

Diagnostic Imaging in the Evaluation of Two Cases of Cognitive Decline



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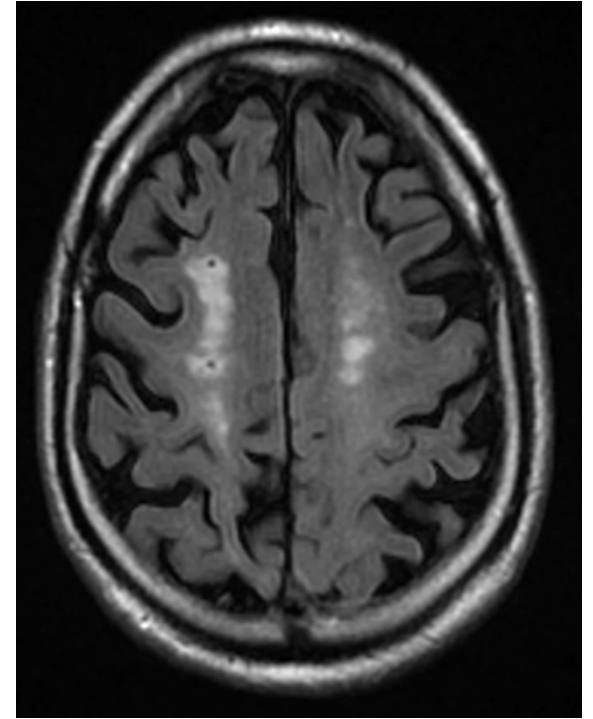
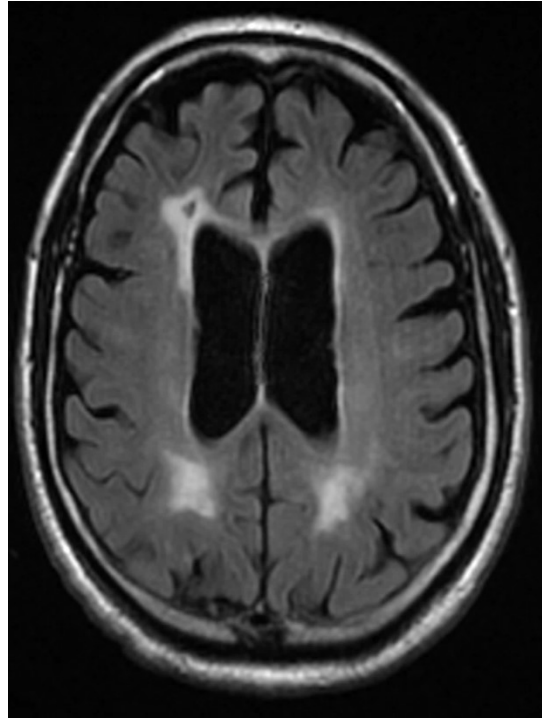
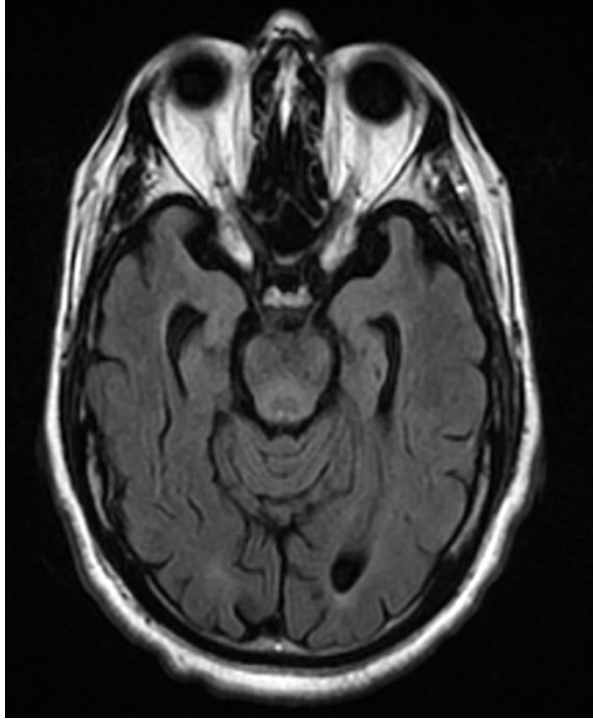
17th Annual Mild Cognitive Impairment Symposium



Case 1

- 86 yo L handed professor with short-term memory loss for 1 y
 - Gradual onset but relatively stable
 - Mildly repetitive, wife reminds him for medication
 - Drives without difficulty including Boston
 - Still writing and doing research part-time
- More withdrawn and mildly depressed on sertraline, upset about memory loss
- Rivastigmine patch caused sleepiness

- HTN, HLD, 4 years earlier episode of left leg weakness with some ischemic changes in the R MCA territory
- Meds-HCTZ, lisinopril, doxazocin, sertraline, atorvastatin, ASA 81
- No fam hx of dementia
- MMSE 26 1/3 delayed recall, MOCA 21, 0/5 delayed recall, 4/5 with prompting
- No rest or action tremor, left hip flex 4+
- Gait-mildly wide-based and mildly slow with a multi-step turn



Cognitive Testing

- Deficits in verbal and visual memory and complex visuoconstruction
- Other domains intact
- Dx-amnestic MCI

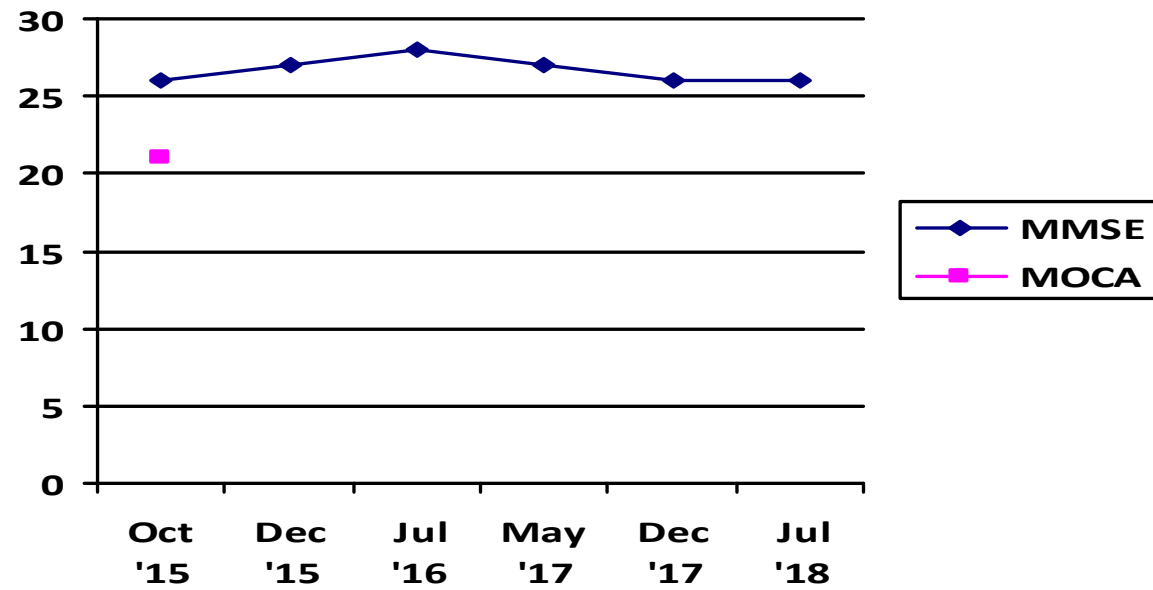
Diagnosis

- Level of impairment
- Features
- Differential diagnosis

Amyloid PET

– SUVR 0.82

MMSE HISTORY



Case 2

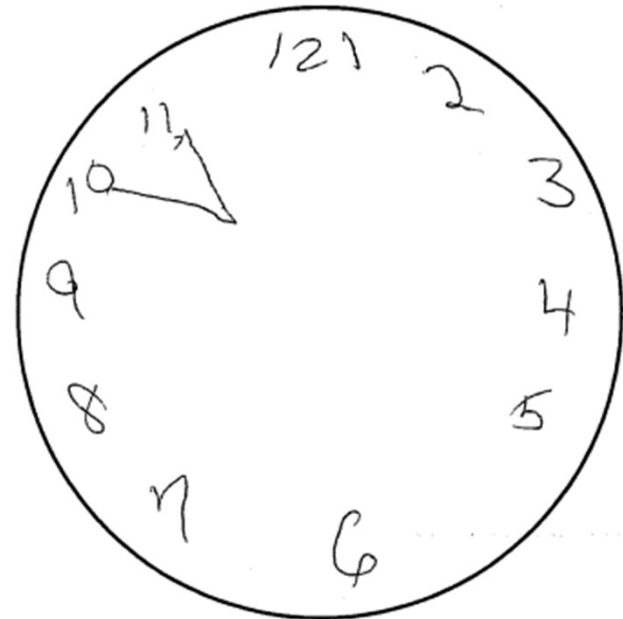
82 yo woman presents with gradual memory decline x 3 years

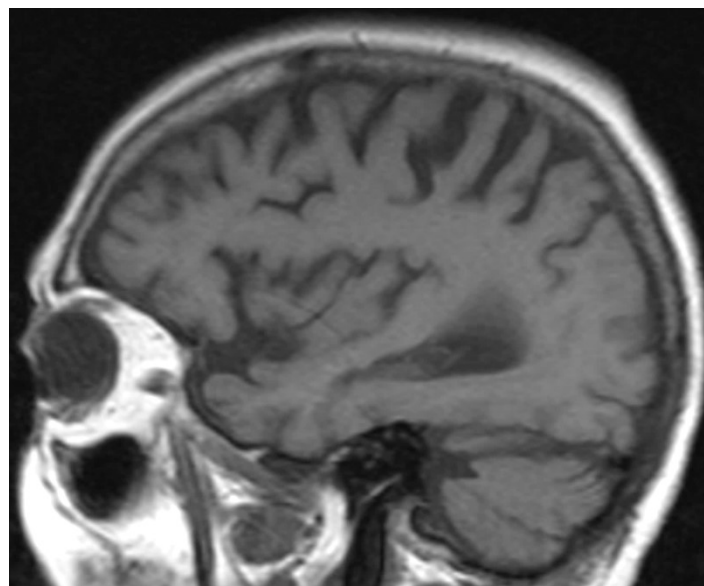
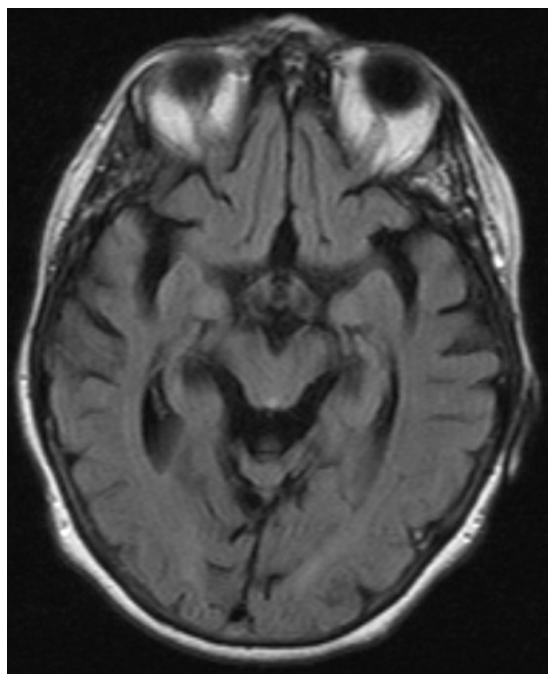
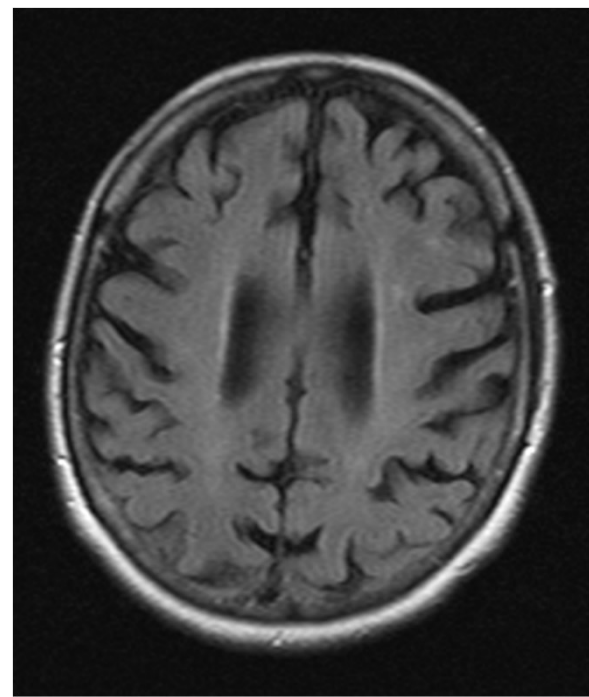
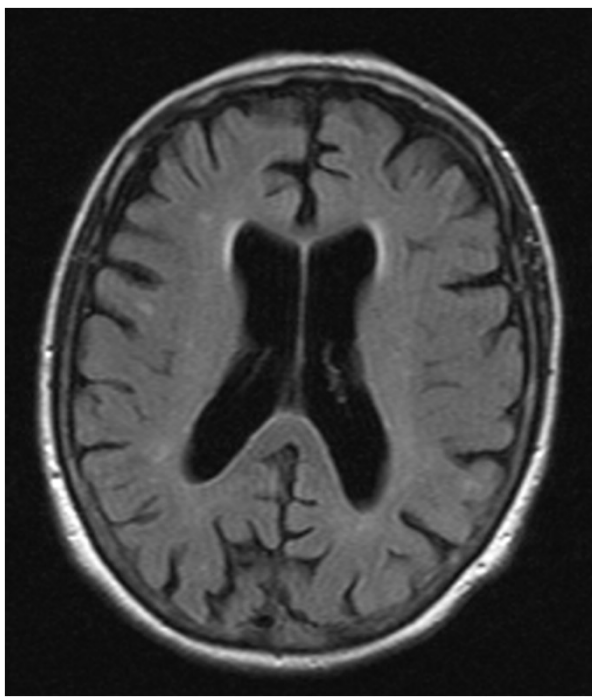
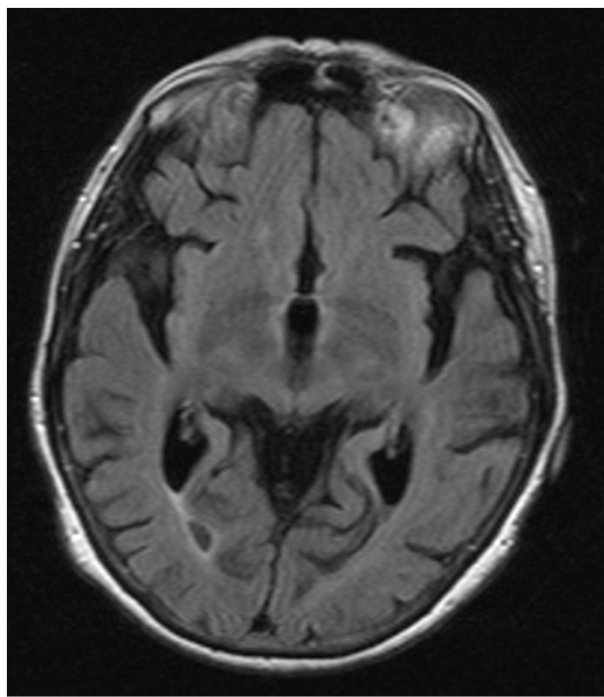
- Repetitive
- Trouble keeping track of dates
- Forgets names of people she knows well
- Mild word-finding difficulty
- Slight fluctuations
- Her husband packs her medication and she now does very limited driving

- PMH: HTN, HLD, GERD, h/o mild depression with good response to citalopram
- Meds: atorvastatin, losartan, omeprazole, citalopram, celecoxib, lorazepam
- FH: Mother died at 98 without cog decline, Father died at 50 of Hodgkins, Brother died at 79 with cog decline since age 70
- SH: Completed 14yrs education

MMSE: **23/30** (Missed 3 on orientation, 0/3 recall, used 10 instead of 2 in setting the time)
She has poor awareness of cognitive difficulty and is repetitive

Neuro: CNs, strength, tone, reflexes, sensation, cerebellar nl,
No frontal release signs, Mild retropulsion, mildly wide based gait





Cognitive Testing

3 yrs prior

- DRS 135
- Borderline to mild deficits in executive functioning, complex visual construction, fine motor dexterity and new learning of unstructured information
- Moderate to severe deficits in delayed recall for unstructured verbal and visual information

Repeat Cognitive Testing

- DRS 131
- Decline on Trails B
- Poor performance on verbal and visual learning and memory

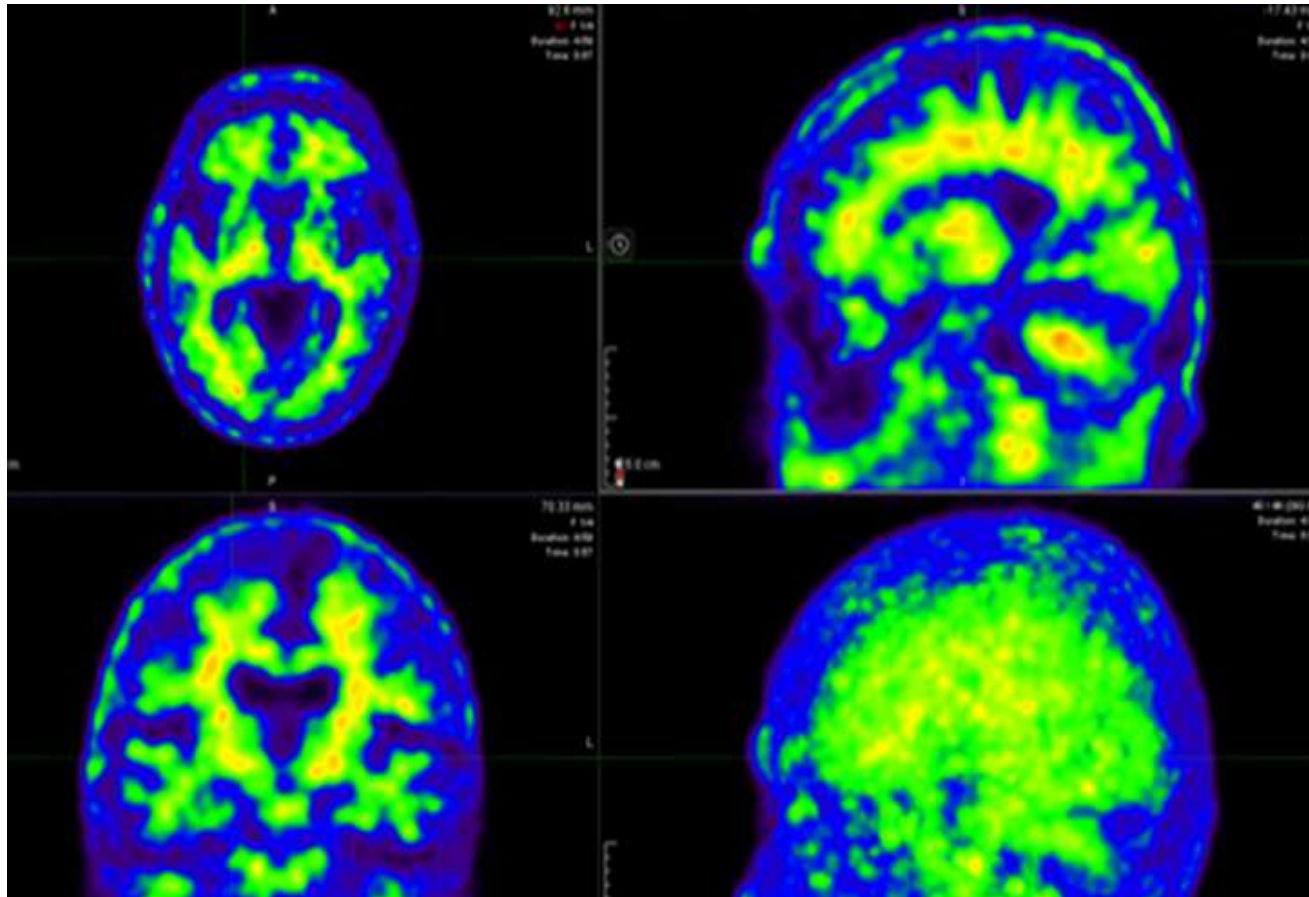
Diagnosis

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Treatment Plan

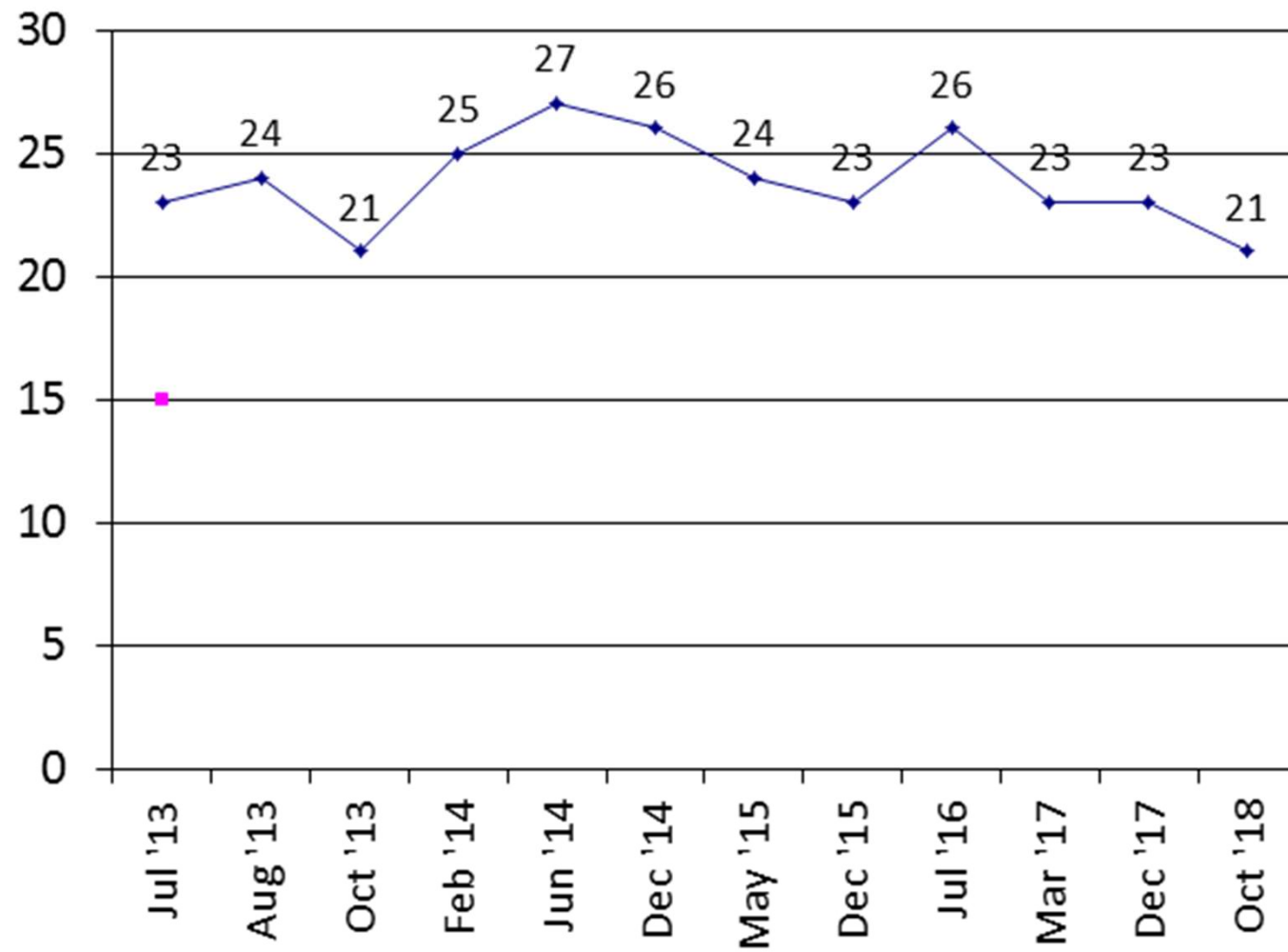
- Donepezil started but switched to rivastigmine patch because of nausea
- Referred to amyloid-lowering clinical trial

Amyloid PET Negative



“Normal and symmetrical pattern of brain ^{18}F -Florbetapir, excluding amyloidopathy”

MMSE HISTORY

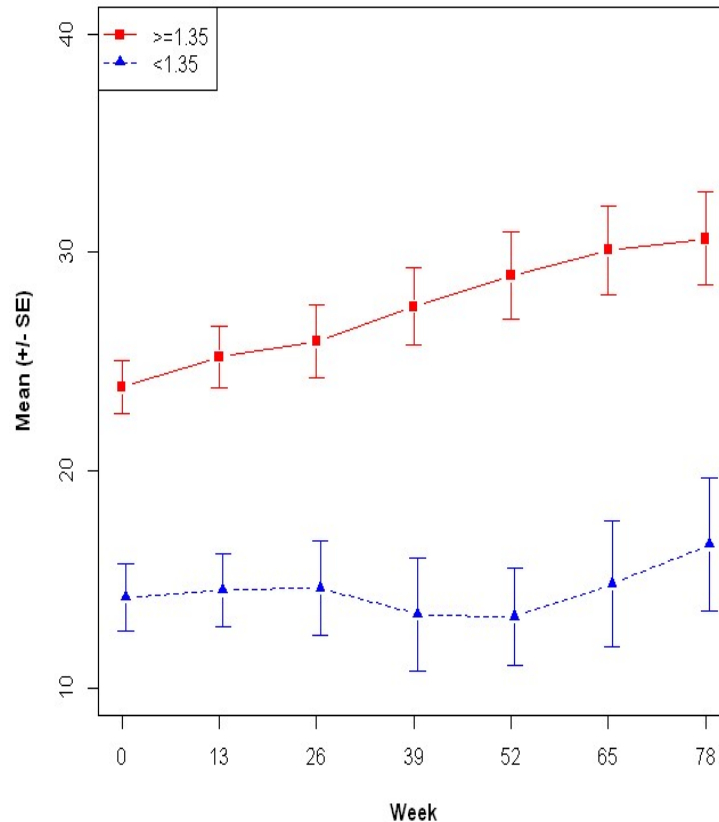


Summary

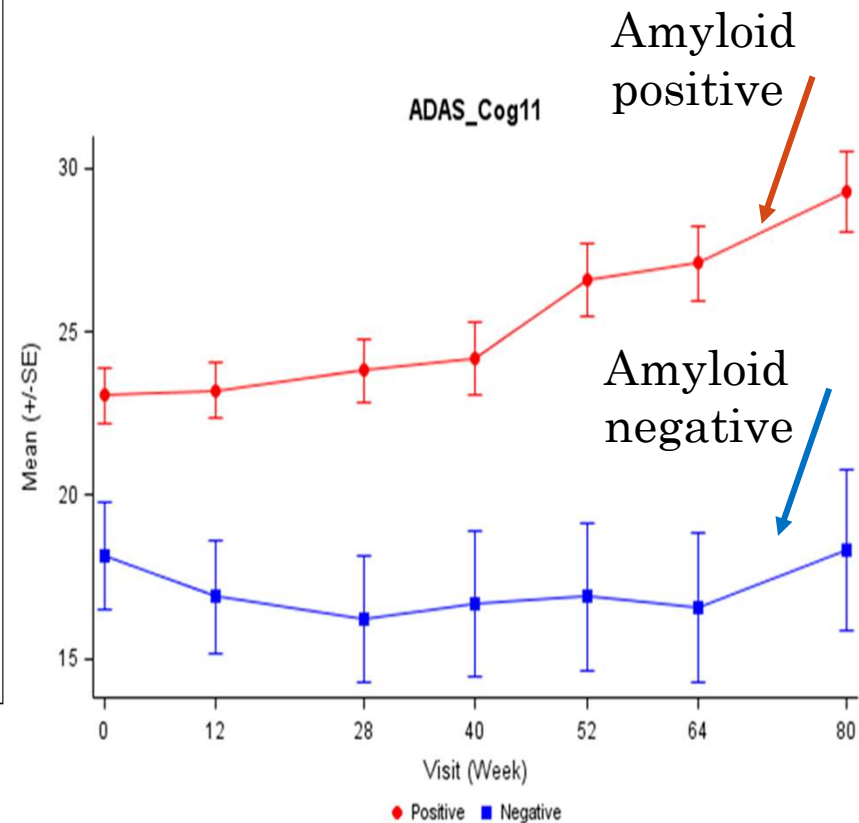
- 2 cases (ages 86, 82) of non-amyloid amnestic cognitive impairment with relatively stable course
- Contributing factors
 - Depression
 - Vascular risk factors and cerebrovascular disease
- Both cases with diffuse cortical and hippocampal atrophy

Change in ADAS-cog/11 in 2 Phase 3 Trials of Mild-Mod AD Dementia

Bapineuzumab



Solanezumab



Slower than expected cognitive and functional decline in amyloid negative subjects

Salloway, Sperling AAIC 2013

Remember patient's brother with cognitive decline

Autopsy on brother completed at Yale

Final Diagnoses:

- Arterio- and Arteriolosclerosis, Moderate to Severe
- Microscopic Infarcts, Remote
- Focal Hippocampal Sclerosis and Neuronal Loss
- Hypoxic Anoxic Injury, Acute

Examples of Non-amyloid Amnestic Syndromes

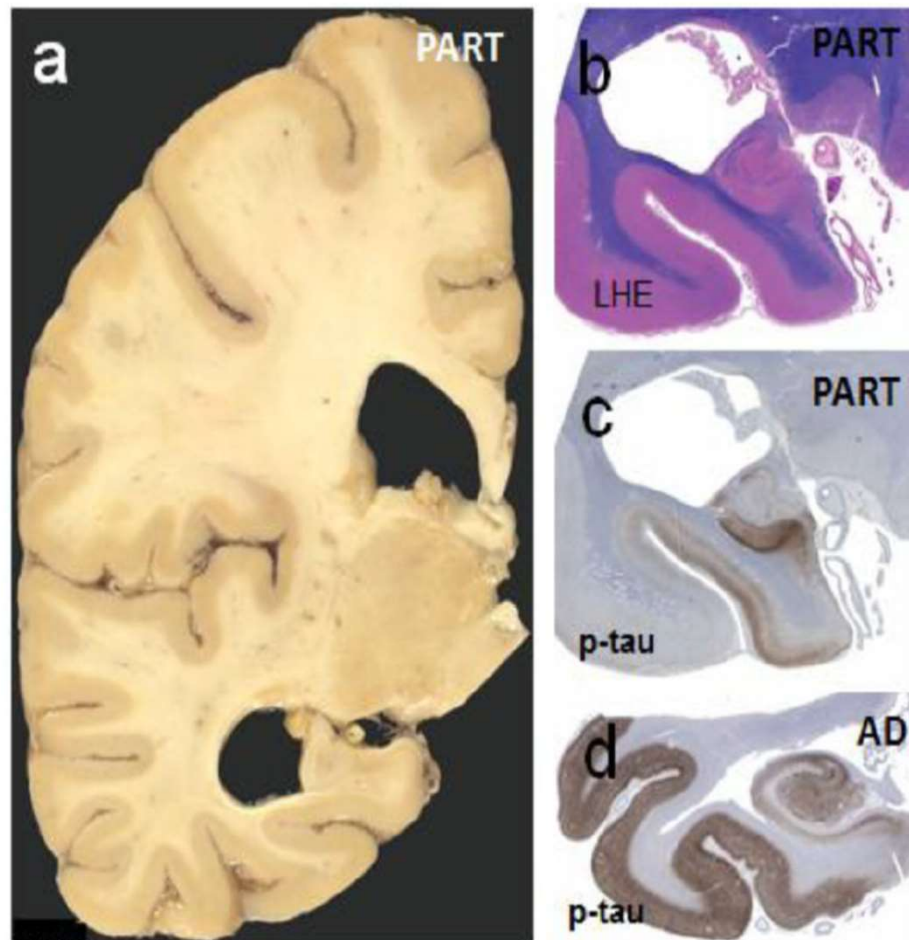
- Hippocampal Sclerosis of Aging (HS-Aging) LATE
- PART (Primary Age-Related Tauopathy)
Tangle only dementia
- Age-related tau astrogliopathy (ARTAG)
- Agyrophyllic grain disease

Hippocampal Sclerosis of Aging

- Neuron loss and astrogliosis in the hippocampal formation, “out of proportion to AD neuropathologic change in the same structures”
- Key pathologic marker is aberrant hippocampal TDP-43 pathology
- HS correlates with impaired cognition, though with a much milder progression
- Can occur concurrently with AD pathology
- Affects > 20% individuals >85yo
- 40-50% of HS-Aging cases have unilateral HS pathology and is associated with cog impairment

Primary Age-Related Tauopathy

- Medial temporal lobe atrophy and tau pathology without or with few amyloid plaques
- Common in clinically normal elderly people
- Increase in prevalence with aging
- Association with cognitive impairment varies



Crary et al. Acta Neuropath, 2014.