Early falls, vertical supranuclear gaze palsy, axial rigidity, no tremor | MRI: midbrain atrophy/hyperintensity* |
| Neurofilament inclusion body disease[23] | Rapidly progressive frontotemporal or corticobasal syndrome, early falls, mutism | |
| Vascular | | |
| Strategic infarct[42] | Discrete thalamic, basal ganglia, or capsular infarct | Computed tomography/MRI: discrete infarction |
| **Multiple cortical infarcts** | Stepwise cognitive decline; predisposing factors | |
| **Small vessel disease** | Predisposing factors, brisk facial reflexes, frontal gait disorder | Computed tomography/MRI: lacunar state (generally involving basal ganglia and brainstem) |
| Prion | | |
| Classical Creutzfeldt-Jakob disease[24] | Rapid, florid myoclonus, cortical blindness | EEG: triphasic periodic complexes<br>MRI: basal ganglia high signal |
| Iatrogenic Creutzfeldt-Jakob disease[26] | History of dural or corneal grafts, exposure to donor human growth hormone; features as in sporadic Creutzfeldt-Jakob disease | CSF: positive 14-3-3 protein |
| New variant Creutzfeldt-Jakob disease[24] | Rapid, early psychiatric symptoms, dysaesthesiae | MRI: pulvinar sign |
| Inflammatory | | |
| Multiple sclerosis[52] | History of acute demyelinating episodes*, frontal-subcortical features, absent abdominal reflexes | VERs/BAERs/SSEPs: delayed<br>MRI: demyelinating changes in brain (corpus callosum involved) and/or spinal cord<br>CSF: unmatched oligoclonal bands |
| **Vasculitis associated with systemic disorders** | Rapid course, headache, fluctuation, seizures, systemic features | EEG: slowing of rhythms<br>MRI: ischaemic lesions<br>CSF: >3 cells, oligodonal bands |
| **Primary angiitis of central nervous system**[47] | Rapid course, headache, seizures, fluctuation | EEG: slowing of rhythms<br>MRI: ischaemic lesions<br>CSF: >3 cells, oligodonal bands |
| **Neurosarcaidosis**[74] | Systemic features, uveitis, hypothalamic dysfunction, cranial nerve signs, or polyradiculopathy | CXR: various patterns<br>MRI: white matter lesions ± meningeal enhancement<br>CSF: chronic lymphocytic meningitis |
| **Behçet's disease**[75] | Racial predilection (especially Turkish/Japanese), oral and genital ulcers, uveitis, skin lesions; posterior circulation strokes | MRI: brainstem, basal ganglia lesions<br>CSF: chronic lymphocytic meningitis |
| Neoplastic/paraneoplastic | | |
| **Tumours (especially frontal/callosal, midbrain)**[76] | Signs of raised intracranial pressure*, focal neurological signs, frontal disconnection syndromes | Computed tomography/MRI: mass lesion(s) |
| **Limbic encephalitis**[54] | Often smoker, constitutional upset, weight loss, rapid course, prominent behavioural changes, hallucinations, seizures | MRI: abnormal temporal lobe signal<br>CSF: oligoclonal bands<br>Serum: positive antineuronal/antivoltage gated potassium channel antibodies |
| Infections | | |
| **Tuberculosis/fungal/"atypical" meningitis**[77] | Risk factors* (including racial origin in tuberculosis, immunosuppression); systemic features, chronic meningitis ± cranial nerve signs | CXR: frequently abnormal<br>Computed tomography/MRI: may have mass lesions (tuberculoma)<br>CSF: lymphocytic meningitis |
| **HIV (AIDS-dementia complex)**[51] | Risk factors; systemic features, AIDS related illnesses, advanced immunosuppression, gait disorder, seizures | MRI: confluent white matter changes<br>Serum: positive HIV serology, low CD4 count |
| **Whipple's disease**[78] | Arthralgia, gut symptoms, facial movement disorder (oculomasticatory myorrhythmia) | CSF: positive Whipple's polymerase chain reaction |
| **Lyme disease**[79] | Suspicion of tick bite/travel to endemic area, skin lesion, arthritis, radiculopathies/ mononeuropathies | CSF: lymphocytic meningitis<br>Serum: positive Lyme serology* |

**Table 2** Continued

| Disease | Clues to diagnosis: Clinical features | Investigations |
|---|---|---|
| **Neurosyphilis**[42] | Risk factors (now rare); chronic meningitis, multiple strokes, Argyll Robertson pupils (light-near dissociation), tremor, seizures, dorsal column signs (tabes dorsalis) | CSF: mononuclear pleocytosis, oligodonal bands<br>Serum: positive syphilis serology |
| Subacute sclerosing panencephalitis[80] | Usually child or adolescent; history of measles, rapid course, fibrid myoclonus and seizures | EEG: periodic burst suppression<br>CSF: oligodonal bands (measles specific antibody) |
| Progressive multifocal leukoencephalopathy[81] | Immunosuppression/haematological malignancies, posterior cortical syndrome | MRI: confluent posterior white matter changes<br>CSF: positive JC virus polymerase chain reaction |
| Metabolic[82] | | |
| **Endocrinopathies** | Clinical and/or biochemical features of specific diagnosis | |
| **Nutritional deficiency** | History of food faddism, features of malabsorption | |
| **Uraemia** | Usually obvious from clinical setting | |
| **Hepatic encephalopathy** | Usually obvious from clinical setting | |
| **Epilepsy**[83] | Discrete episodes, fluctuating course, topographical amnesia | EEG: epileptiform discharges (especially temporal lobe origin)<br>MRI: abnormal mesial temporal signal |
| Alcohol[50] | Usually obvious from clinical setting; may be associated nutritional deficiency | |
| **Toxic** (including carbon monoxide poisoning,[42] lead,[83] prescribed drugs including lithium,[84] interferon α[48] | Suspicion of overt or covert exposure (for example, occupational/environmental, recreational drug use) | Specific screens if available |
| Post-irradiation[46] | History of cranial irradiation (may be delayed), corticospinal signs, ataxia, seizures | MRI: confluent white matter changes |
| Other | | |
| Obstructive sleep apnoea[67] | Obesity, morning headaches, daytime somnolence, excessive snoring | Sleep study: findings consistent with obstructive sleep apnoea |
| **Chronic subdural haematoma**[42] | History of head trauma*, frontal-subcortical signs | Computed tomography: subdural haematoma (may be isodense depending on chronicity; may be bilateral) |
| **Hydrocephalus (any cause)**[42] | History of meningitis, subarachnoid haemorrhage or neurosurgical procedure; gait apraxia, urinary incontinence | Computed tomography/MRI: findings of hydrocephalus (disproportionate ventricular enlargement) and/or causative lesion |
| Dementia pugilistica[85] | History of repeated head trauma; parkinsonism | |

BAERs, brainstem auditory evoked potentials; CSF, cerebrospinal fluid; CXR, chest radiograph; EEG, electroencephalography; EMG, electromyography; MRI, magnetic resonance imaging; SSEPs, somatosensory evoked potentials; VERs, visual evoked potentials.

**REVIEW**

# Young onset dementia

**E L Sampson, J D Warren, M N Rossor**

*Postgrad Med J* 2004;**80**:125–139. doi: 10.1136/pgmj.2003.011171