NACC Neuropathology Data Form
Version 10, October 11, 2013

Frontotemporal Lobar Degeneration and Other Tauopathies (*Section 17*)

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Presenter's Disclosure of Interest

Name & Presentation Date: Nigel Cairns, October 11, 2013

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  - 3. NIA/NACC U01 AG16976
  - 4. Alzheimer's Drug Discovery Foundation

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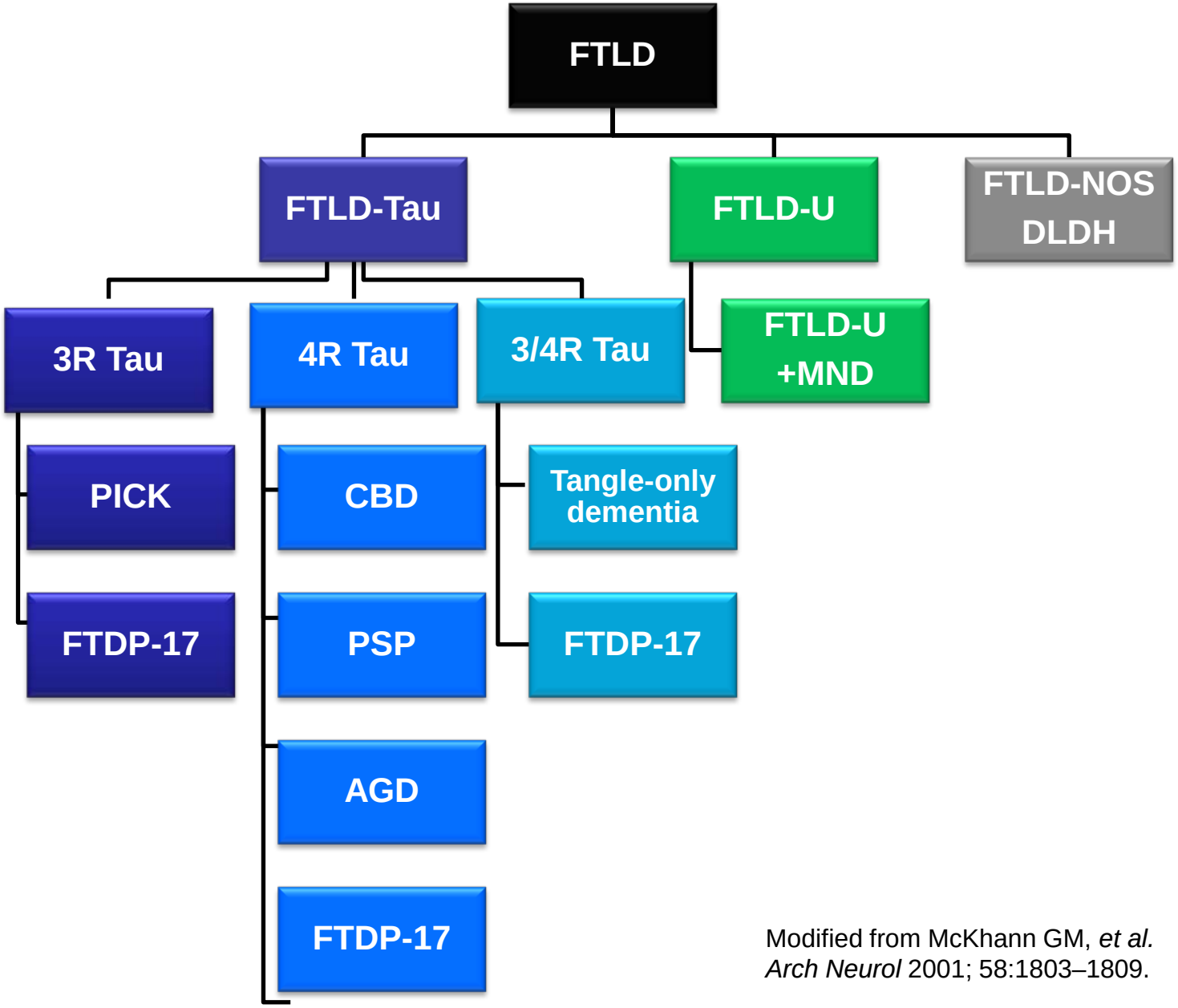
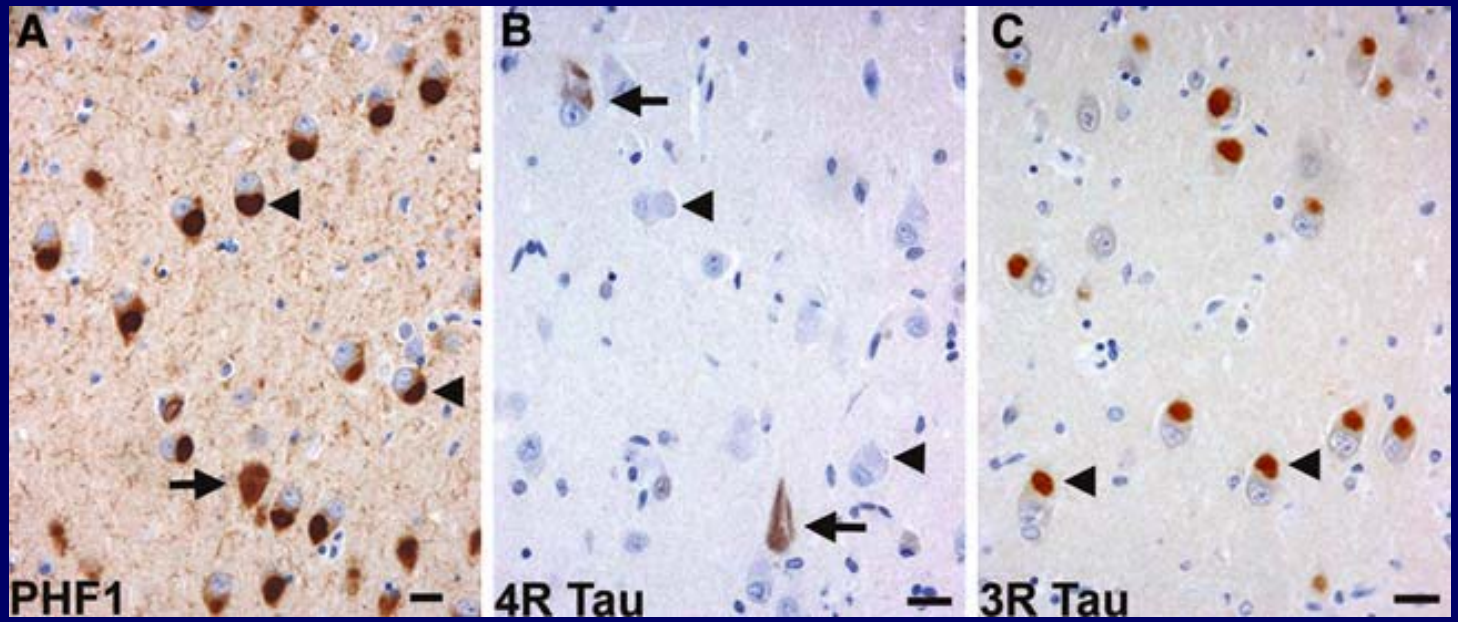
- Stock Equity: None

NACC NP Form V9.1 – FTLD *Section 14*



Modified from McKhann GM, *et al.* *Arch Neurol* 2001; 58:1803–1809.

Tau isoform-specific antibodies may be used to distinguish between 3R and 4R tauopathies



Pick's disease

Phosphorylation-dependent anti - tau (PHF1)	Anti - 4R tau (RD4)	Anti - 3R tau (ET3)
Pick bodies +	-	+
NFT na	+	na

Why revise the NACC NP diagnosis coding of FTLD?

Frontotemporal Lobar Degeneration: New Nosological Entities

New Molecular Pathologies

- TDP-43 proteinopathy
- FUS proteinopathy

New FTD Genetics

- *GRN, VCP, TARDBP, FUS, C9orf72, CHMP2B*

New entities

- Globular glial tauopathy
- Chronic traumatic encephalopathy

Acta Neuropathol (2007) 114:5–22
DOI 10.1007/s00401-007-0237-2

CONSENSUS PAPER

Neuropathologic diagnostic and nosologic criteria for frontotemporal lobar degeneration: consensus of the Consortium for Frontotemporal Lobar Degeneration

Nigel J. Cairns · Eileen H. Bigio · Ian R. A. Mackenzie · Manuela Neumann · Virginia M. -Y. Lee · Kimmo J. Hatanpaa · Charles L. White III · Julie A. Schneider · Lea Tenenholz Grinberg · Glenda Halliday · Charles Duyckaerts · James S. Lowe · Ida E. Holm · Markus Tolnay · Koichi Okamoto · Hideaki Yokoo · Shigeo Murayama · John Woulfe · David G. Munoz · Dennis W. Dickson · Paul G. Ince · John Q. Trojanowski · David M. A. Mann

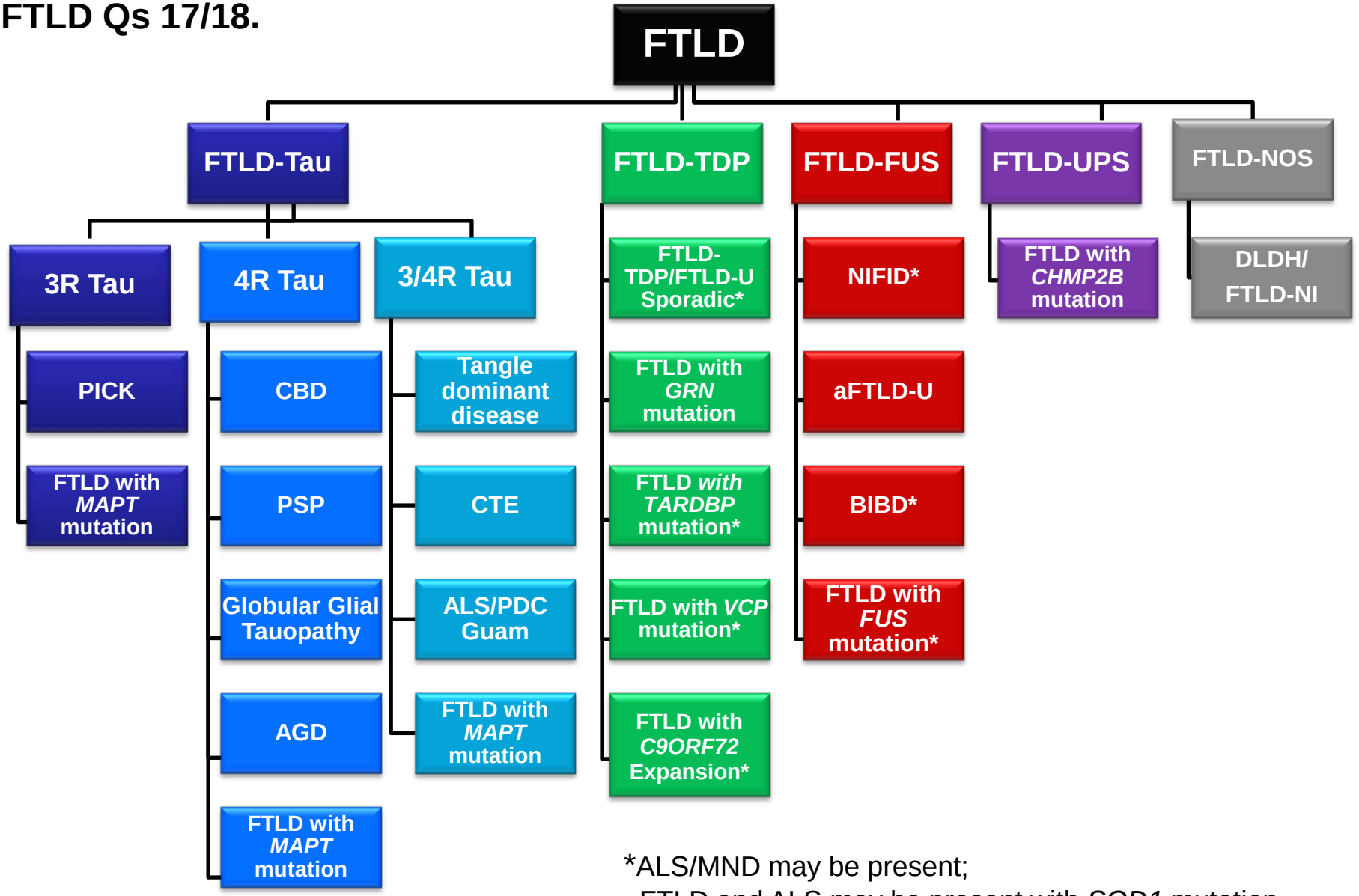
Acta Neuropathol (2009) 117:15–18
DOI 10.1007/s00401-008-0460-5

EDITORIAL

Nomenclature for neuropathologic subtypes of frontotemporal lobar degeneration: consensus recommendations

Ian R. A. Mackenzie · Manuela Neumann · Eileen H. Bigio · Nigel J. Cairns · Irina Alafuzoff · Jillian Kril · Gabor G. Kovacs · Bernardino Ghetti · Glenda Halliday · Ida E. Holm · Paul G. Ince · Wouter Kamphorst · Tamas Revesz · Annemieke J. M. Rozemuller · Samir Kumar-Singh · Haruhiko Akiyama · Atik Baborie · Salvatore Spina · Dennis W. Dickson · John Q. Trojanowski · David M. A. Mann

NACC NP Form V10
FTLD Qs 17/18.



*ALS/MND may be present;
FTLD and ALS may be present with *SOD1* mutation

Additional Help?

NACC NP Guidebook - Version 10

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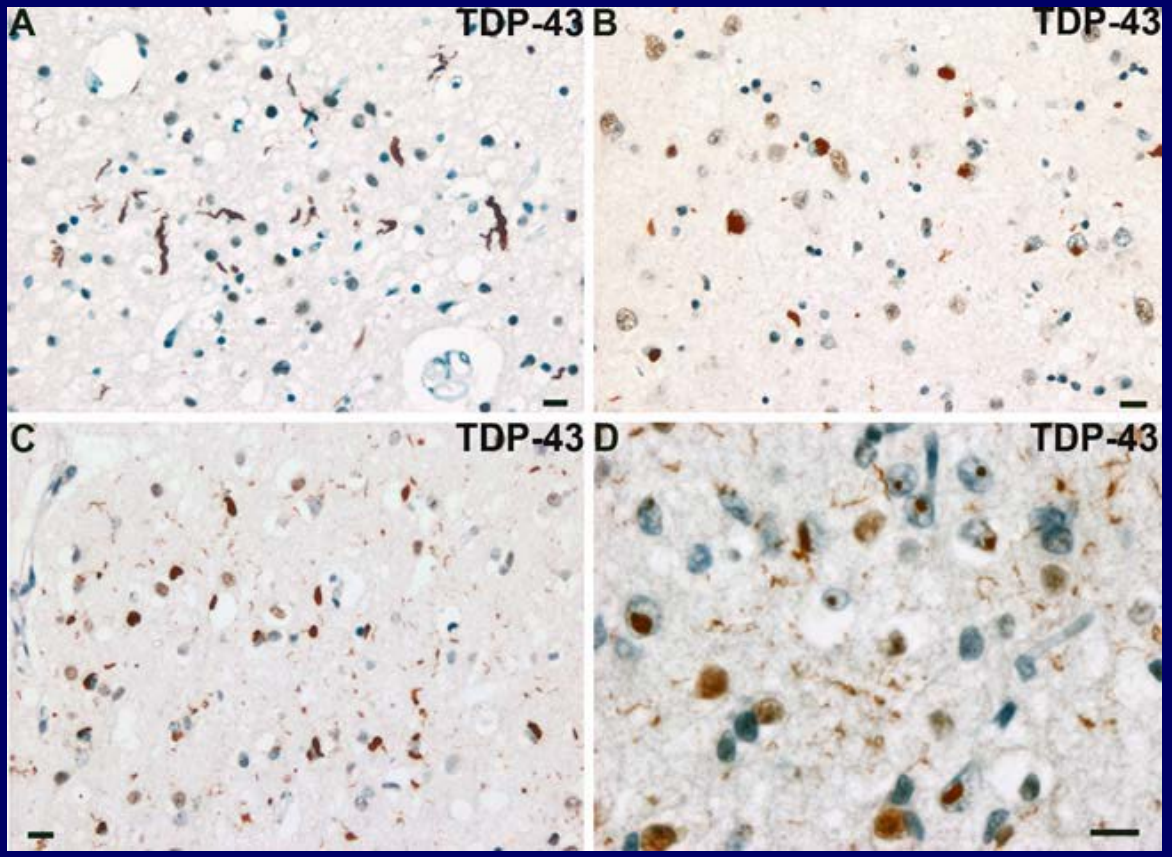
NIH/NIH U01 AG016976

FTLD-U/FTLD-TDP Subtypes. Consortium for FTLD
Acta Neuropathol (2007) **114**:5–22**.**

Type 1
Sporadic

Type 2
C9-linked/
C9orf72
Sporadic



Type 3
GRN
Sporadic

Type 4
VCP

Type 1: Long and tortuous dystrophic neurites (DNs) in laminae II/III with relatively few neuronal cytoplasmic inclusions (NCIs) and no neuronal intranuclear inclusion (NII).
Type 2: Numerous NCIs, relatively few DNs, and no NII.
Type 3: Numerous NCIs and DNs and an occasional NII in lamina II.
Type 4: Numerous NII and DN, but few NCI.

Neuropathological heterogeneity in frontotemporal lobar degeneration with TDP-43 proteinopathy: a quantitative study of 94 cases using principal components analysis

Richard A. Armstrong, William Ellis, Ronald L. Hamilton, Ian R. A. Mackenzie, John Hedreen, Marla Gearing, Thomas Montine, Jean-Paul Vonsattel, Elizabeth Head, Andrew P. Lieberman, and Nigel J. Cairns

J. Neural Transm. 2010; **117**: 227-239

Methods

Case selection:

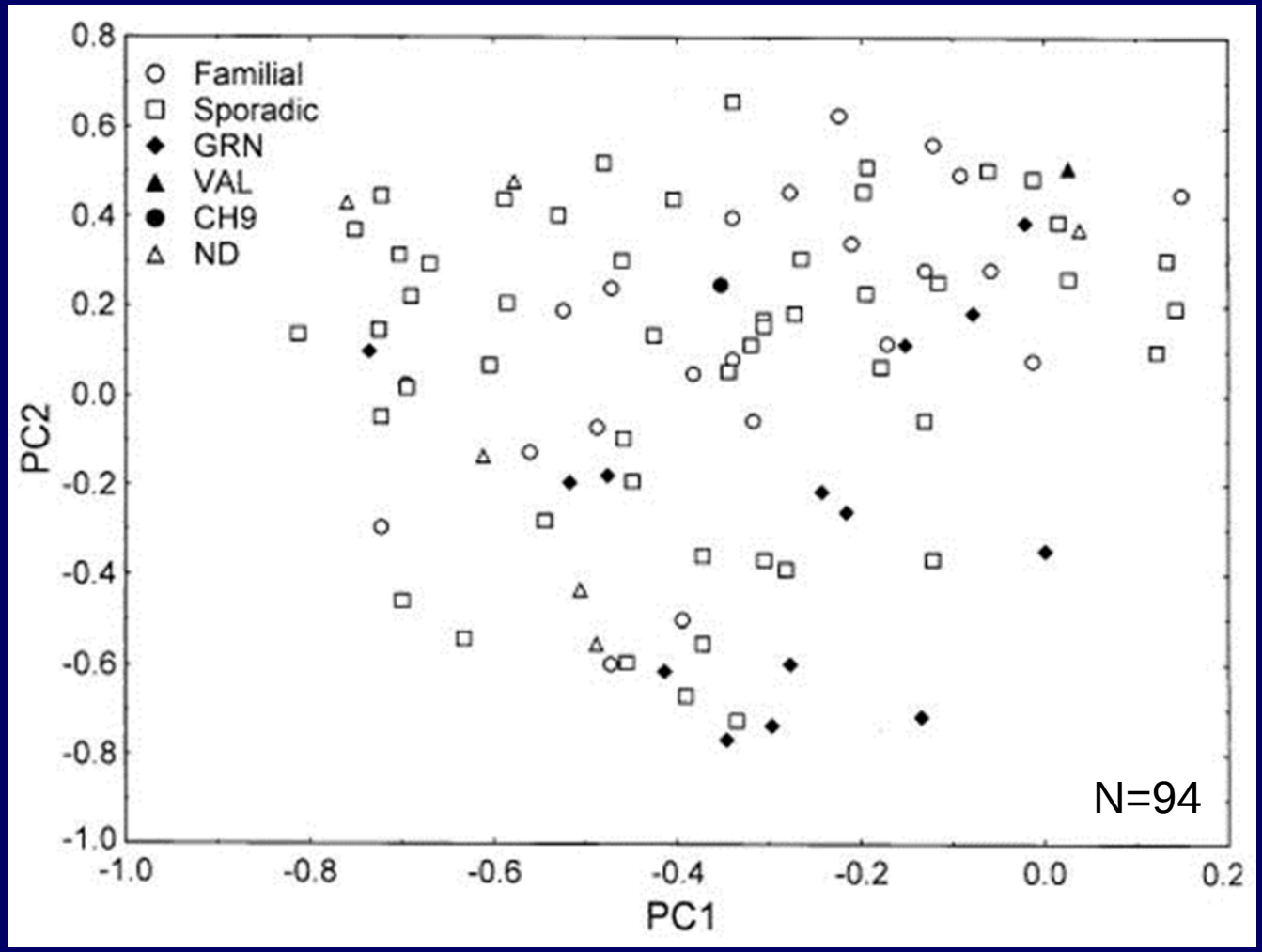
FTLD-TDP (n=94 from 10 sites of which 37 familial: 14 *GRN*, 1 *VCP*, 1 *C9orf72*)

Density of TDP-43 immunoreactive lesions in FL and TL (PHG, CA1):

- Neuronal cytoplasmic inclusions
- Oligodendroglial inclusions
- Neuronal intranuclear inclusions
- Dystrophic neurites
- Neuron number
- Microvacuolation (vacuoles > 5 μm diameter)

Results PCA suggests that cases are not segregated into distinct subtypes.

Neuropathological overlap between FTLD-TDP phenotypes



PCA of 94 cases of FTLD-TDP. PCA 1: TDP-43 lesions (variance explained: ~80%); PCA 2, neuron number/vacuolation (~10%). The plot displays sporadic and familial cases with progranulin (GRN), valosin-containing protein (VAL),and chromosome 9-linked (C9orf72) mutations. ND, genetic status of familial cases not defined.