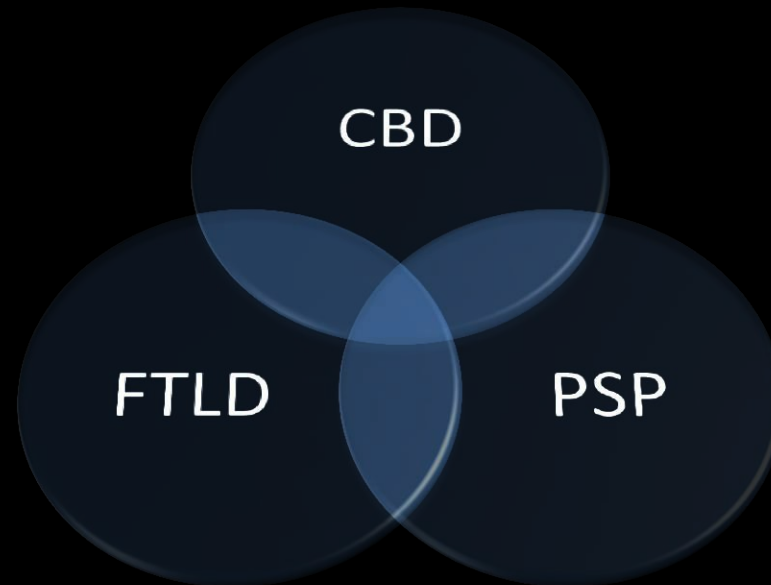


CORTICOBASAL SYNDROME,
CORTICOBASAL DEGENERATION,
AND PROGRESSIVE SUPRANUCLEAR
PALSY:
WHAT ARE THE
TAUOPATHIES?

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Sciences Stanford Center for Memory Disorders

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TAUOPATHIES

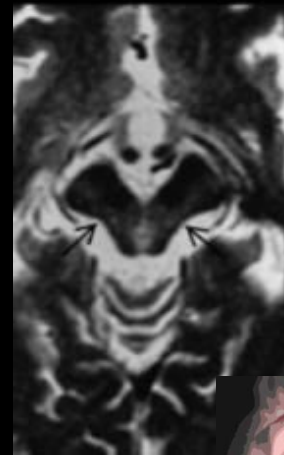
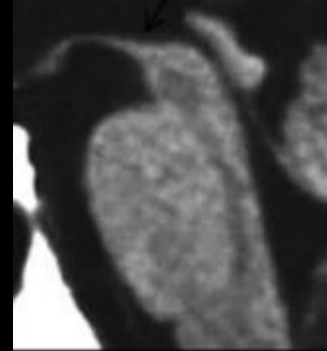


MANY DISEASE ARE TAUOPATHIES

Disorder	Anatomy (major areas affected in typical cases)
4R TAUOPATHIES	
Corticobasal degeneration	Cortex and basal ganglia
Progressive supranuclear palsy	Basal ganglia, brainstem and cerebellum
FTDP-17 T	Cortex, basal ganglia and brainstem
3R TAUOPATHIES	
Pick's disease	Cortex and limbic lobe
FTDP-17 T	Cortex, basal ganglia and brainstem
3R+4R TAUOPATHIES	
Alzheimer disease	Cortex and limbic lobe
FTDP-17 T	Cortex and limbic lobe

PSP CLINICAL FEATURES

- Behavior:
 - Apathy, obsessive/compulsive behaviors, utilization
- Cognitive profile: executive dysfunction
- Motor:
 - Parkinsonism: axial rigidity, postural instability, bradykinesia, reduced blink
 - Supranuclear gaze palsy
 - Dysphagia/dysarthria

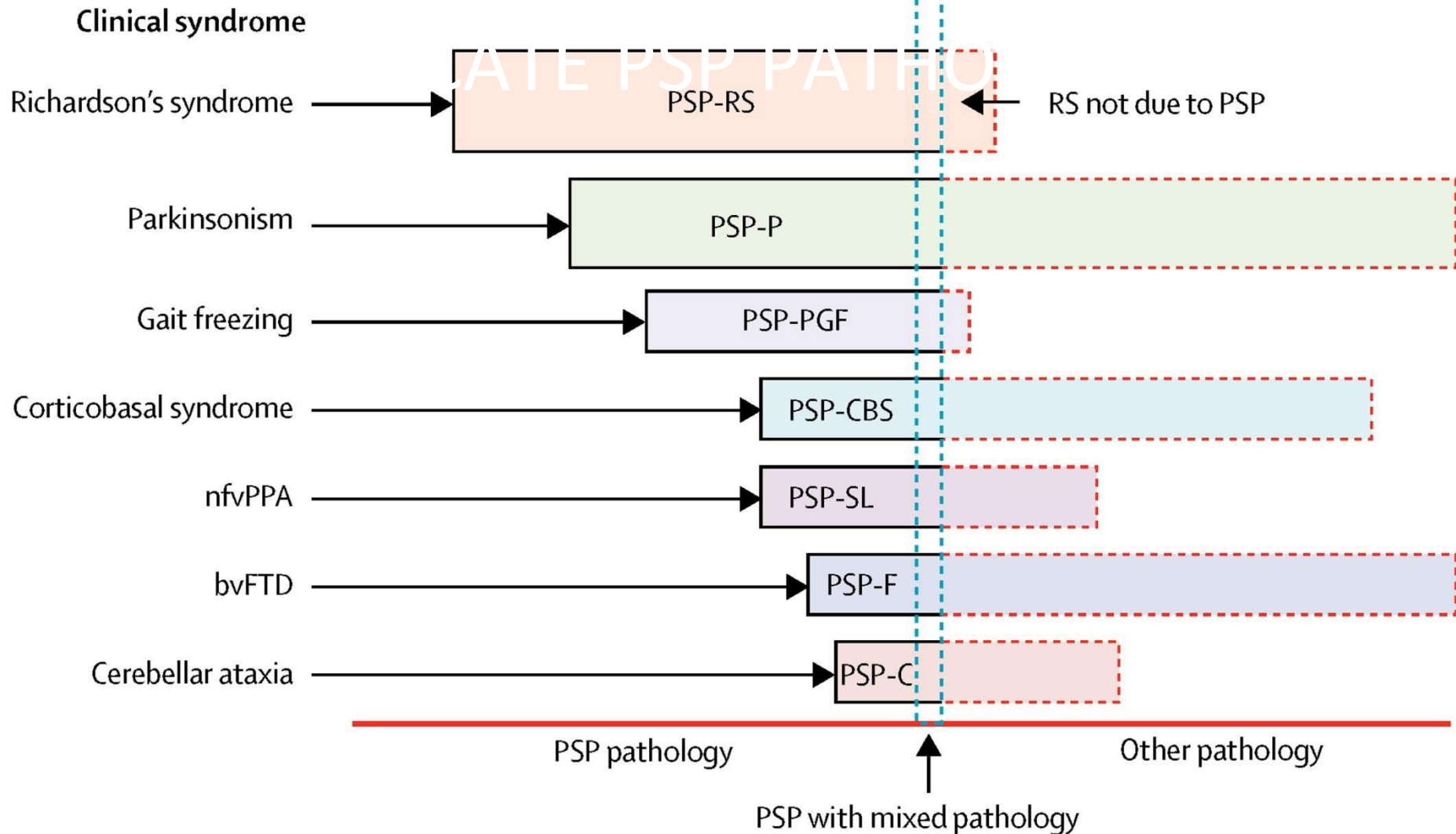


PSP CRITERIA UPDATED THIS YEAR

- Sporadic occurrence Hooger et al 2017
- Age 40 or older at onset
- Gradual progression of PSP-related symptom
- Core features:
 - Oculomotor dysfunction
 - Postural Instability
 - Akinesia
 - Cognitive dysfunction

Certainty	Oculomotor	Postural Instability	Akinesia	Cognitive Dysfunction
Level 1	O1: Vertical supranuclear gaze palsy	P1: Repeated unprovoked falls within 3 years	A1: Progressive gait freezing within 3 year	C1: Speech/language disorder (nf/agrammatic PPA or AOS)
Level 2	O2: Slow velocity of vertical saccades	P2: Tendency to fall on the pull-test within 3 years	A2: Parkinsonism, akinetic-rigid, predominantly axial, and levodopa resistant	C2: Frontal cognitive/behavioral presentation
Level 3	O3: Frequent macro square wave jerks or <u>o</u> leLjelid opeŶiŶg apradŹa_	P3: More than two steps backward on the pull-test within 3 years	A3: Parkinsonism, with tremor and/or asymmetric and/or levodopa responsive	C3: Corticobasal syndrome

SOME VARIANTS ARE MORE LIKELY TO



PSP-CORTICOBASAL SYNDROME

Corticobasal syndrome



PSP-CBS

- Variable combo of:
 - Progressive limb rigidity
 - Apraxia
 - Cortical sensory loss
 - Alien limb
 - Bradykinesia
 - Unresponsive to levodopa

PSP-SPEECH/LANGUAGE

nfvPPA

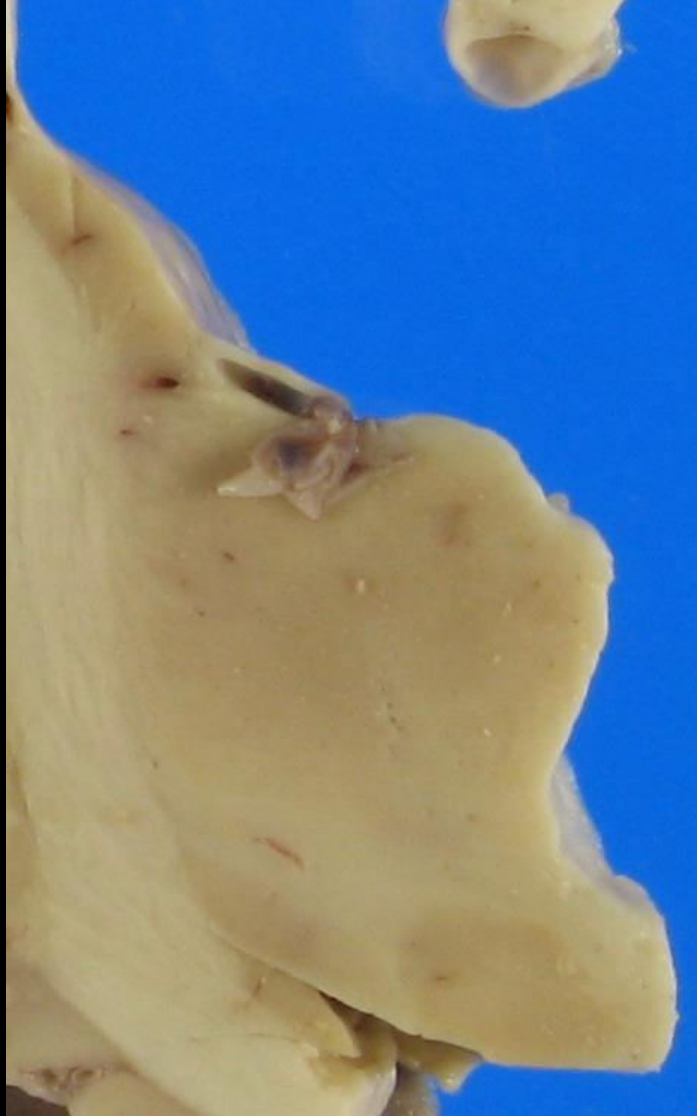


PSP-SL

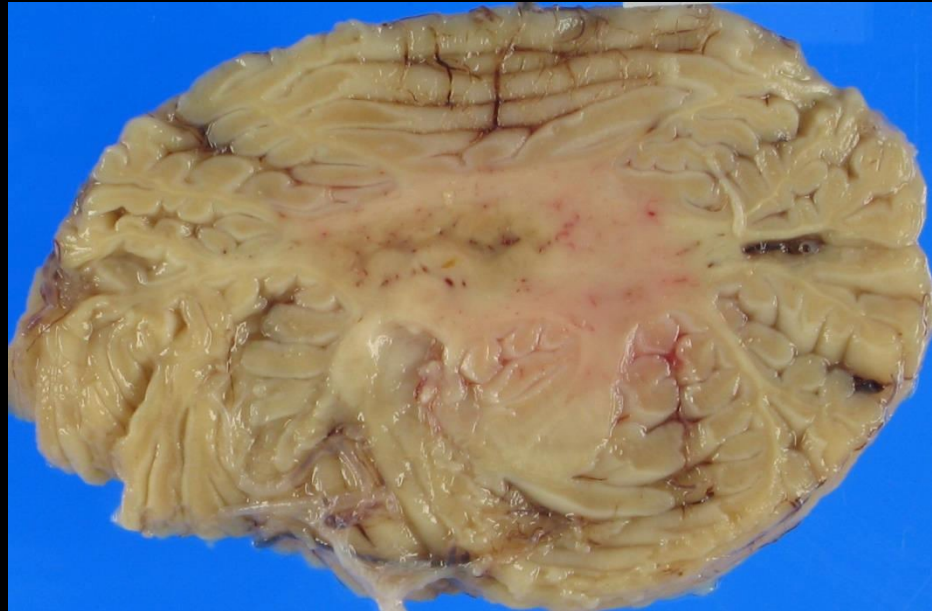
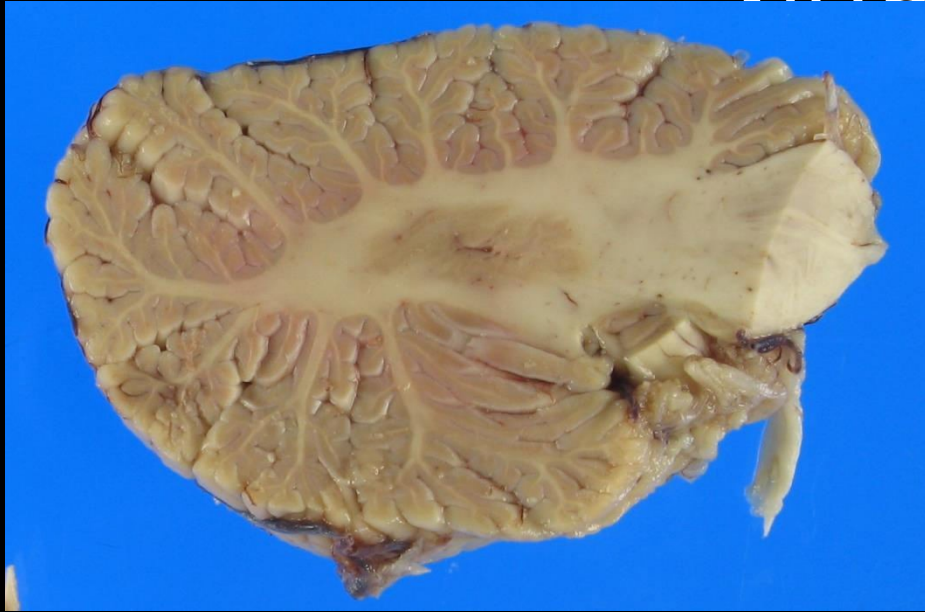


- nfvPPA
- Agrammatism
- Effortful, halting speech with inconsistent speech sound errors and distortions (AOS)

STN ATROPHY

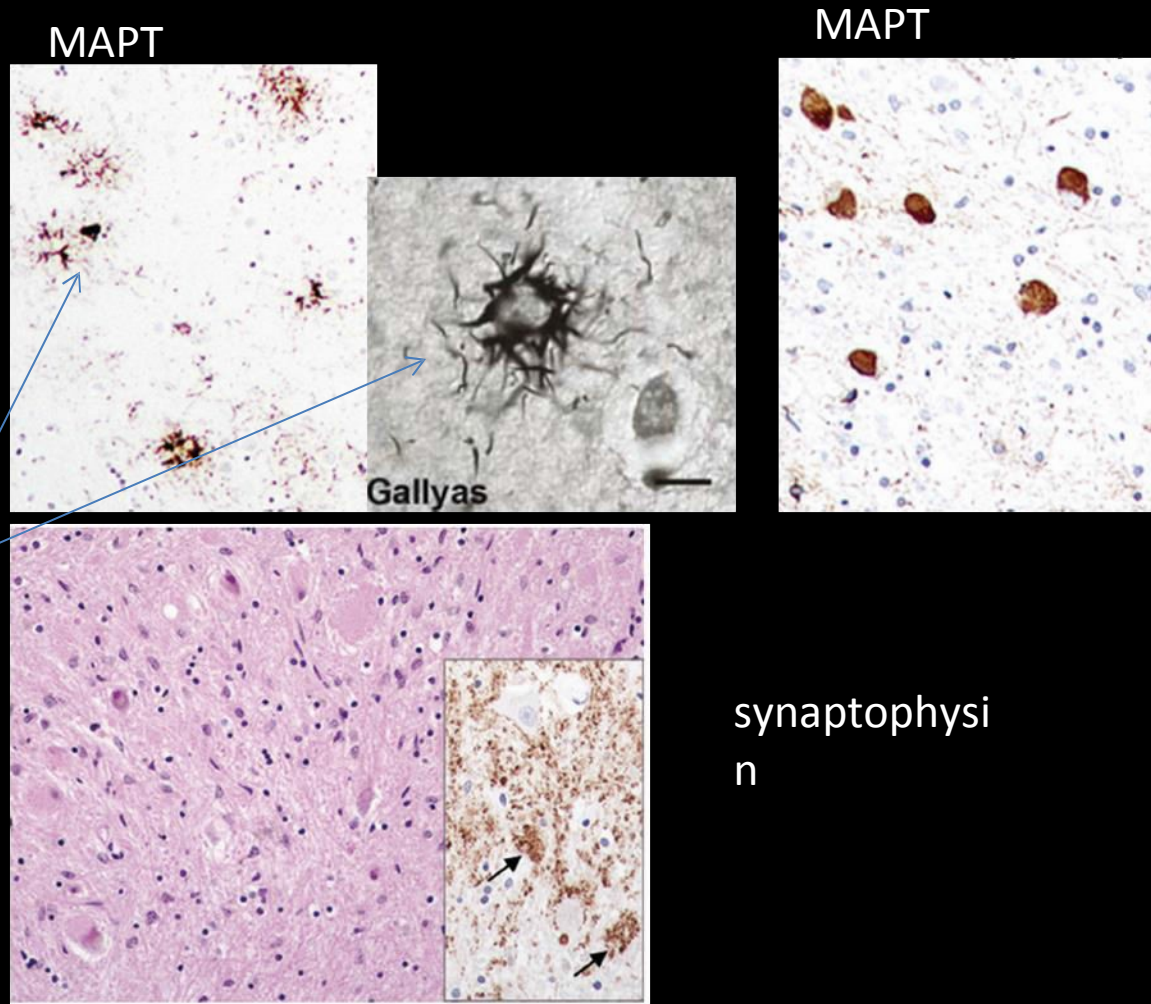


ATROPHY OF CEREBELLAR DENTATE NUCLEUS



PSP PATHOLOGY

- Neuronal loss and gliosis
- Hyperphosphorylated MAPT accumulation
 - Glial tauopathy:
 - tufted astrocytes



CORTICOBASAL SYNDROME: MULTIPLE PATHOLOGIES

- Dystonia, Parkinsonism, apraxia, cortical sensory loss, loss of voluntary limb control
- Syndrome now associated with several pathologies:
 - CBD
 - PSP
 - DLB
 - AD
 - FTLD-TDP43
 - Prion disease

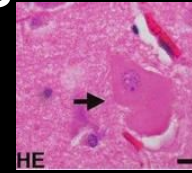
Syndrom



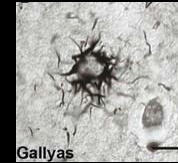
CBS

Patholog

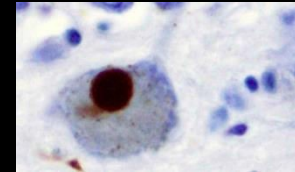
y
CBD



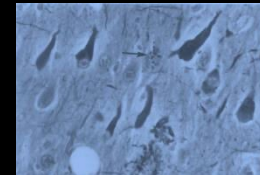
PSP



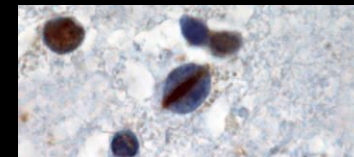
DLB



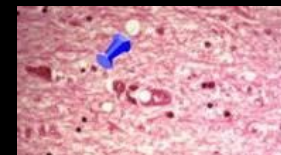
AD



TDP-43



Prion

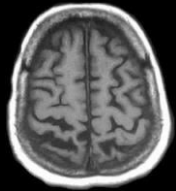


CORTICOBASAL DEGENERATION: MULTIPLE CLINICAL

PRESENTATIONS

- Different presenting syndromes can have CBD pathology:
 - Behavioral syndrome (FTD)
 - Non-fluent aphasia syndrome
 - PSP syndrome
 - CBS

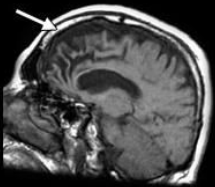
Syndrom



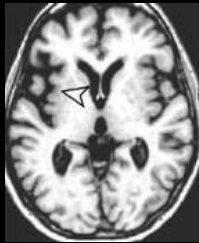
CBS



PSP



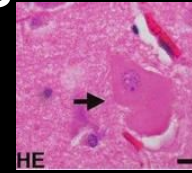
FTD



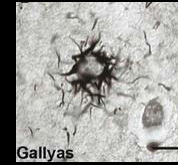
Non-fluent PPA

Patholog

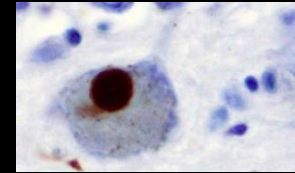
y
CBD



PSP



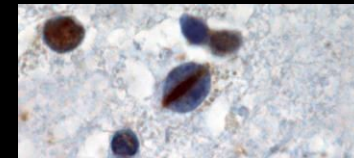
DLB



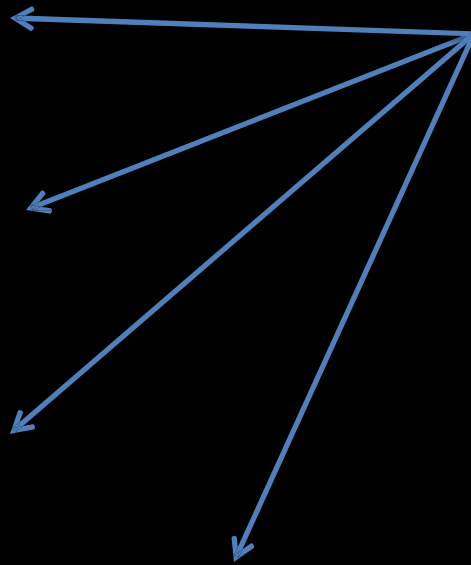
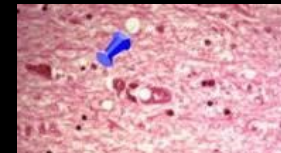
AD



TDP-43



Prion



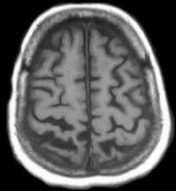
PROPOSED CLINICAL PHENOTYPES OF CBD

Probable
CBS Asymmetric presentation of 2 of: a) limb rigidity or akinesia, b) limb
 dystonia,
 c) limb myoclonus plus 2 of: d) orobuccal or limb apraxia, e) cortical

FBSS Two of: a) executive dysfunction, b) behavioral or personality changes,
 c) visuospatial deficits

PSPS Three of: a) axial or symmetric limb rigidity or akinesia, b) postural
 instability or falls, c) urinary incontinence, d) behavioral changes, e)
 supranuclear vertical gaze palsy or decreased velocity of vertical saccades

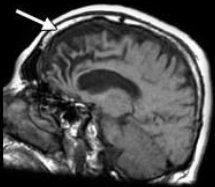
Syndrom



CBS



PSP



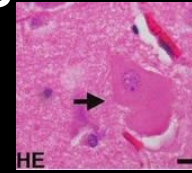
FTD



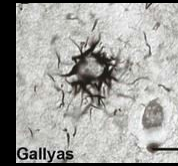
Non-fluent PPA

Patholog

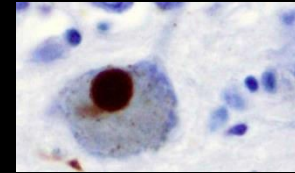
y
CBD



PSP



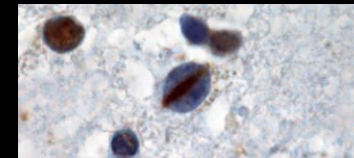
DLB



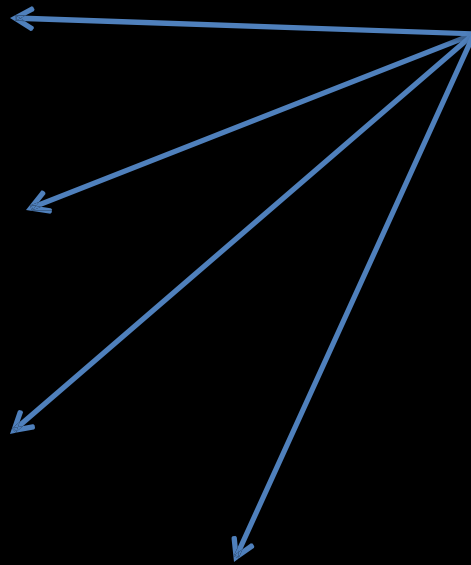
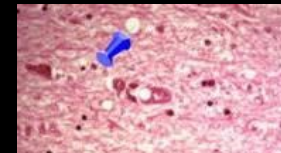
AD



TDP-43



Prion



PATIENT 1



58 RH F 1 year Left sided
clumsiness

- Difficulty descending stairs: hold railing with RUE
- 6 months later difficulty with sequence of starting car
- Handwriting worse, tremor b/l

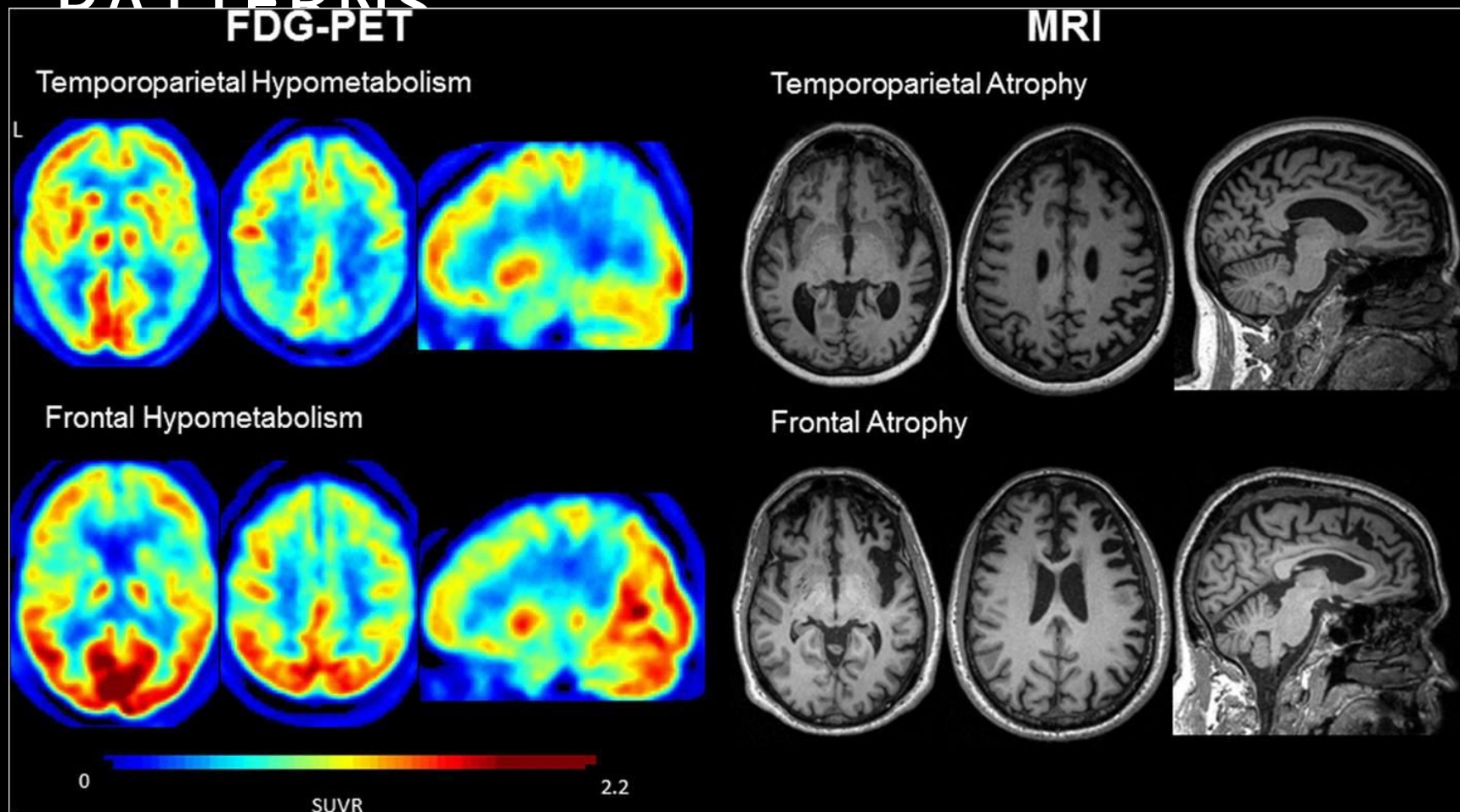
PATIENT 1



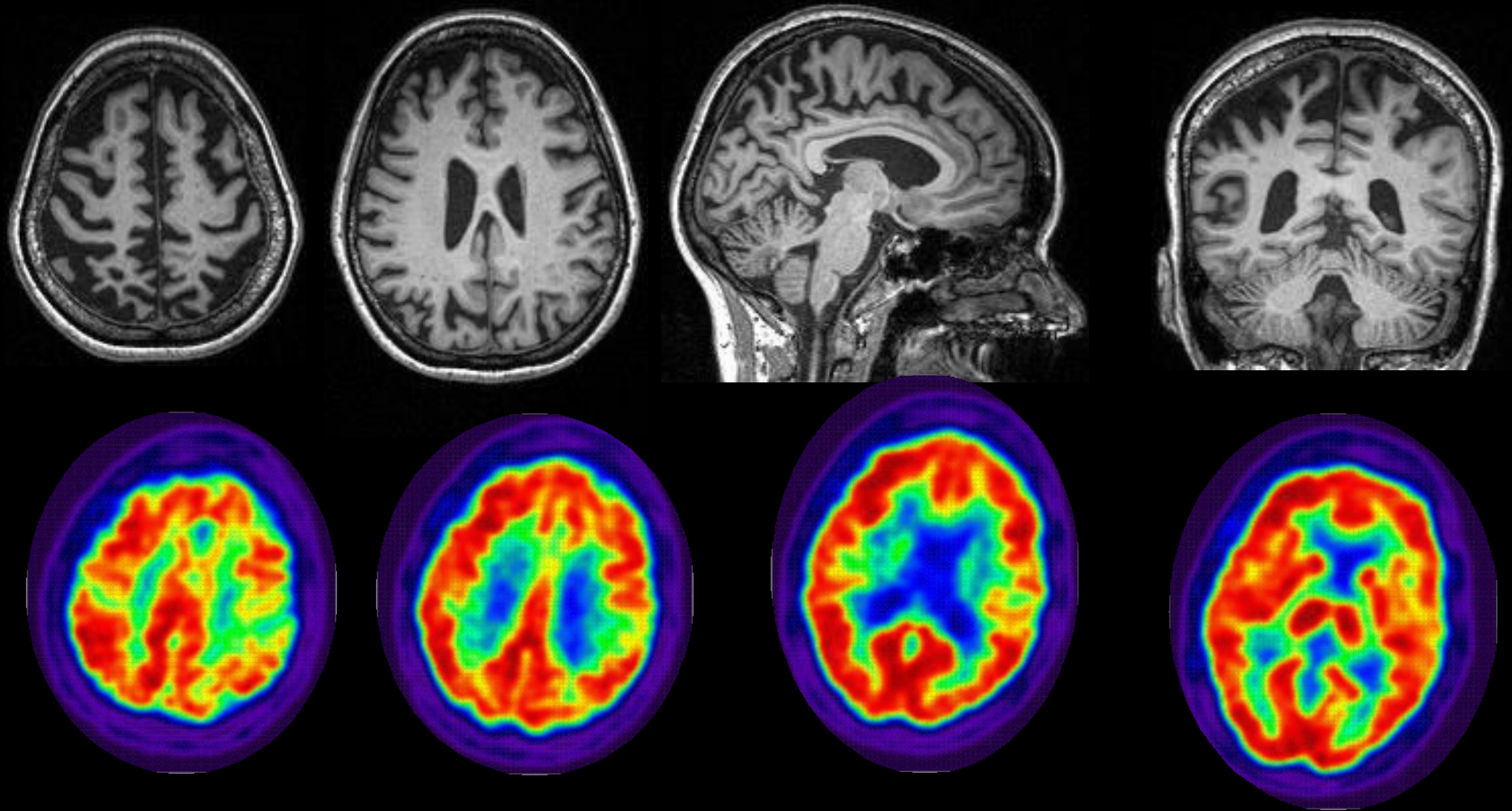
- Exam
 - Praxis worse L
 - Tone increased, cogwheel
 - Coordination worse on left, slow
- Cognitive testing:
 - Pretty good overall with minor problems in calculations and copying, but impaired phonemic fluency

TYPICAL FDG PET AND MRI

PATTERNS



PATIENT 1 MRI AND FDT PET



PATIENT 2

70 M 1.5 years of progressive motor and cognitive changes

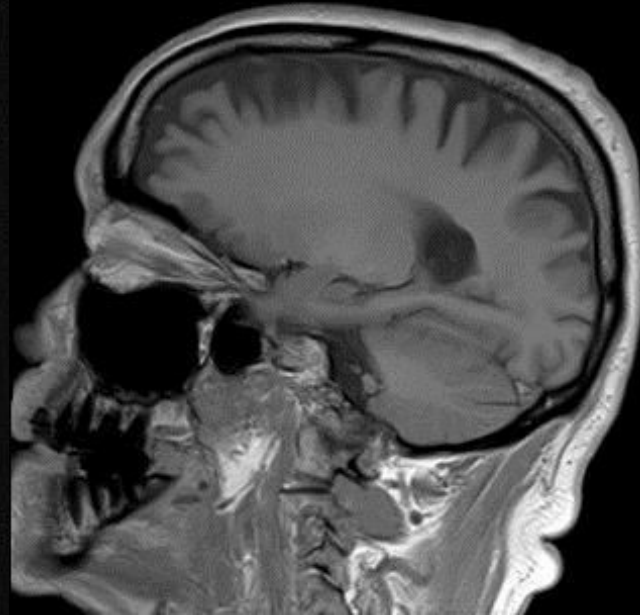
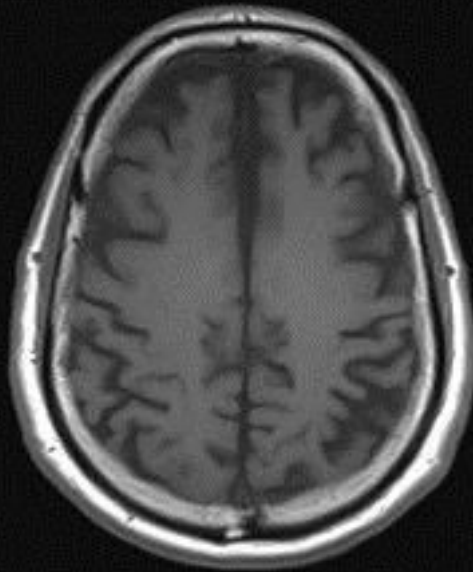
- Skiing accident with concussion
- R hand dystonia: Can't write, Can't eat
- Speech slow and slurred
- Memory problems, difficulty with details, planning

Exam:

- Memory loss recall 1/5, names 4 F words
- Eye movements with overshoot, saccadic
- Slurred speech and slow
- Right hand dystonic with increased tone
RUE, RLE



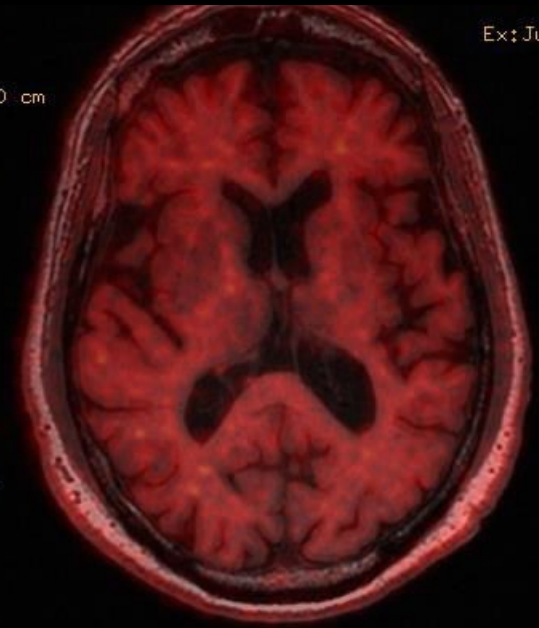
AMYLOID PET IS SUGGESTIVE OF AD PATHOLOGY



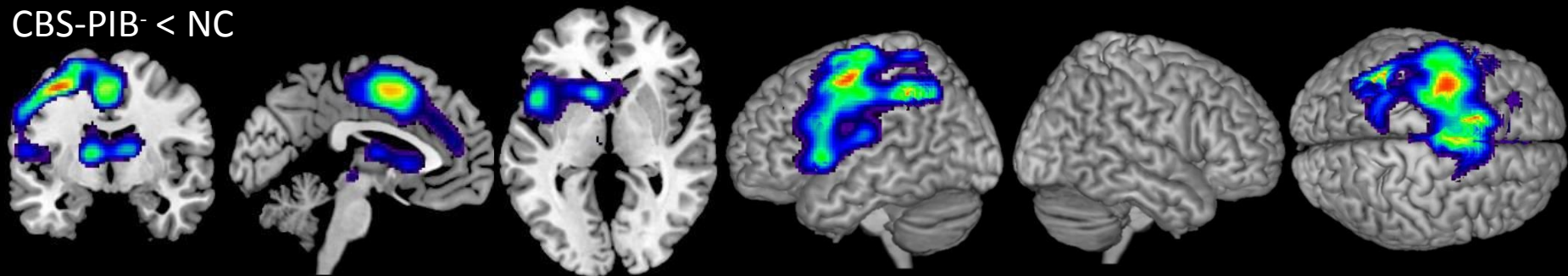
S: 12.2
Im: 45
DFOV 26.0 cm



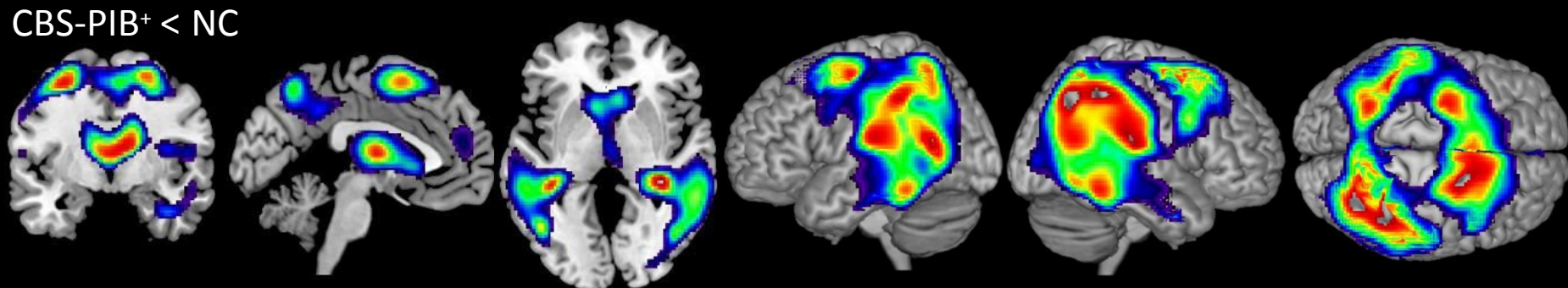
50 % PET
2.78



CBS-PIB⁻ < NC



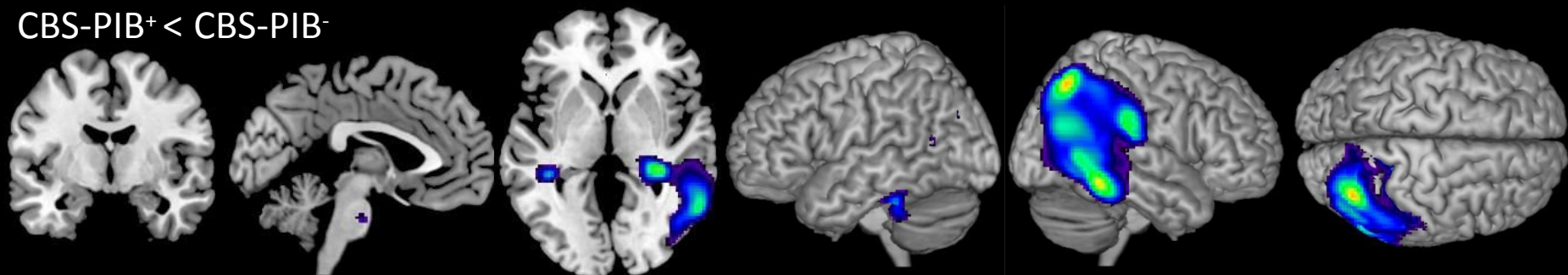
CBS-PIB⁺ < NC



CBS-PIB⁻ < CBS-PIB⁺



CBS-PIB⁺ < CBS-PIB⁻

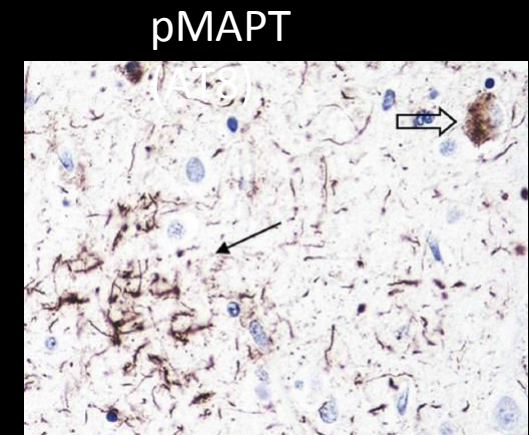
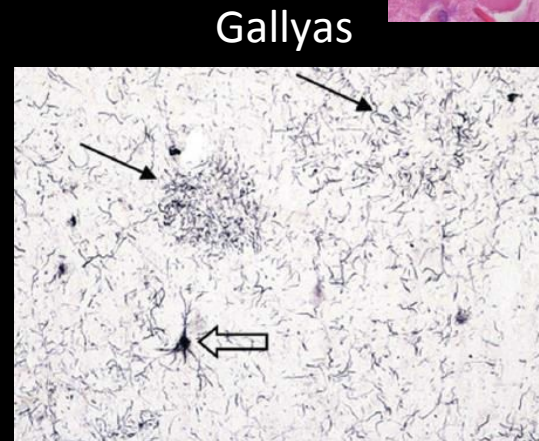
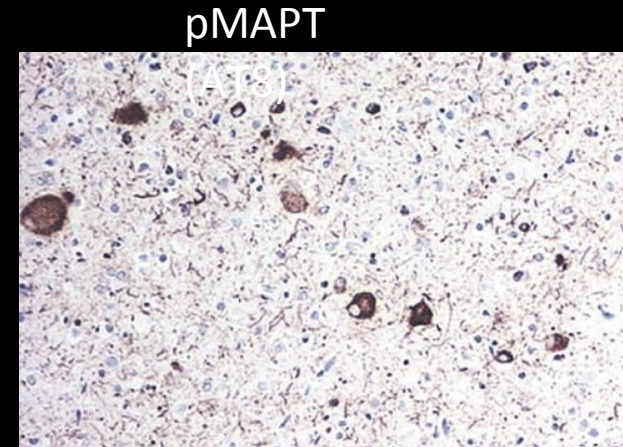
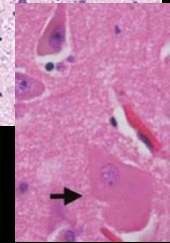
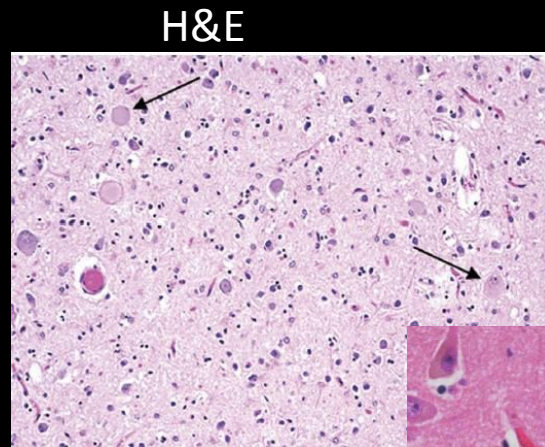


CORTICOBASAL DEGENERATION

- Macroscopic Pathology
 - Narrowing of cortical gyri especially frontal; **pre- and postcentral gyri atrophic** to varying degrees; **atrophy is often asymmetric**
 - May be flattening of caudate nucleus; brown discoloration of globus pallidus
 - Loss of neuromelanin pigment in the substantia nigra with better pigmentation in locus ceruleus
 - **Subthalamic nucleus (STN) usually preserved**

FTLD-MAPT (CBD)

- Abundant swollen cortical neurons
- Glial Tauopathy:
 - Coiled bodies
 - Astrocytic plaques



N.J. Cairns et al. (2007). *Acta Neuropathol.* 114:5-22.

E.H. Biggio (2013). *Arch Pathol Lab Med.* 137: 314-

CONCLUSIONS

- PSP and CBD can have different clinical presentations
- PSP-RS is the most common and most predicts PSP pathology
- CBS usually indicates CBD but can have alternate pathologies

STANFORD ADRC



- Free exercise and wellness classes (Yoga, Tai Chi, Dance, Qi Gong)
- Free support services (caregiver workshops, support groups, classes)
- Travel reimbursement, participation incentives, and feedback to share with your family and health care provider
- Stanford Neuroscience Supportive Care Program: www.stanfordhealthcare.org/nscn

650-721-2409

cwysscoray@stanfordhealthcare.org

<https://med.stanford.edu/adrc.html>

Thank you!

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