

The Diagnostic Dilemma of Subjective Cognitive Concerns

Case Presentation of a 70 y/o woman

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Psychosocial History

- 70 y/o, right-handed woman, married 40 years, 2 older children, average EIQ= 130

Education:

- Graduated Boston College with Bachelor of Science degree in Education
- Special training in Italian from Florence, Italy

Occupation:

- Taught English and Italian at the High School level for 13 years prior to raising her family
- Sales and merchandising for Hershey chocolates

Medical / Psychiatric History

- Rheumatoid Arthritis (1969)
- Hypertension
- Hypercholesterolemia
- Congestive heart failure (2003)
- s/p Endometrial cancer treated with hysterectomy and chemotherapy (2006)
- Mild depression (2006) successfully treated for 8 years with SSRIs
- Sleep Initiation Disorder

Family History

- Mother died at age 73 with forgetfulness in the setting of Parkinson's disease
- Father died at age 80 with myocardial infarction related to a surgical procedure. He was repeating himself prior to his death.
- 3 uncles with late-life dementia, presumably Alzheimer's disease (AD)
- Maternal cousin diagnosed with AD
- 2 sisters (ages 72 and 67) who remain in good health without memory difficulty

2007 Case Presentation Summary

Mrs. V (age 64) initially referred for a neuropsychological evaluation because of subjective concerns about her memory.

- ADLs were normal.
- Continued to pay bills in husband's business.
- No difficulty with driving or becoming lost.
- No name or word-finding problems.
- Family had not noticed any changes.

Neurological exam and laboratory workup were normal

She was diagnosed as having cognitive changes related to depression secondary to her cancer diagnosis

2011 Case Presentation Summary

- **Mrs. V (age 68) complains of being more forgetful**
 - Gave up bill paying in husband's business because she was forgetting to pay bills on time
 - More difficulty preparing elaborate meals
 - More withdrawn and less active in her hobbies
 - Family thought she was functioning quite well and remained unconcerned
 - Neurological exam and laboratory workup were normal

She was diagnosed as having amnestic Mild Cognitive Impairment due to declines in memory on exam and changes and achieving an CDR of 0.5

Case Presentation

- **2013 : Mrs. V (age 70) feels that her memory is “*all right because I do not forget on a daily basis*”.**
 - She forgot that she had an appointment at BWH two weeks in a row despite being reminded by her daughter the night before.
 - She is forgetting to take her medications
 - Doesn't recall what medications she is actually taking
 - Recently took a trip to Italy, surprised she could still speak Italian but could not describe what she did when she returned home
 - Unlike previous years, she is not troubled by her memory loss
 - Continues to drive without incident but may get lost.
 - She does all the grocery shopping but forgets items
 - Her family are now more concerned

2013 Review of Systems

- Mood is *good*. She feels optimistic and maintains a good sense of humor
- She takes ¼ pill of Mirtazapine for sleep. She generally falls asleep about 10:30 PM and wakes at 8 AM feeling rested.
- She denied being in any significant pain
- She drinks a glass of red wine 2-4 times per month.
(AUDIT C = 2)
- When physically able, she walks 3 times per week or rides an exercise bike
- Further review of systems is negative for tobacco or illicit drug use, gait or balance disturbance, auditory or visual hallucinations, paranoia, suicidal or homicidal ideations. She feels safe in her home environment.

2013 Current Medications

- Arava 20 mg,
- Cardura 4 mg,
- Citalopram 40 mg,
- Folic Acid 1 mg,
- Humira 40 mg,
- Imodium 2 mg,
- Mirtazapine 7.5 mg for sleep,
- Prednisone 2 mg,
- Resveratrol 250 mg,
- Vitamin B6 100 mg,
- Vitamin B12 50 mcg
- Vitamin D3 2000 units.

2013 Physical and Neurological Exam

- Her physical examination was notable for multiple deformities due to her arthritis with limited range of motion in her neck and hands.
- Her BP was 132/84, heart rate of 72. Her lung and heart examination was unremarkable.
- Her elemental neurologic examination revealed slightly diminished sense of smell. Visual fields were full. Visual acuity was normal with reading correction.
- She had slight restriction of upgaze but otherwise intact extraocular movements without saccadic intrusions. Her facial sensation and movement was symmetric. Her hearing was intact to whisper and her palate elevated symmetrically, and she had normal tongue movements.

2013 Motor and Sensory Exam

- Motor examination revealed symmetric strength.
- No evidence of upper or lower motor neuron deficits. Tone was normal without evidence of cogwheeling.
- She had no evidence of dysmetria. Gait was narrow based, and slow due to her arthritis.
- Her sensory examination revealed mild loss of vibration in both feet, intact at the ankles. Her temperature sense was also slightly diminished in both feet. Deep tendon reflexes were 1+ and symmetric. Plantar reflexes were flexor.

2013 Laboratory Workup

- Basic blood work was unrevealing. She had normal complete blood count, chemistries, thyroid tests.
- Vitamin B12 was normal, and Lyme and syphilis tests were negative on previous blood work.

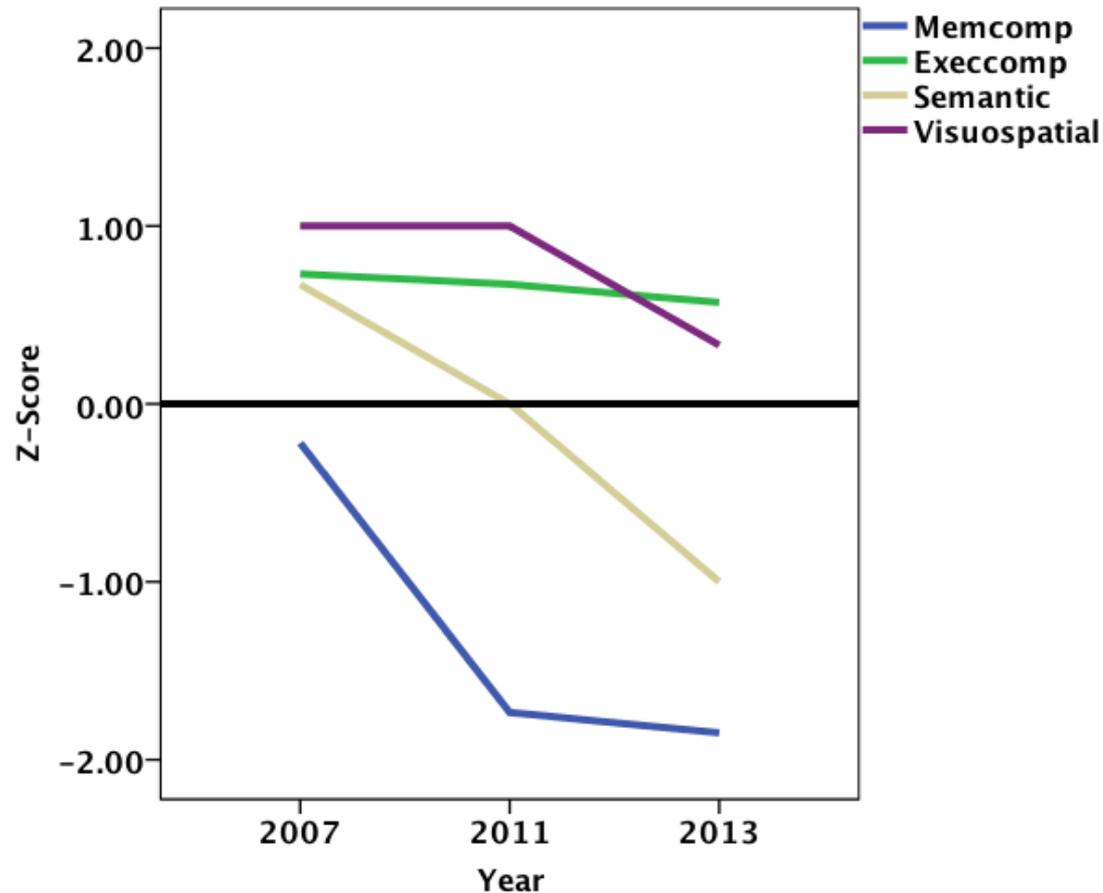
Procedures

- Neuropsychological Testing
 - 11/13/2007
 - 11/7/2011
 - 10/17/2013
- MRI Imaging (3/11/2011)
- PiB PET Imaging (4/19/2011)
- Tau PET Imaging (10/17/2013)

Neuropsychological Exam

- MMSE
- Blessed Dementia Rating Scale
- Attention Span
- Word fluency (FAS and 3 Categories)
- Tests of mental control
- CERAD 10-Word List
- WMS-R Logical Memory
- Free and Cued Selective Reminding Test
- Boston Naming Test
- Visual Form Discrimination Test
- WAIS-III Similarities
- Beck Depression and Anxiety Inventories

Cognitive Performance in 70-y/o woman with initial Subjective Cognitive Concerns



IMAGING

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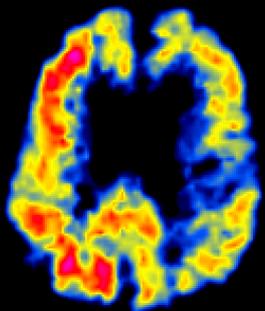
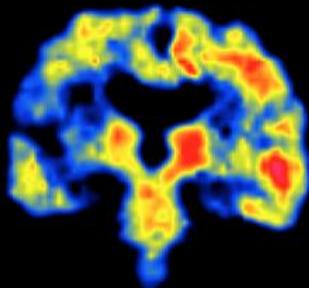
MR WMA



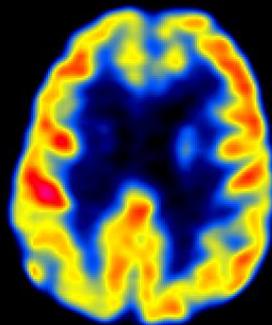
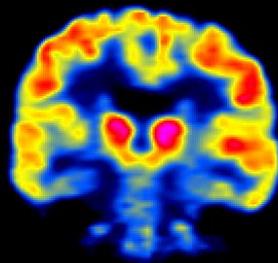
MRI



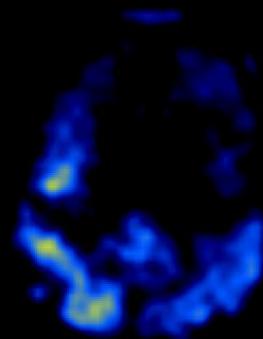
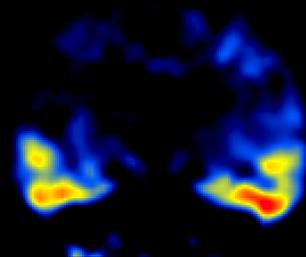
PiB



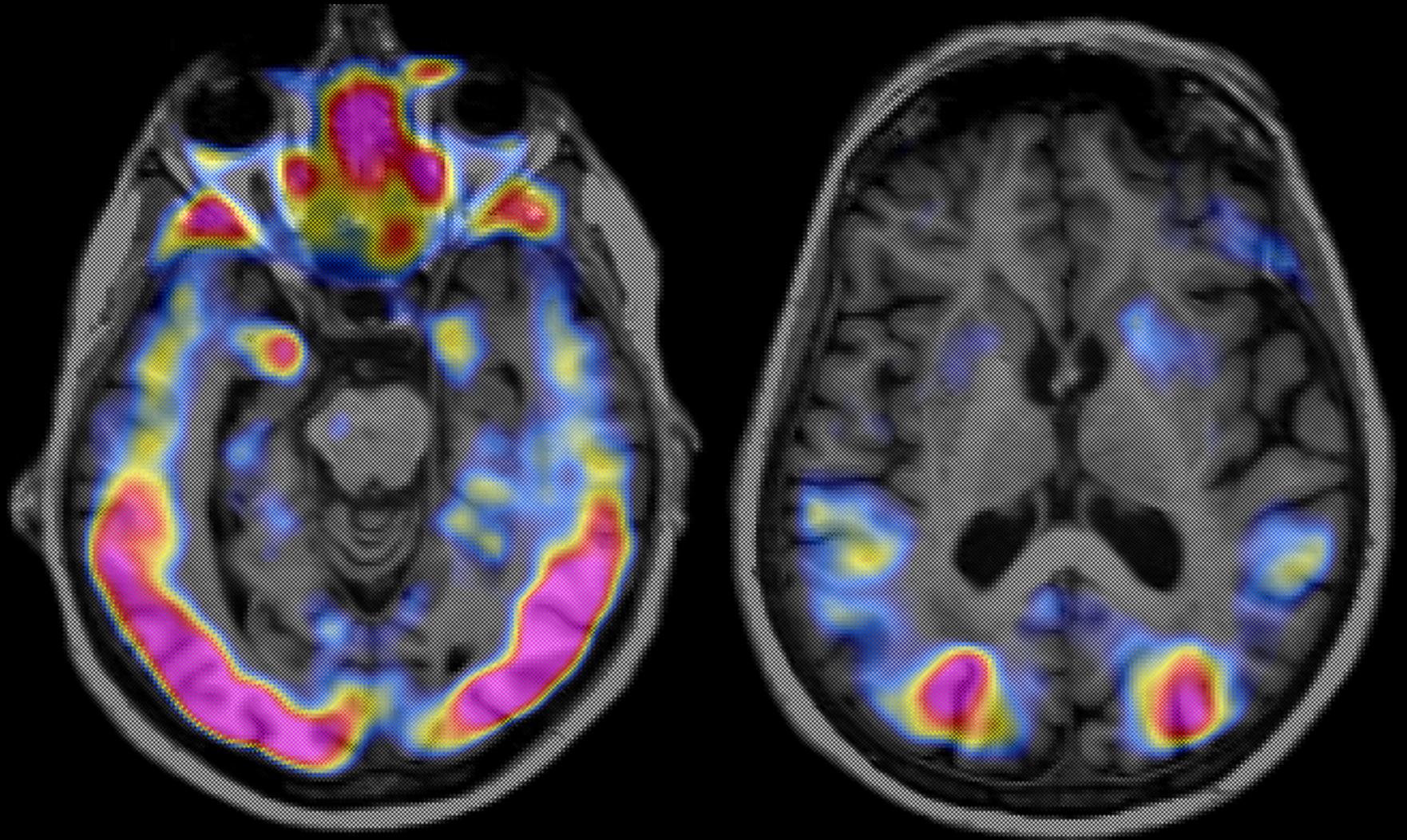
FDG



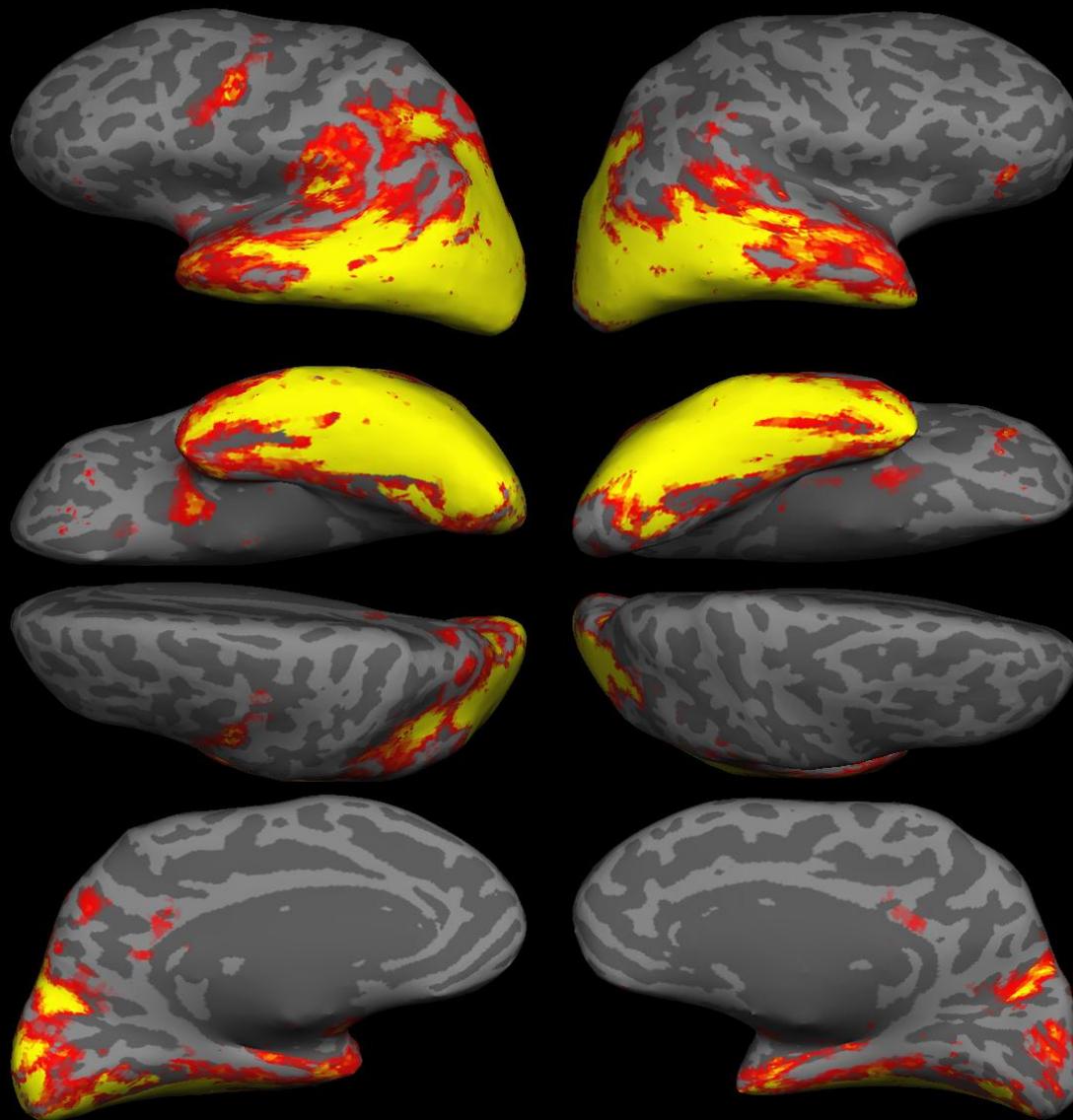
T807



Axial Overlay of MR and Tau



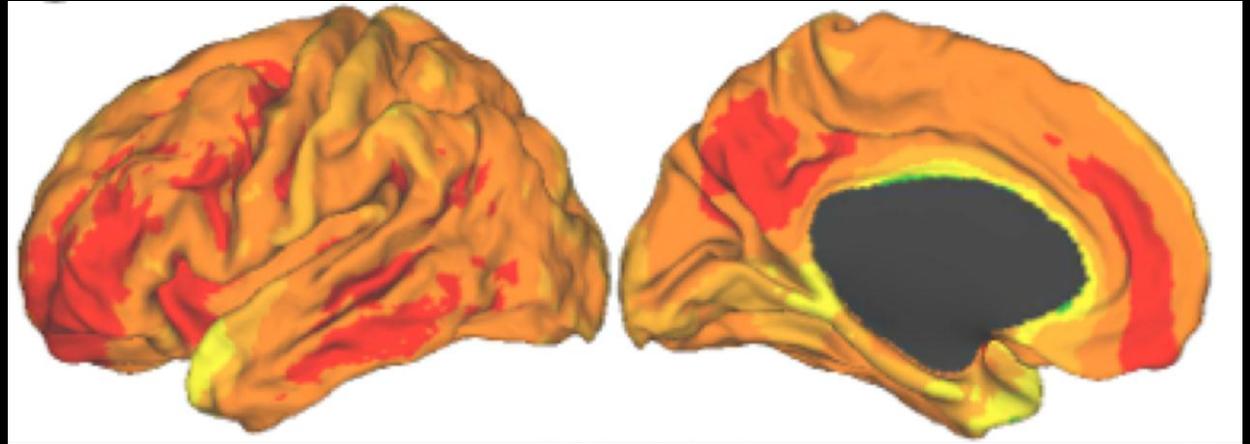
Tau Surface Projection



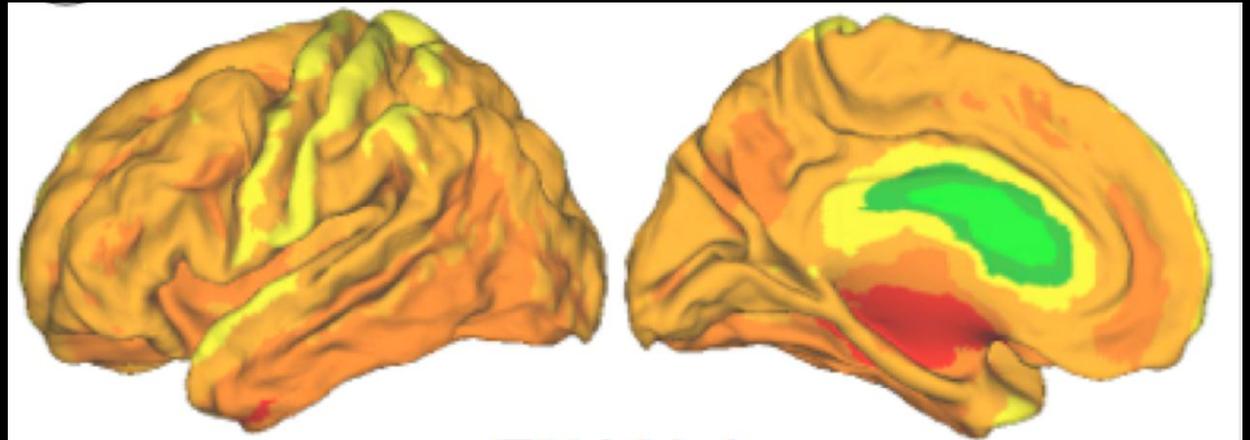
PiB PET vs. FT807 PET

cognitively normal controls, mean age 72, N = 12

11C PiB
Fibrillar
Amyloid- β



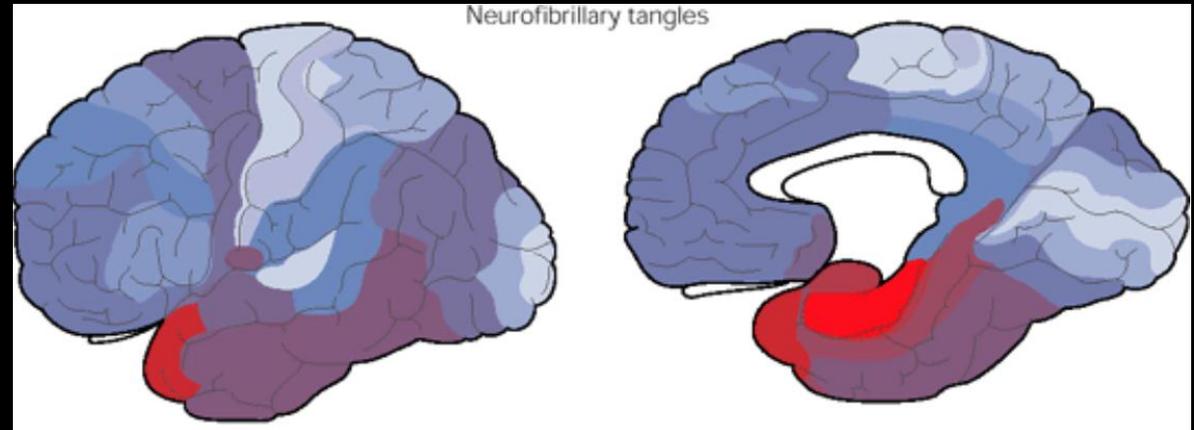
18F T807
PHF Tau



Silver stain vs. T807 PET

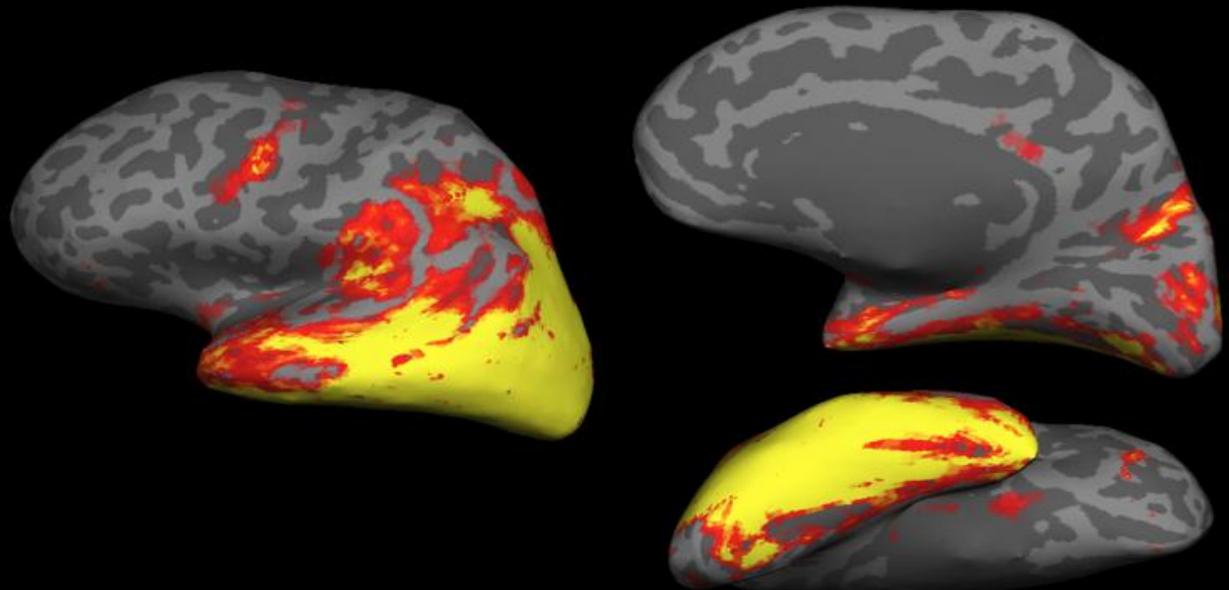
Neuro-
Fibrillary
Changes

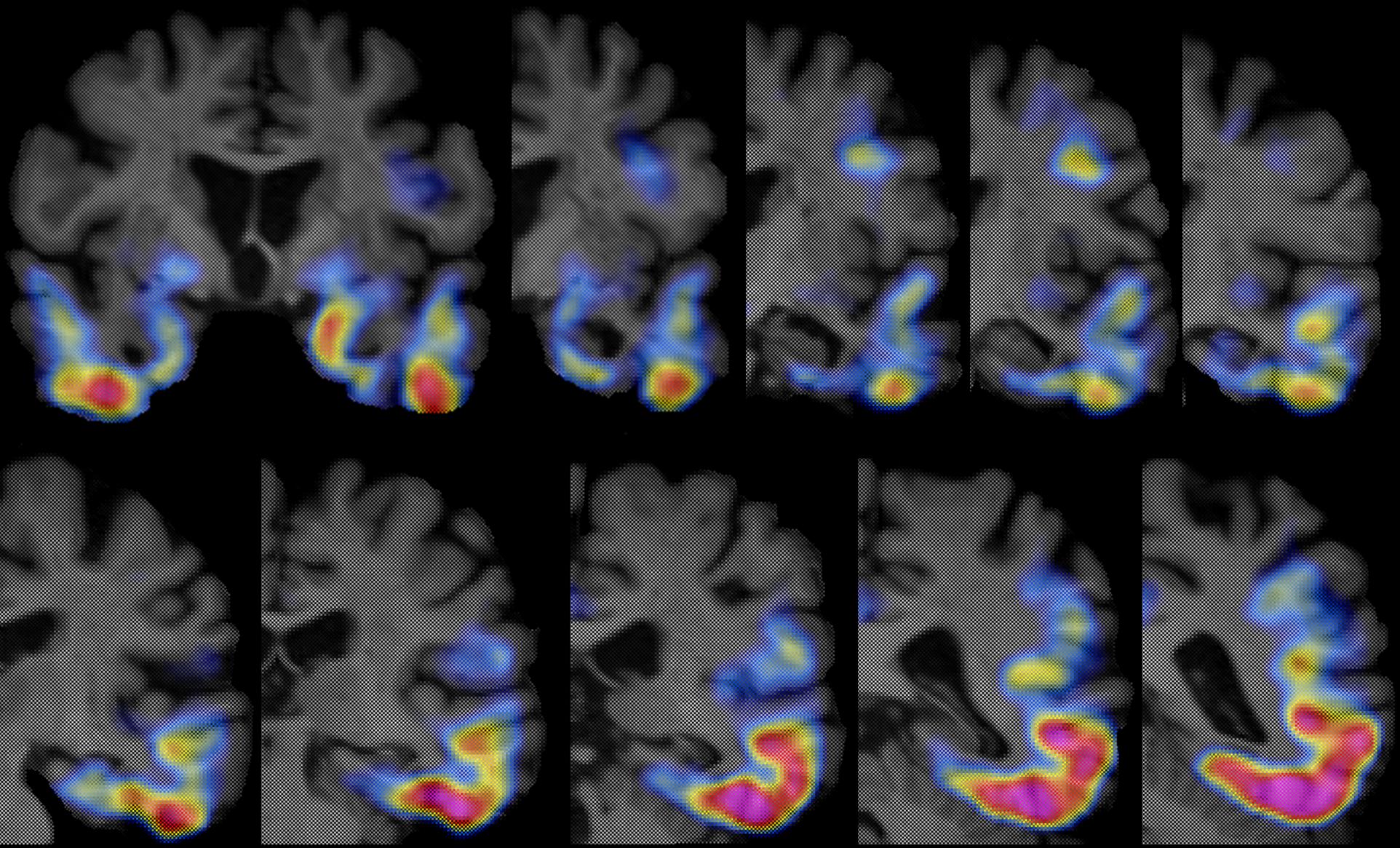
Arnold et al., 1991



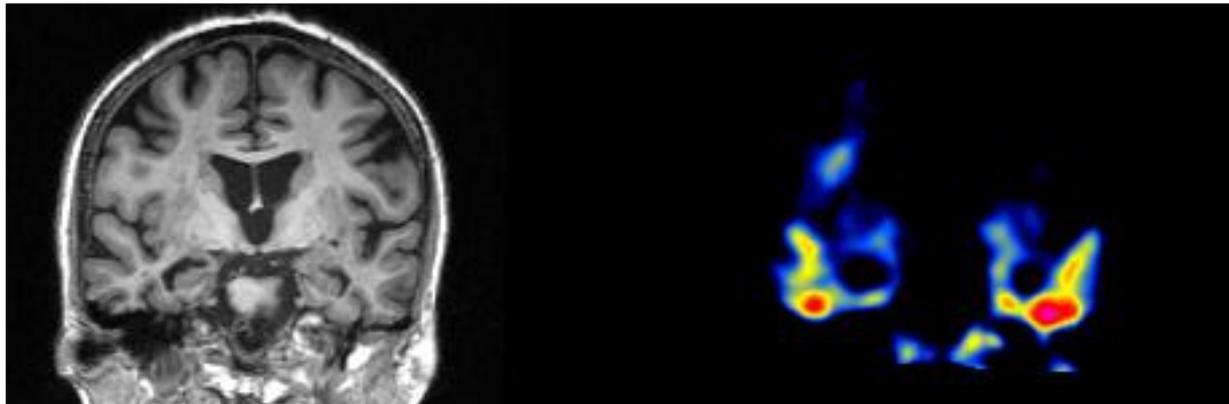
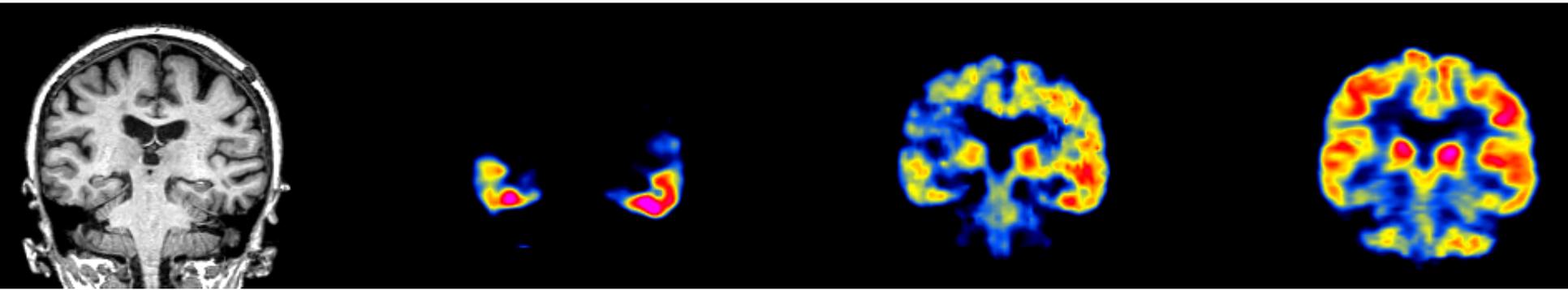
^{18}F T807
PHF Tau

MCI age 70





Axial Overlay of MR and Tau



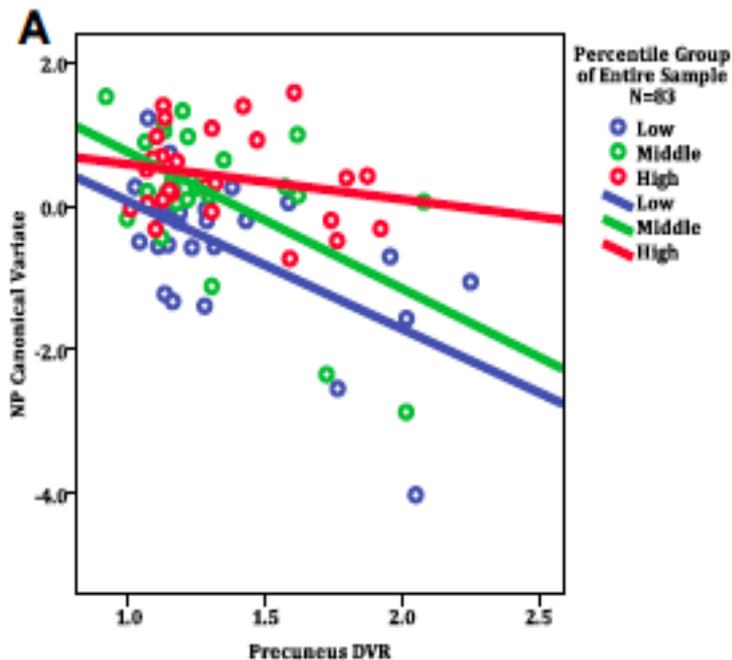
Conclusions/ Discussion

- Mrs. V came to initial evaluation in 2007 (age 64) with subjective cognitive complaints in the context of preserved ADLs and no family concerns of deteriorating function
 - At that time, memory was still within the normal range in the context of preserved cognitive functions consistent with her overall superior abilities.
 - Cognitive changes were attributed to recent cancer treatments and changes in mood
- 2011- (age 68) returns with persistent cognitive complaints
 - Memory changes now involved deficits in encoding, retrieval and storage suggestive of a temporolimbic amnesia.
 - Greater difficulties with complex ADLs (bill paying, driving, large family meal preparations
 - Diagnosis of Amnestic Mild Cognitive Impairment was made

Conclusions/ Discussion

- 2013 (Age 70) Mrs. V no longer has subjective cognitive concerns, thinks her memory is okay, however her family now has concerns about her memory
 - In contrast to 2007 and 2011 evaluations, there were further declines in memory, naming and semantic processing suggestive of a neurodegenerative process. She is now given a diagnosis of mild Alzheimer's disease.
- Several issues are raised:
 - How important are subjective cognitive complaints?
 - How does high cognitive reserve impact early diagnosis?
 - What role does amyloid and tau imaging play in early diagnosis?

Cognitive Performance vs. Precuneus A β Is Modified by Cognitive Reserve AD and NCs N=83

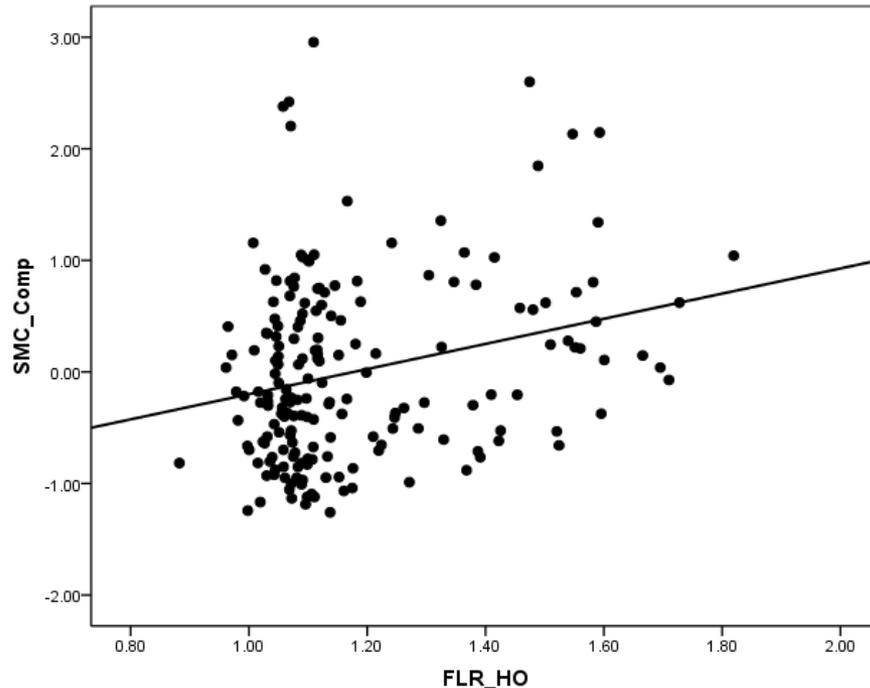


Predictor Variable	Correlations of Predictor Variables with Their Own Canonical Variate	Regression Analysis of the NP Canonical Variate and Predictors	
		Parameter Estimate ^a	<i>p</i>
Age	0.3191	0.026	0.0133 ^b
Education	0.2389	0.038	0.3152
rAMNART	0.5814	-0.072	0.1568
Precuneus PiB	-0.6742	-1.545	<0.0001 ^b
Precuneus PiB rAMNART interaction	0.6189	0.087	0.0278 ^b

DM Rentz, et al. *Ann Neurol* 2010; 67:353-364.

Conclusions/ Discussion

- Subjective Cognitive Concerns were significantly related to amyloid burden in clinically normal older adults



	β	p
SCC-Total	0.188	0.025
GDS	-0.383	0.70

THANK YOU!!

COMMENTS / DISCUSSION