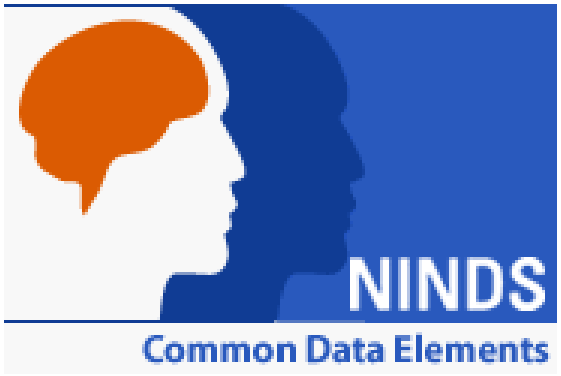
Proposed NACC Neuropathology Database Changes

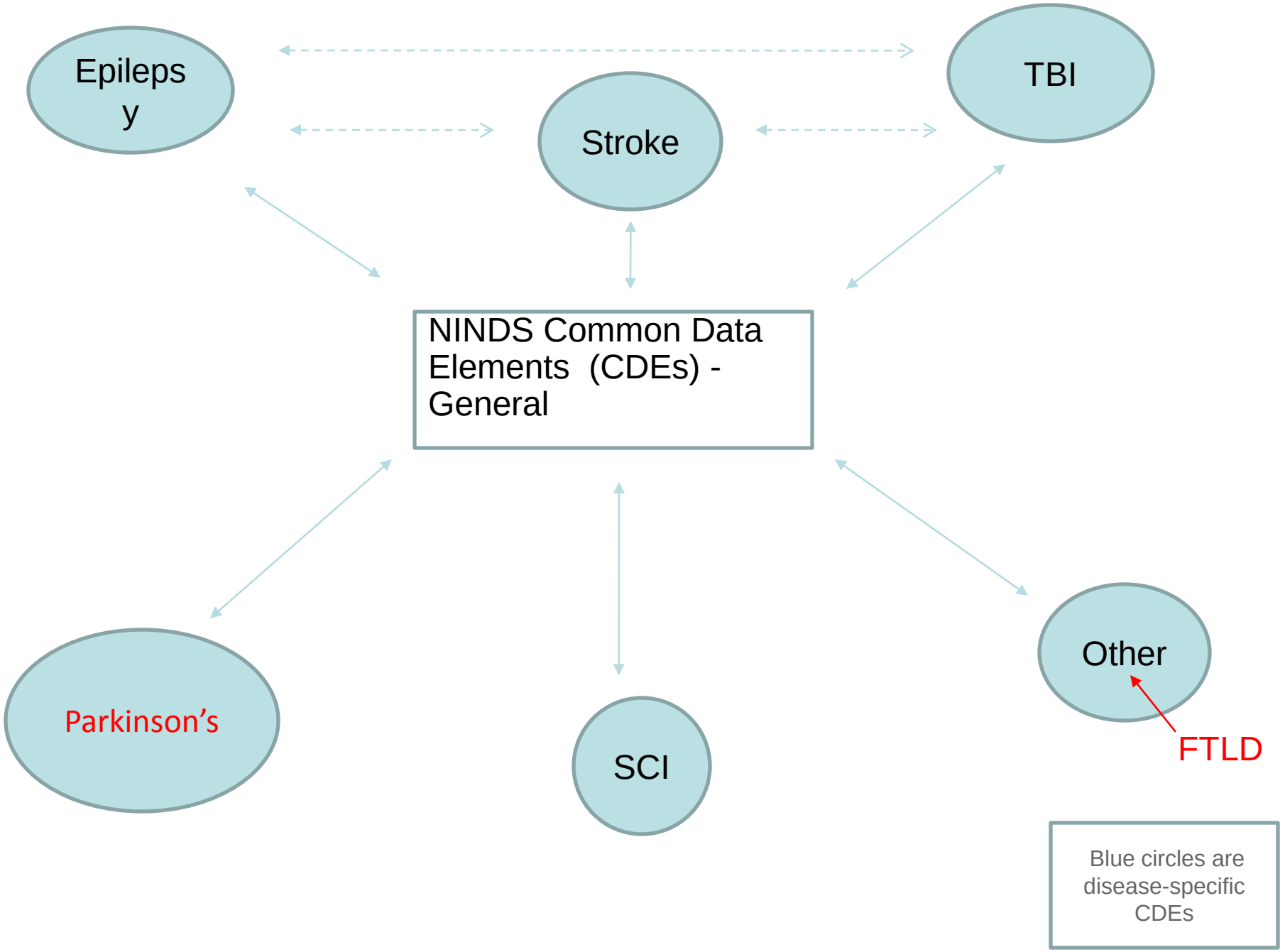
NIA/NINDS Common Data Element Initiatives for Frontotemporal Dementia and Parkinson Disease



NINDS Common Data Element (CDE) Project

http://www.nindscommondataelements.org/

NINDS CDE Project Team


Epilepsy
TBI
Stroke
NINDS Common Data Elements (CDEs) - General
Parkinson's
SCI
Other
FTLD
Blue circles are disease-specific CDEs

What do we hope to gain from CDEs?

- Create system-independent data elements $\Rightarrow$ Facilitate data sharing
- Increase overall data quality
- Encourage parsimonious data collection $\Rightarrow$ reduce burden on investigators and participants

Parkinson's Disease CDE Working Group
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General and Motor subgroup:
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David Oakes, PhD

NIA, NINDS & AFTD Initiative on Common Data Elements for FTD

- **Neuropathology working group**
  - Dennis Dickson, Mayo Clinic - Chair
  - Eileen Bigio, Northwestern University
  - Nigel Cairns, Washington University
  - Bernadino Ghetti, Indiana University
  - Ian MacKenzie, University of British Columbia
  - John Trojanowski, University of Pennsylvania
- **Propose changes to NACC database to accommodate advances in FTLD**
  - Refined classification of tauopathies
  - TDP-43
  - FUS

Tauopathies

3R TAUOPATHIES

Pick's Disease
1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

4R TAUOPATHIES

Corticobasal degeneration
1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

Progressive supranuclear palsy
1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

Argyrophilic grain dementia (including diffuse AGD)
1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

Other 4R tauopathy (e.g., multisystem tauopathy)
1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

3R+4R TAUOPATHIES

Tangle-predominant dementia, including Parkinson dementia complex
1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

OTHER TAUOPATHIES

Tauopathy, not otherwise specified or incompletely characterized)
1 = Yes (describe:)
2 = No
3 = Not assessed
9 = Missing/unknown

TDP-43 proteinopathies

IS ABNORMAL TDP-43 PATHOLOGY PRESENT?

TDP-43 associated with pathology consistent with frontotemporal degeneration (FTLD-TDP)*

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

**** No need to subtype at this time given poor interrater reliability and lack of generally accepted subtyping scheme.***

TDP-43 associated with other well defined neurodegenerative pathology (e.g., Alzheimer disease)

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

TDP-43 associated with hippocampal sclerosis of the elderly

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

TDP-43 associated with motor neuron disease or amyotrophic lateral sclerosis (ALS)

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

Other FTLD

IS ABNORMAL FUS PATHOLOGY PRESENT?

FUS associated with pathology consistent with frontotemporal degeneration (FTLD-FUS)*

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

**** Includes neuronal intermediate filament inclusion disease (NIFID) and dementia with basophilic inclusions***

FUS associated with familial amyotrophic lateral sclerosis (ALS-FUS)

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

IS ANOTHER TYPE OF FTLD PRESENT?

FTLD-UPS (ubiquitin-positive inclusions, but tau, TDP-43 and FUS negative)

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

FTLD-NI (No inclusions)

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

FTLD-NOS (not otherwise specified or incompletely characterized)

1 = Yes
2 = No
3 = Not assessed
9 = Missing/unknown

Neuropathology CDE for PD

- Start with NACC forms and definitions – refine and add elements
- Additions
  - Final clinical diagnosis
  - Other banked specimens (e.g., blood, spinal cord, nerve, muscle)
  - Macroscopic photographs
  - Brain weight (type of tissue weighed)
  - Hydrocephalus
  - Amyloid phase
  - Lewy body distribution
  - Substantia nigra neuronal loss
  - Multiple system atrophy
  - Spinocerebellar degeneration
  - FTD/ALS module (as above)
  - Final pathologic diagnosis for 1) cognitive status & 2) motor (i.e. extrapyramidal) status

Additions

Brain weight

Record brain weight:_____

Type of tissue weighed

0 = Whole fresh brain
1 = Whole fixed brain
2 = Fixed hemibrain (calculated whole brain weight)
9 = Missing/unknown

Hydrocephalus

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
5 = Not assessed
9 = Missing/unknown

Amyloid phase (Thal et al., 2002)

1 = Phase 1 (cortex)
2 = Phase 2 (cortex & hippocampus)
3 = Phase 3 (cortex, hippocampus & basal ganglia)
4 = Phase 4 (cortex, hippocampus, basal ganglia & brainstem)
5 = Phase 5 (cortex, hippocampus, basal ganglia, brainstem & cerebellum)
6 = Amyloid plaques not present
7 = Not assessed
9 = Missing/unknown

Density of "Lewy related pathology."

For each region record: 0 = Absent; 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Very severe; 5 = Not assessed; 9 = Missing/unknown

a. Sympathetic ganglia (paravertebral)
b. Parasympathetic ganglia (GI, GU)
c. Spinal cord
d. Olfactory bulb
e. Dorsal motor nucleus/glossopharyngeal
f. Locus ceruleus
g. Raphe nucleus
h. Substantia nigra, pars compacta
i. Amygdala
j. Basal nucleus/diagonal band
k. Hypothalamus
l. Caudate/putamen
m. Entorhinal cortex
n. Cingulate cortex
o. Hippocampus
p. Temporal cortex
q. Frontal cortex
r. Parietal cortex
s. Primary cortex (motor and/or visual)

Lewy body type
1 = Brainstem predominant type
2 = Intermediate or transitional (limbic) type
3 = Diffuse (neocortical) type
4 = Amygdala predominant
5 = Lewy body pathology, unspecified or not further assessed
6 = Not assessed
9 = Missing/unknown

Likelihood that pathology is consistent with Lewy related cognitive syndrome
1 = Low (brainstem LBs & NIA-Reagan low, intermediate or high; transitional LBs & NIA-Reagan high)
2 = Intermediate (transitional LBs & NIA intermediate; diffuse LBs & NIA-Reagan high)
3 = High (diffuse LBs & NIA-Reagan low or intermediate; transitional LBs & NIA-Reagan low)
4 = Lewy body pathology, unspecified or not further assessed
6 = Not assessed
9 = Missing/unknown

Estimate degree of substantia nigral neuromelanin-containing neurons neuronal loss
0 = None
1 = Mild
2 = Moderate
3 = Severe
4 = Not assessed
9 = Missing/unknown

Alpha-synuclein pathology consistent with multiple system atrophy (MSA)
1 = Striatonigral predominant
2 = Olivopontocerebellar predominant
3 = Mixed striatonigral and olivopontocerebellar
4 = MSA (not specified or incompletely characterized)
5 = Not assessed
9 = Missing/unknown

What are the primary and contributing pathologic diagnoses or features which you judge to be responsible for the subject's extrapyramidal signs, if present?

Primary (1 only; code as 1); Contributing (no limit; code as 2)

No significant pathology
Lewy body disease
Multiple system atrophy
Progressive supranuclear palsy
Corticobasal degeneration
FTLD-TDP
Vascular Parkinsonism
Normal pressure hydrocephalus
Idiopathic nigral degeneration
Other (specify):