TC 49 (Danube symposium)

Frontotemporal dementias

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Conflict of interests

- There is no conflict of interests

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Aims of the TC

- Review of the concept of frontotemporal lobar degenerations (FTLD)
- Clinical criteria
- Neuroimaging
- Pathogenetic subtypes

Clinical spectrum of frontotemporal lobar degeneration (FTLD)

- Frontotemporal dementia behavioral variant (bvFTD) inkluding Pick‘s disease and FTDPark-17
- Corticobasal degeneration (CBD)
- Progressive supranuclear palsy (PSP)

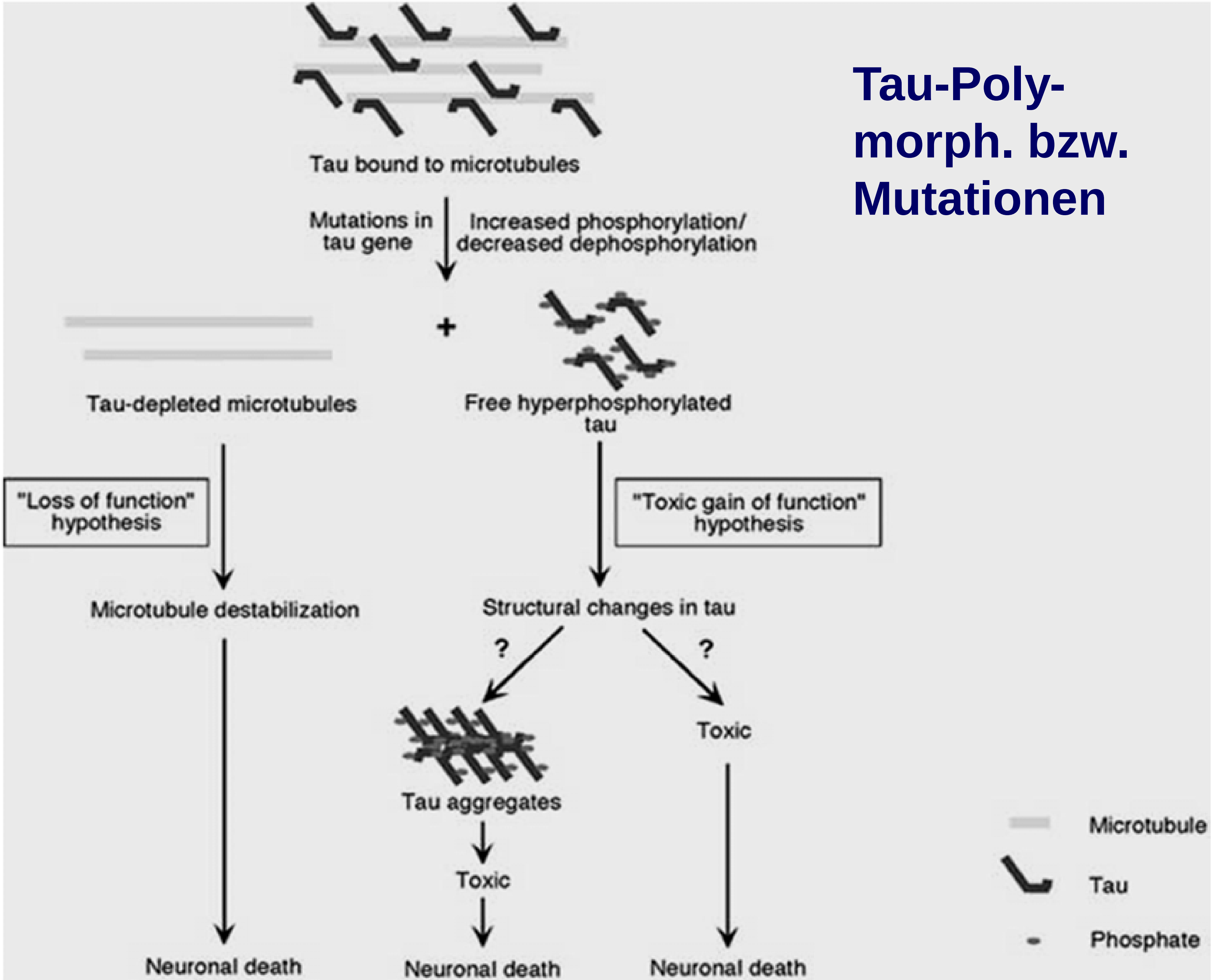
Primary Progressive Aphasias

- Semantic dementia (SD)
- Primary progressive non-fluent/agrammatic aphasia (PPnf/aA)

Common features of FTLD

- **Neuropathological similarities/diversities**
  - FT lobar degeneration
  - Histology details:
    - **FTLD-Tau**: Pick‘s disease, CBD, PSP, FTDP-17, sporadic multi-system taupathy, argyrophilic grain disease
    - FTLD-transactive response **TAR DNA - binding protein TDP43**
    - FTLD-fused in sarcoma (FUS)
    - FTLD-ubiquitin or P62 (UPS)
    - FTLD-intermed. filament pos (IF)
    - Basophilic inclusion body disease
    - FTLD-ni NOS

Tau-Poly-morph. bzw. Mutationen



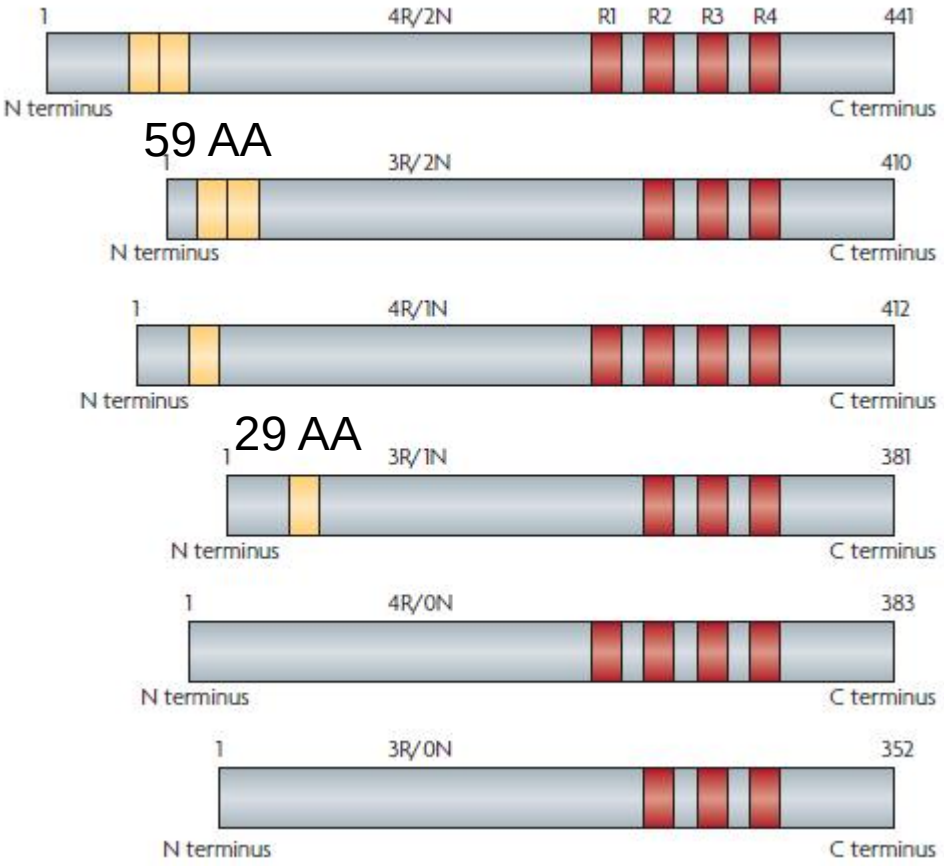
Mudher u. Livestone Trends Neurosci 2002; 25:22

Tau (Chromosome 17q)

Projection domaine Tubulin binding domaine

6 Tau isoforms

3- and 4 repeat tau

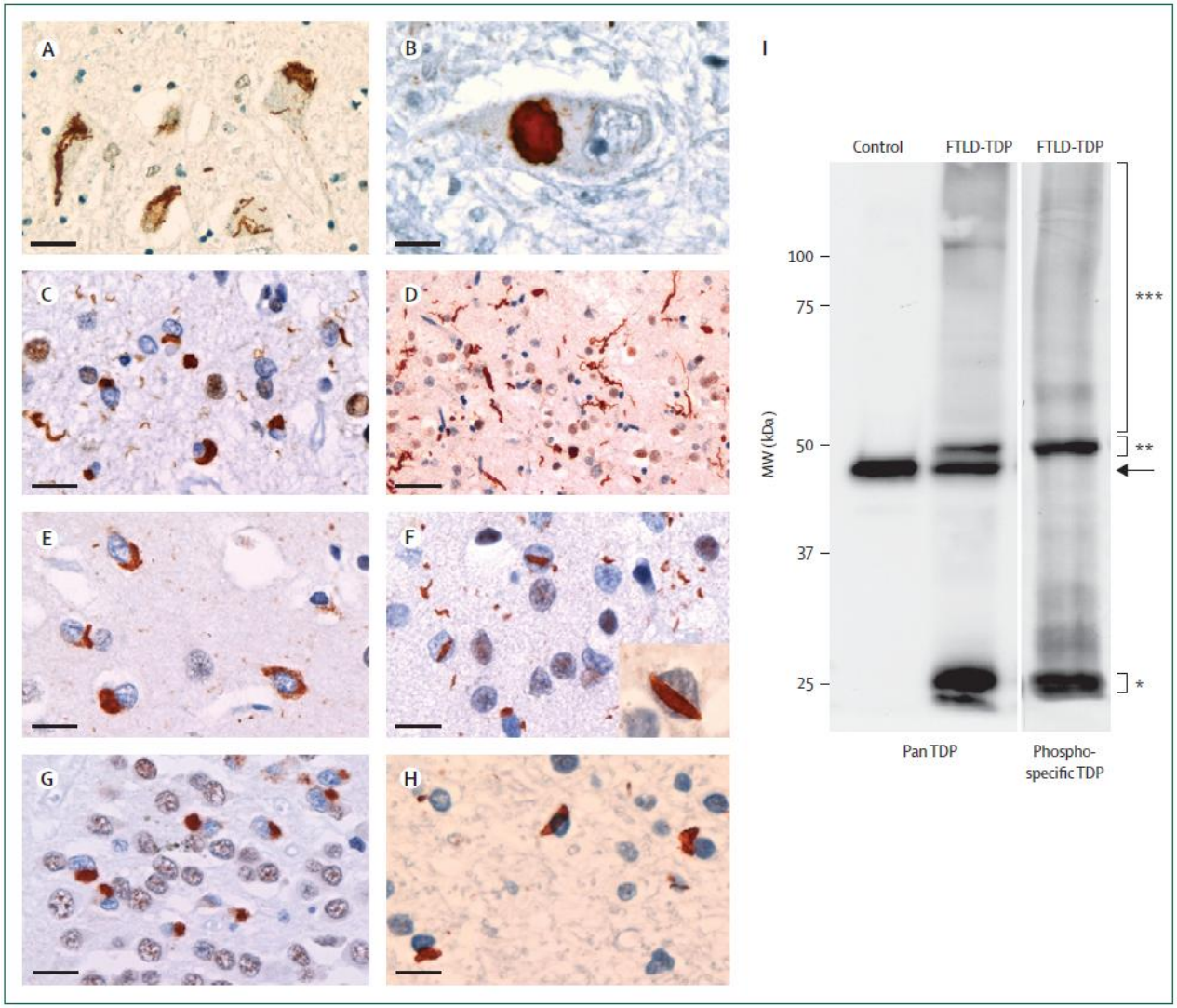


TDP-43-pos. Inclusions

ALS (left)

FTD (right column)

Mackenzie et al. 2010



Clinical diagnostic criteria of bvFTD

(Rascovsky K et al-FTDC criteria Brain 2011)

- Progressive deterioration of behaviour/cognition (history, observation)
- **Possible bvFTD**: ?3 of the following 6 symptoms:
  - **Disinhibition**
  - Early **apathy** and inertia
  - Early **loss of sympathy or empathy**
  - Early perseverative, stereotyped or compulsive/ritualistic behaviour
  - Hyperorality and dietary changes
  - Impaired in executive tasks, but episodic memory and visuospatial function relatively spared

Clinical diagnostic criteria of bvFTD

(Rascovsky K et al-FTDC criteria Brain 2011)

- **Probable bvFTD**

  Criteria of possible bvFTD fulfilled

  Significant functional decline in

  Caregiver report,

  Clinical Dementia Rating or

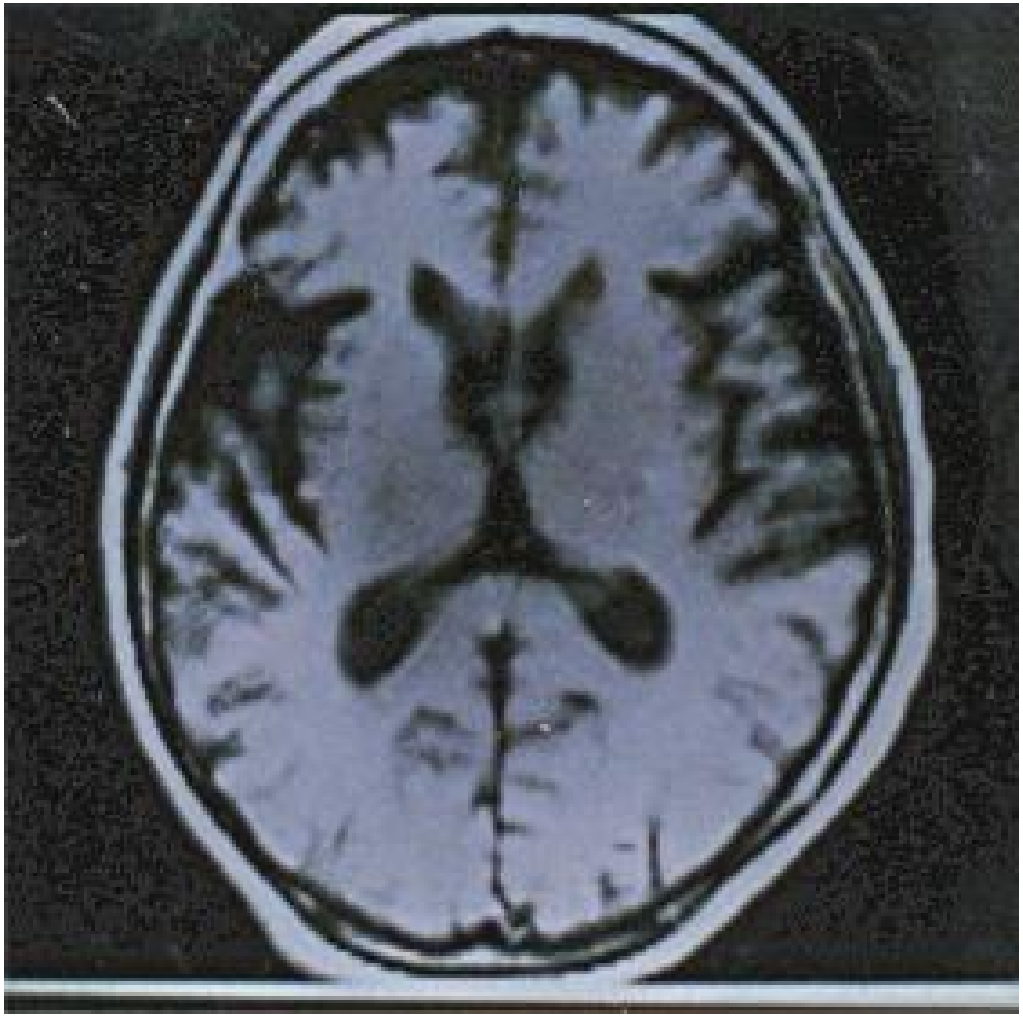
  Functional Activities Questionnaire

  Frontal a/o temporal atrophy in **MRI or CT**

  or:

  Frontal a/o temporal hypometabolism or hypoperfusion on **PET or SPECT**

MRI in bvFTD



Differences of bvFTD to Alzheimer‘s disease (AD)

- Earlier age at disease onset (comparable age at onset in arount 20%)
- Behavioral impairment prevails over cognitive decline
- Underdiagnosed disease
- Frontal a/o temporal lobar atrophy vs. temporo-parietal atrophy in AD

- Caregiver burden bvFTD >> AD
- Prognosis bvFTD worse than in AD

Diagnostic criteria of primary progressive aphasias (Gorno-Tempini Neurology 2011)

Semantic variant PPA

- **Clinical diagnosis**
  - **Both core features must be present**
    - Impaired confrontation naming
    - Impaired single-word comprehension
  - **?3 of the following 4 features must be present**
    - Impaired object knowledge (low-familiarity, low-frequency objects)
    - Surface dyslexia or dysgraphia
    - Spared repetition
    - Spared speech production (grammar and motor speech)

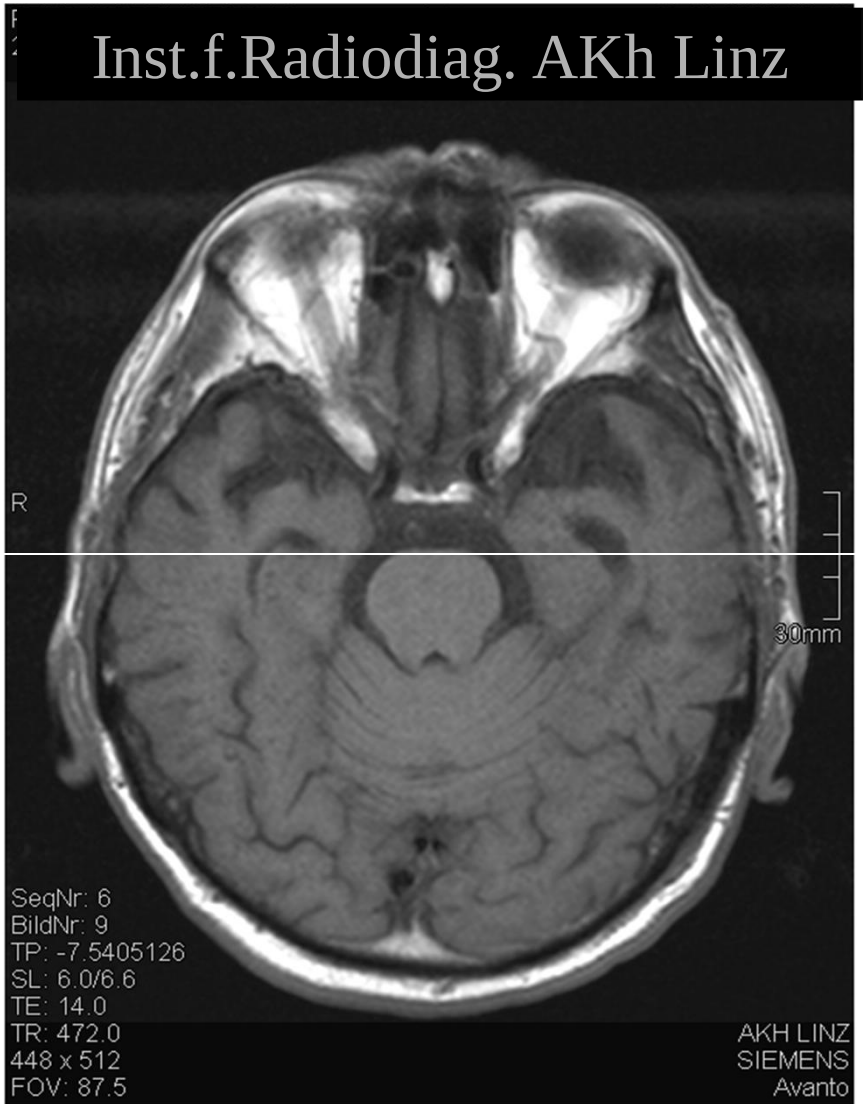
Diagnostic criteria of primary progressive aphasias (Gorno-Tempini Neurology 2011)
Semantic variant PPA cont‘d

- **Imaging supported diagnosis:**

  clinical diagnosis+

- one of the following must be present
- predominant anterior temporal atrophy on MRI
- or hypoperfusion/hypometabolism on SPECT/PET

MRI in sematic dementia

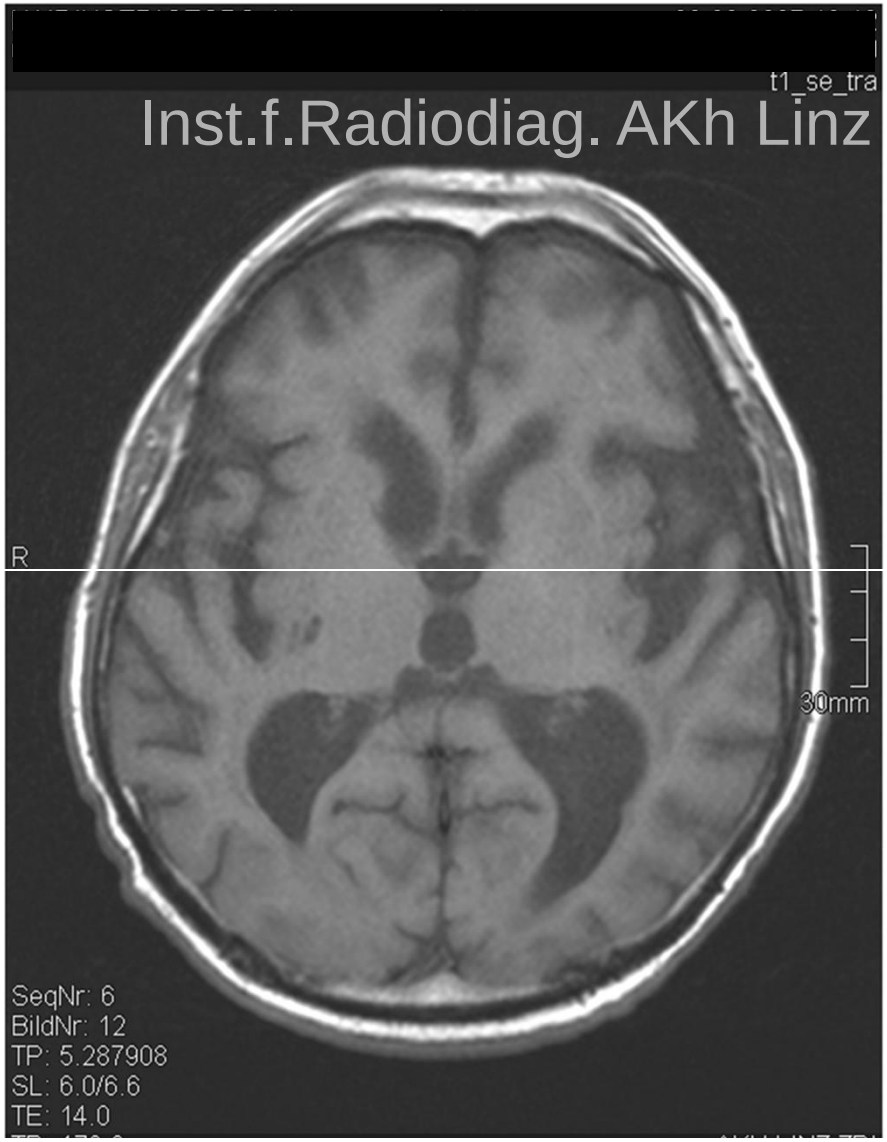


Left > right anterior and lateral temporal atrophy

Diagnostic criteria of primary progressive aphasias (Gorno-Tempini Neurology 2011)
Non fluent/agrammatic variant PA

- **Clinical diagnosis**
  - **One of the following core features**
    - Agrammatism in language production
    - Effortful, halting speech + inconsistent speech sound errors and distortions (apraxia of speech)
    - **?Ê2 of the 3 following 3 features**
    - Impaired comprehension of syntactically complex sentences
    - Spared single-word comprehension
    - Spared object knowledge
- **Imaging supported diagnosis**: clinical diagnosis +
  - One of the following: predominant left posterior fronto-insular atrophy (MRI) or hypoperfusion/hypometabolism (SPECT, MRI)

MRI primary progress., non-fluent/agrammatic Aphasia



Atrophy left operculum frontale (BA 44,45)

Clinical criteria of progressive supranuclear palsy (PSP) (Richardson-type)

NINDS-SPSP 1996 Litvan et al. 1996

Onset after 45, gradually progressive disorder, mostly sporadic

Possible
Vertical supranuclear palsy or slowing of vertical saccades and
Marked postural instability with falls within the 1st year

Probable
Vertical supranuclear palsy and
Marked postural instability with falls within the 1st year

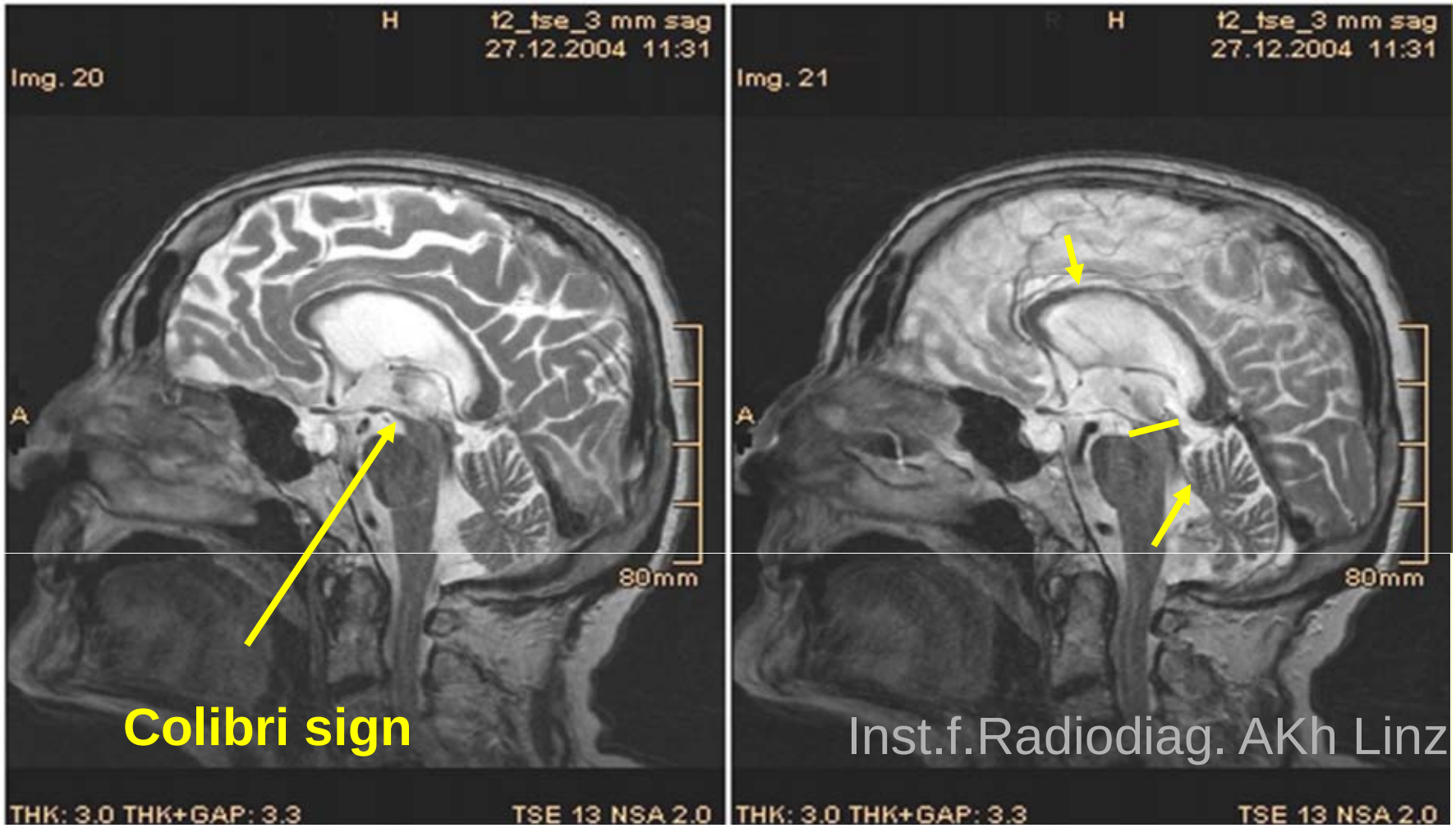
Definitive PSP
Clinical possible or probable PSP +
neuropatholog. confirmation

Applause sign
(?¨co, FTD, PD)

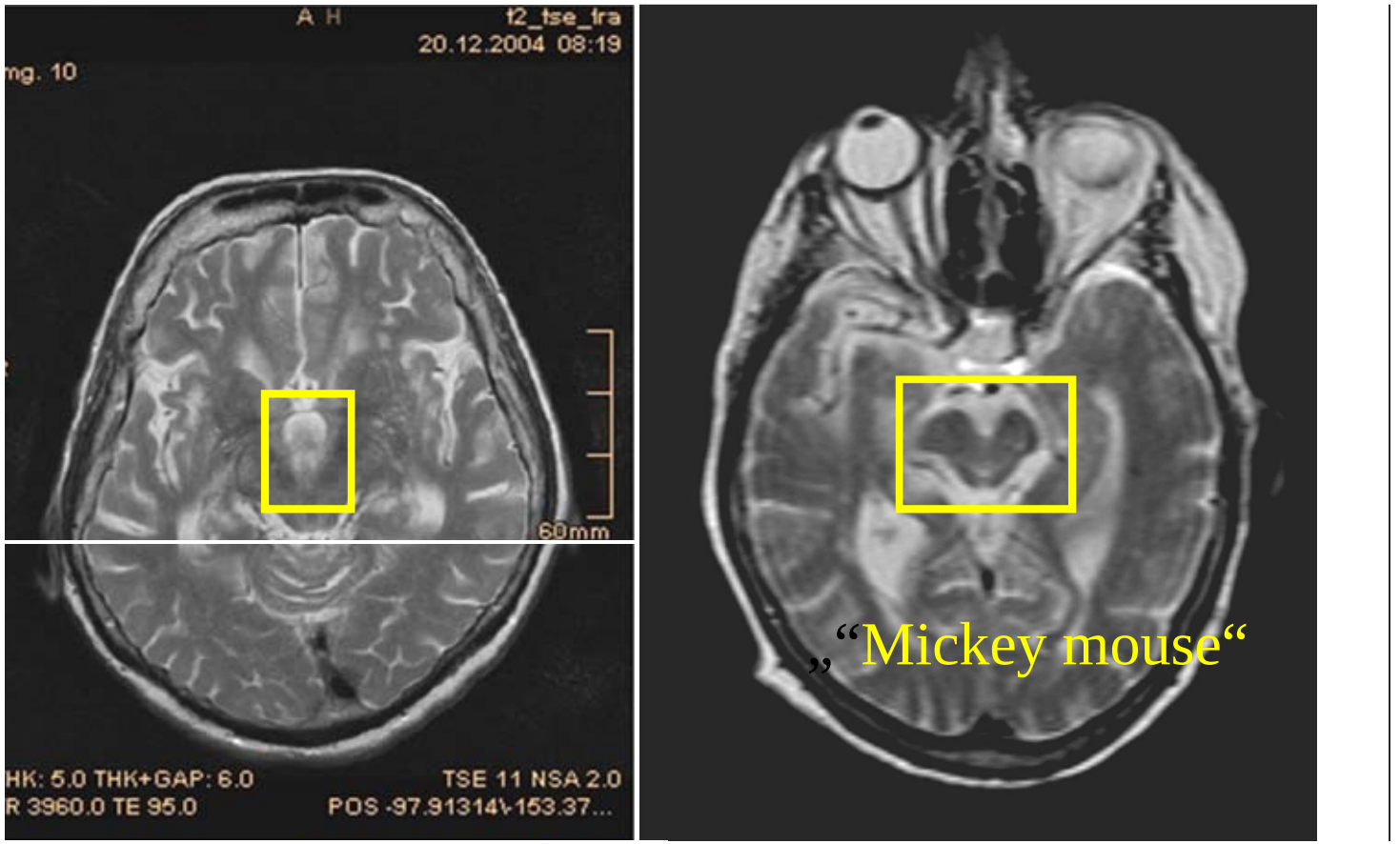
Dubois Neurology
2005;64:2123

MRI in PSP-Richardson

Atrophies frontal lobe, callosal body, midbrain, sup. cerebell peduncle



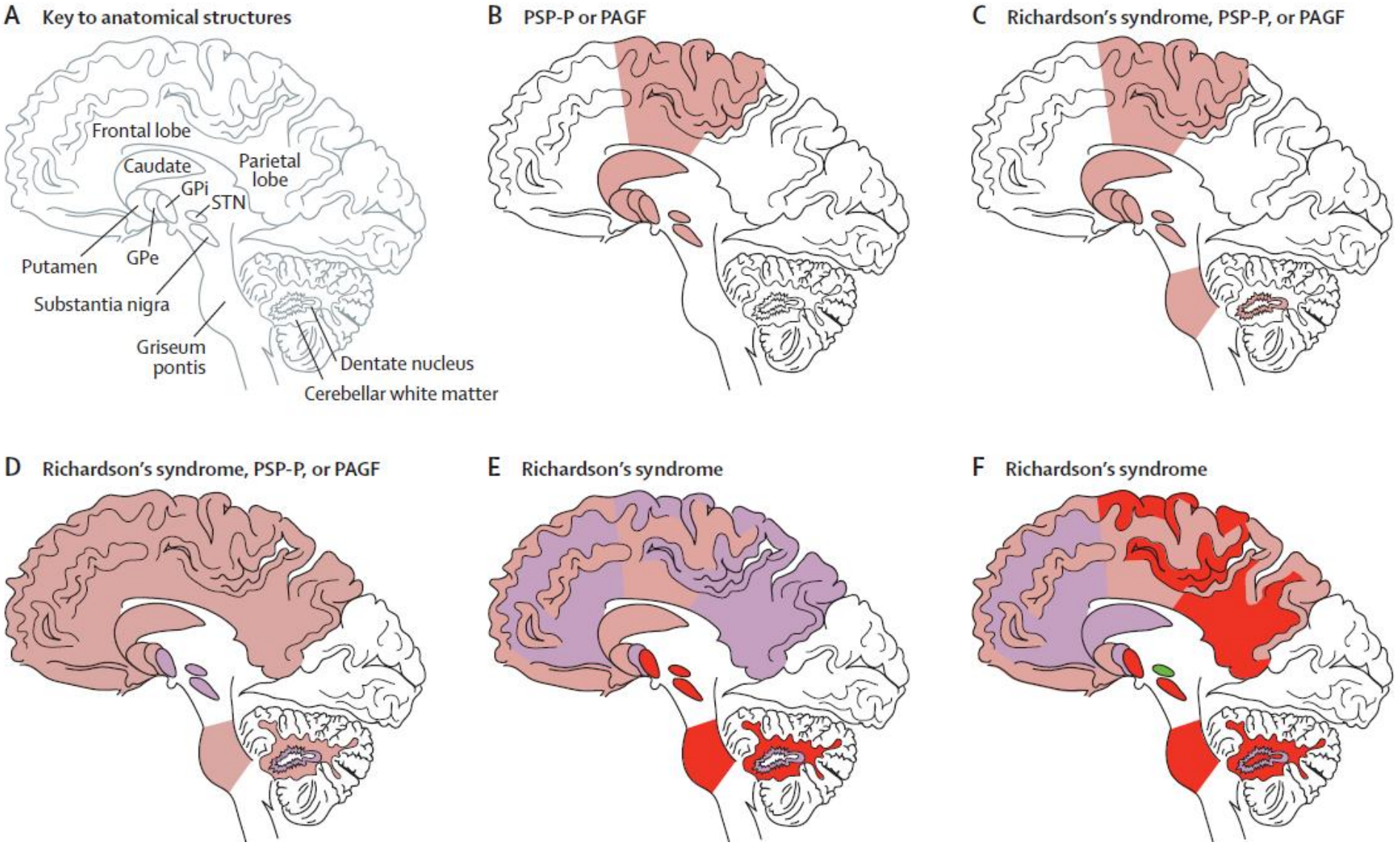
MRI in PSP-Richardson



Wide 3rd ventricle and midbrain axial diameter reduced

The clinical syndrome of progressive supranuclear palsy (PSP)

- PSP-Richardson Type (classical PSP)
- PSP-Parkinsonism
- Pure akinesia with gait freezing
- PSP-corticobasal syndrome
- PSP-progressive non-fluent aphasia



Differences in extent of neuropathological involvement in relation to clinical subtype

Clinical criteria of CBD

Armstrong et al 2013

A) Probable CBD: 2 of limb rigidity or akinesia, dystonia, myoclonus; 2 of orobuccal or limb apraxia, cortical sensory deficit, alien limb

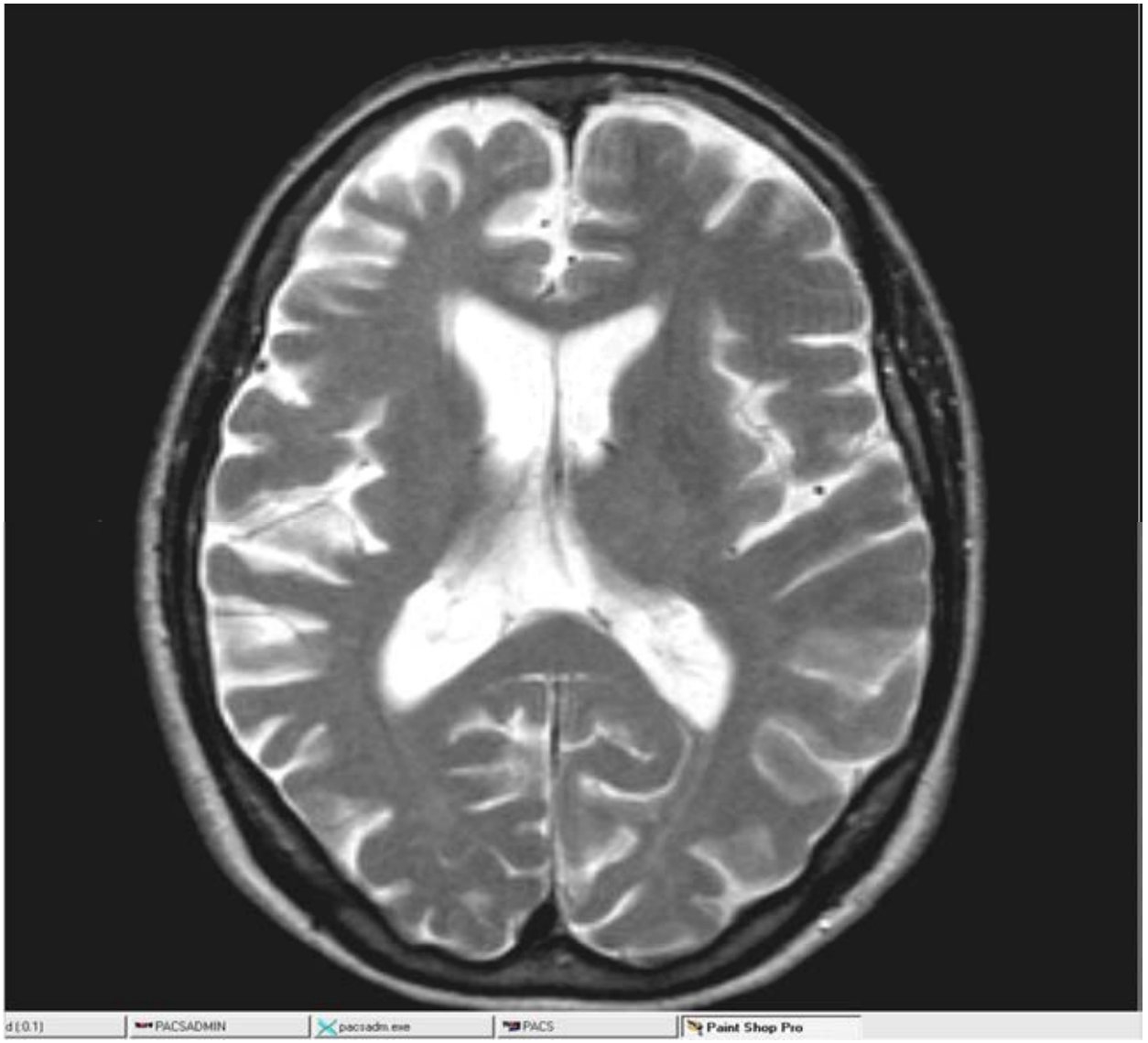
B) Possible CBD: 1 of the 1st and 1 of the 2nd 3 of A)

C) Frontal behovioral-spatial syndrome:
2 of executive dysfunction, behavioral or personality changes, visuospat. deficits

D) Nonfluent/agrammatic PPA

E) PSP syndrome

MRI bei CBD



Inst. f. Radio Diagnostik
AKh Linz

Literature

Armstrong et al Neurology 2013; 80:496
Gorno-Tempini et al. Neurology 2011;76:1006
Litvan et al. Neurology 1996;47:1
Mackenzie et al. Lancet Neurology 2010;9:995
Raskovsky et al. Brain 2011;134:2456