SPECT and PET in Epilepsy and dementia and Parkinson's syndromes

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Epilepsy

- Various forms of epilepsy
- In childhood and young adults ca be spontaneous
- Often triggered or stopped by life events
  - Menarche
  - Pregnancy
- In older patients related to organic pathology CVA or tumour

What is epilepsy

- It is not a fit
- Anyone if pushed enough will have a fit
  - Pyrexia
  - Metabolic
- To make a diagnosis of epilepsy need history of more than one fit
- In some a trigger identified – flashing lights
- Important diagnosis legal issues

Types of epilepsy

- Petit mal-episodes of non-attention normally disappears by puberty
- Temporal lobe epilepsy-often suffer from deja vu or smelling an odd smell often mildy unpleasent
- Grand mal, the most common type tends to be worse in children classic fit can result in cerebral ischaemia and other injuries
- Tonic-clonic aggressive form of above may only affect one limb

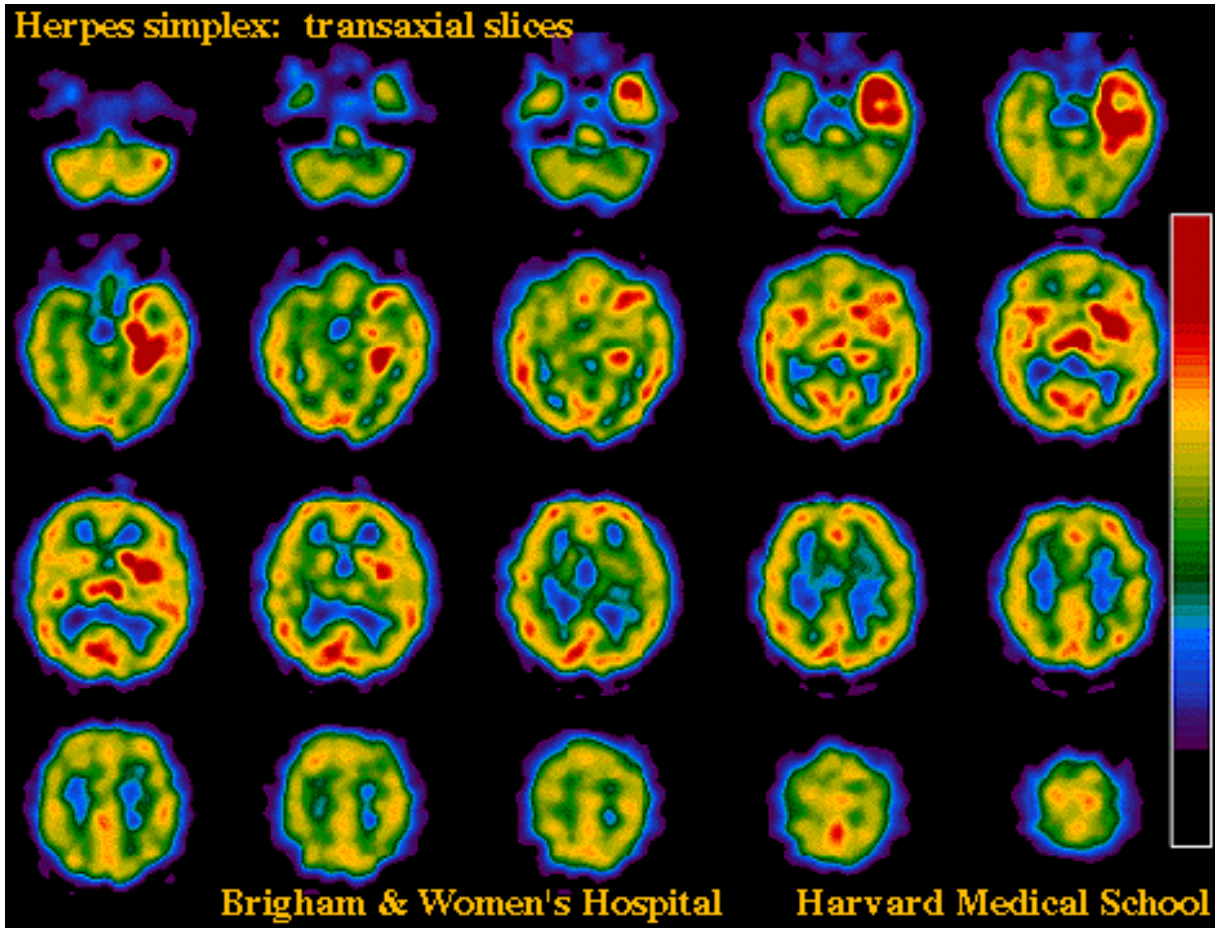
Diagnosis and treatment

- History
- Observation
- EEG for delta waves
- CT or MRI to exclude organic disease
- Treatment with anti-epileptic drugs
- Older drugs can affect cognitive function
- May not control severe fits

Role of Nuclear Medicine

- The role is limited
- May be used to find nidus of fit
- This may be used to direct surgery
- However inter-ictal scan can be normal
- So need to inject tracer during fit
- Therefore tends to be in patients with frequent fits and in whom a trigger can be identified

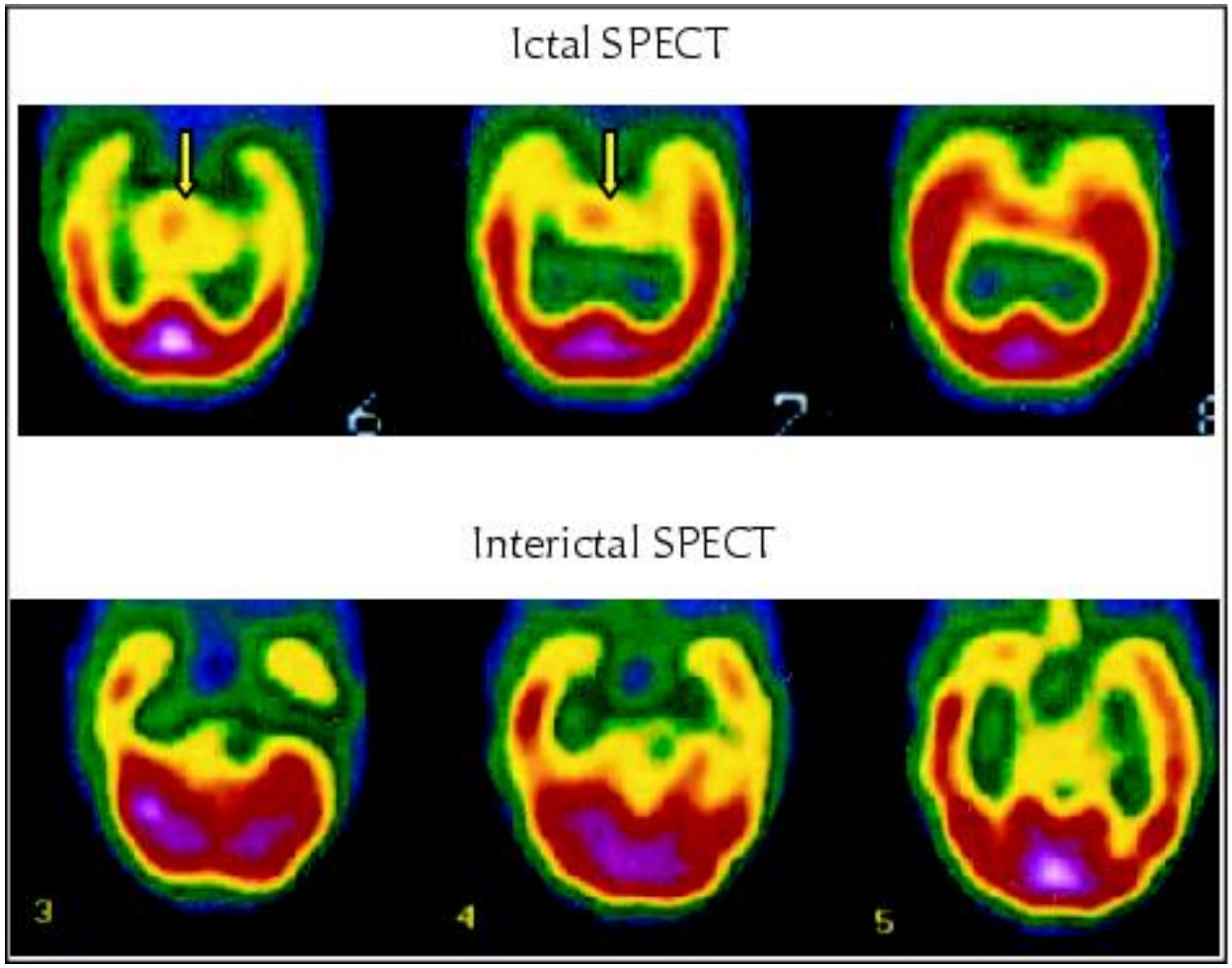
Tc-99m ECD SPECT imaging ictal showing increased perfusion of the left temporal lobe



SPECT in epilepsy

- 1600 papers published
- Not widely used
- Most used inter-ictal and ictal imaging
- Often used subtraction imaging
- Image fusion with MRI for localisation

Use of ictal and interictalimaging



Subtraction imaging

- Ideal method
- Give 350MBq Tc-99m HMPAO
- Image for 30minutes
- Keep patient still
- Induce fit (normally with visual stimulus)
- During fit inject 350MBq Tc-99m HMPAO
- Image for 15 minutes
- Subtract image 1 from image 2

Subtraction imaging

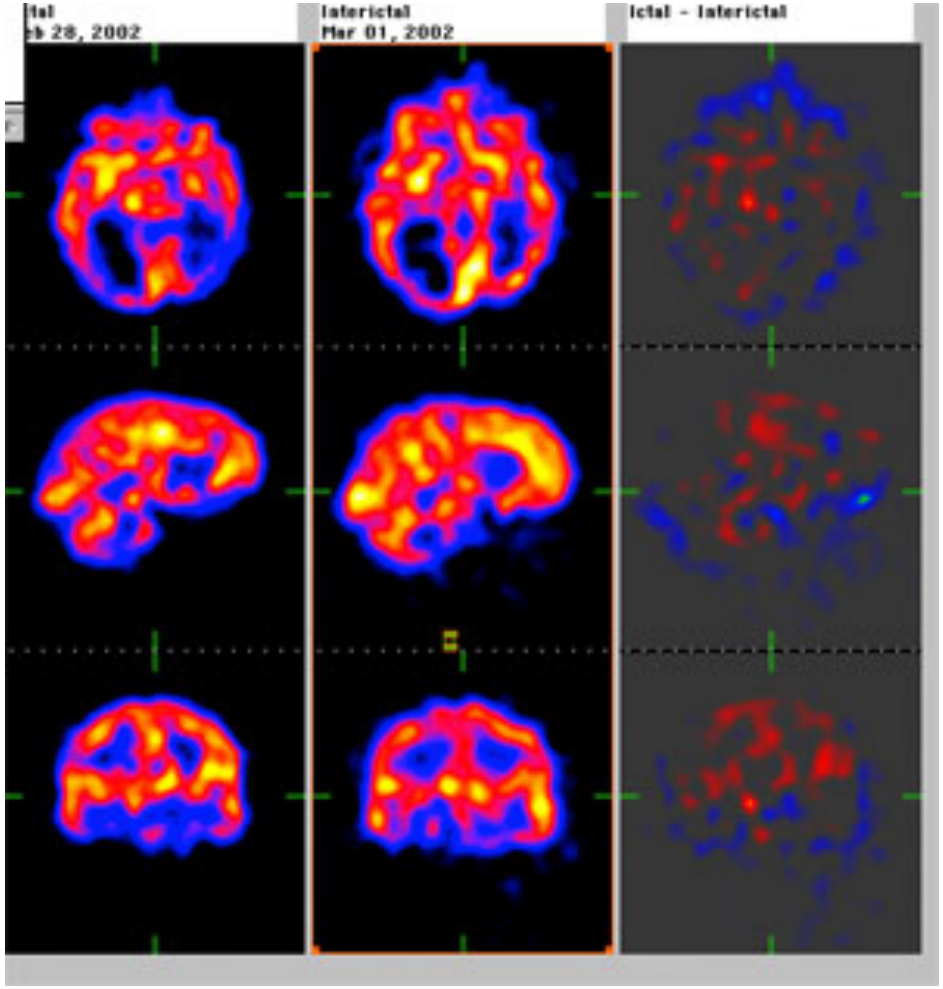
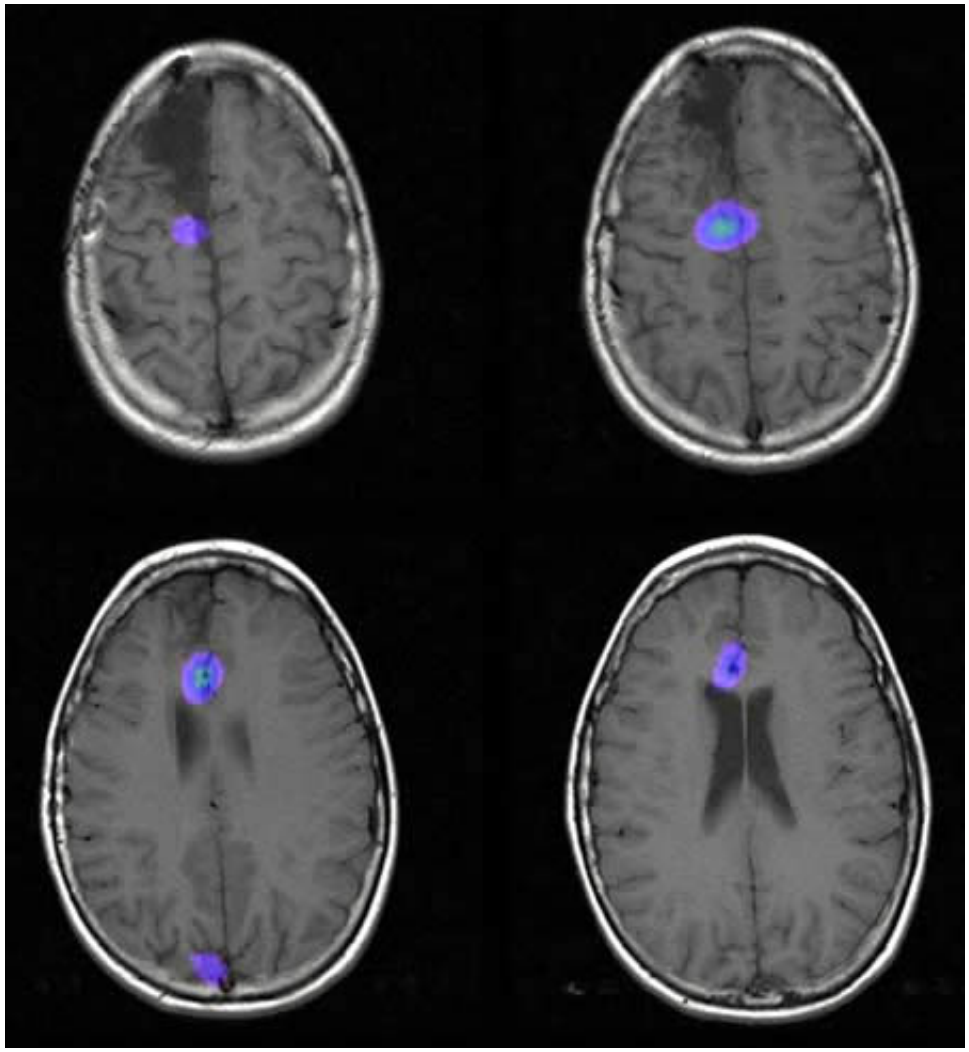


Image fusion



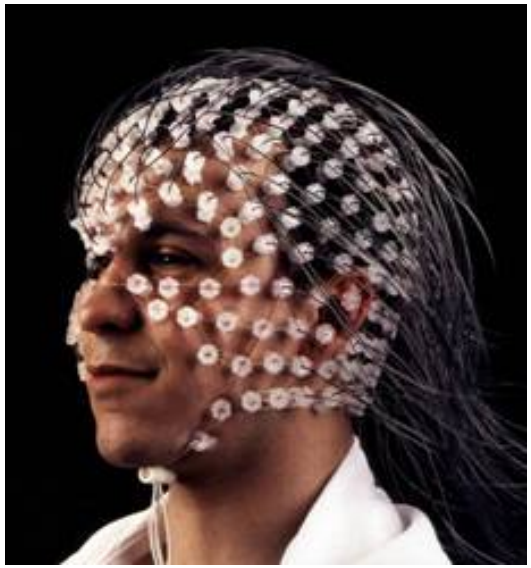
Results

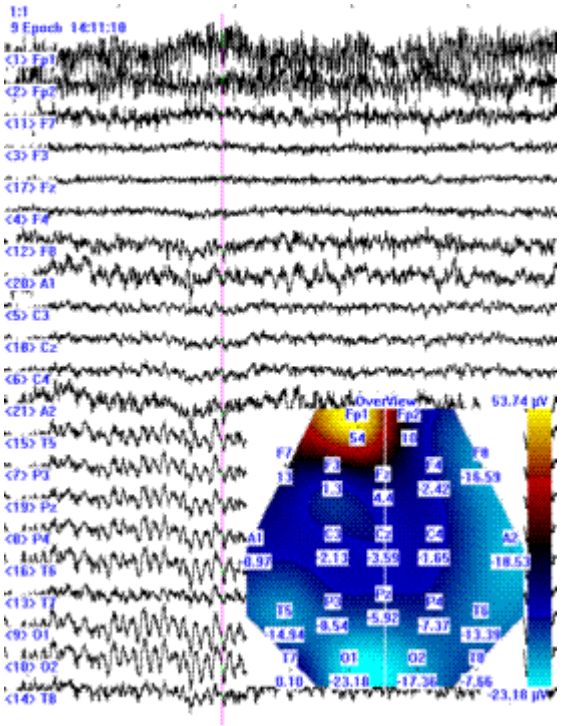
- Matsada et al Japan Ann Nuc Med 2009
  - Demonstrated that when Subtraction SPECT was used with MRI fusion 12x better localisation than not using this technique
- Goltan et al Semin Nuc Med 2008
  - Compared ictal and inter-ictal FDG PET and Tc-99m HMPAO
  - FDG response variable but Tc-99m HMPAO increase uptake at site of epilepsy in ictal scan
- Wichart-Ann Semin Nuc Med 2008
  - Used subtraction SPECT and MRI fusion of 9/17 patients with localisation of epilespy all cured by surgery

Why not more widely used

- Some concern on role of surgery
- New drugs based on GABA receptors better control
- Some patients resistant to idea of surgery
- Other imaging techniques such as EEG imaging

EEG imaging




1:1
9 Epoch 14:11:10
(1) Fp1
(2) Fp2
(11) F7
(3) F3
(17) Fz
(4) F4
(12) F8
(20) A1
(5) C3
(18) C2
(6) C4
(21) A2
(15) T5
(7) P3
(19) Pz
(8) P4
(16) T6
(13) T7
(9) O1
(10) O2
(14) T8
Overview
53.74 µV
-23.18 µV

SPECT and dementia

- Dementia
- Loss of cognitive function
- Loss of emotional stability
- Some patients additional mobility problems
- Causes
  - Alzheimer's
  - Pick's
  - Vascular
  - Lewy body
  - Parkinson plus inc MSA

Lewy body Parkinson plus

- Identified by loss of cognitive function
- If frontal lobe syndrome and movement disorders-Lewy body
- If movement disorder then cognitive function-Parkinson's plus
- Imaging with DAT for both
- However may also need MIBG for Parkinson's plus where MSA cardiac MIBG reduced

Diagnosis

- History
- Type of cognitive dysfunction eg behaviour or memory
- Smooth deteriation or “step wise”
- Family history (HD)
- Other risk factors
  - Al ingestion
  - Brain surgery or even brain surgeon-NvCJD

Lab tests

- BP
- Vascular studies to carotid arteries
- Blood sugar
- TFTs
- Plasma Calcium
- CT or MRI of brain (to look for atrophy, infarcts or tumour)

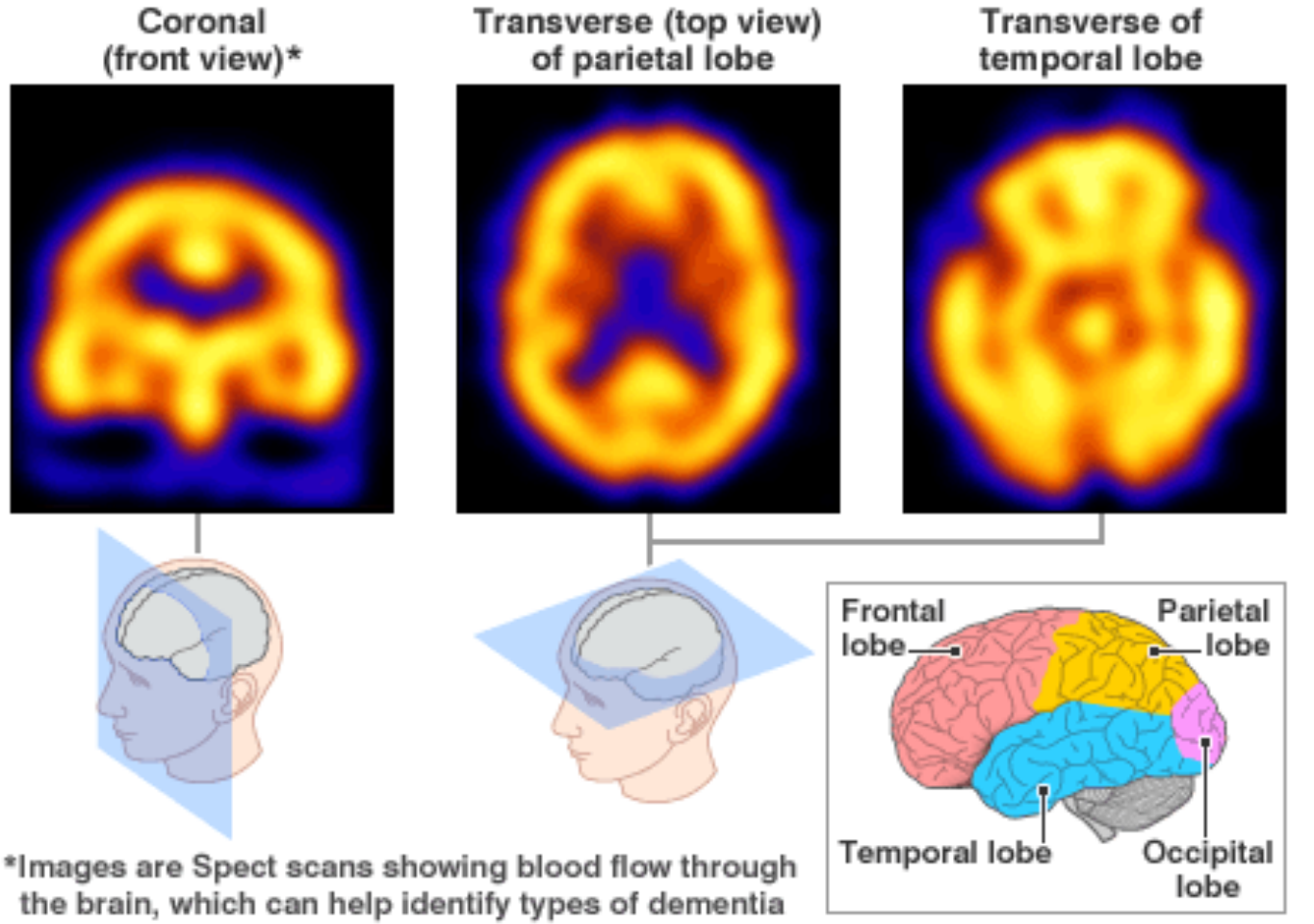
NM

- SPECT
  - I-123 IMP
  - Tc-99m HMPAO
  - Tc-99m ECD
  - (I-123 Ioflupane)
- PET
  - F-18 FDG
  - F-18 amyloid imaging
  - N-13 Ammonia

Tc-99m HMPAO and ECD

- HMPAO
  - Advantage uptake proportional to rCBF
  - Unless stabalised must be used within 30 minutes of manufacture
  - Start SPECT at 5 mins p.i.
- ECD
  - Uptake high at low flow rates and low at high flow rates
  - Uptake in medical temporal lobe reduced
  - Start SPECT at 30 mins p.i.

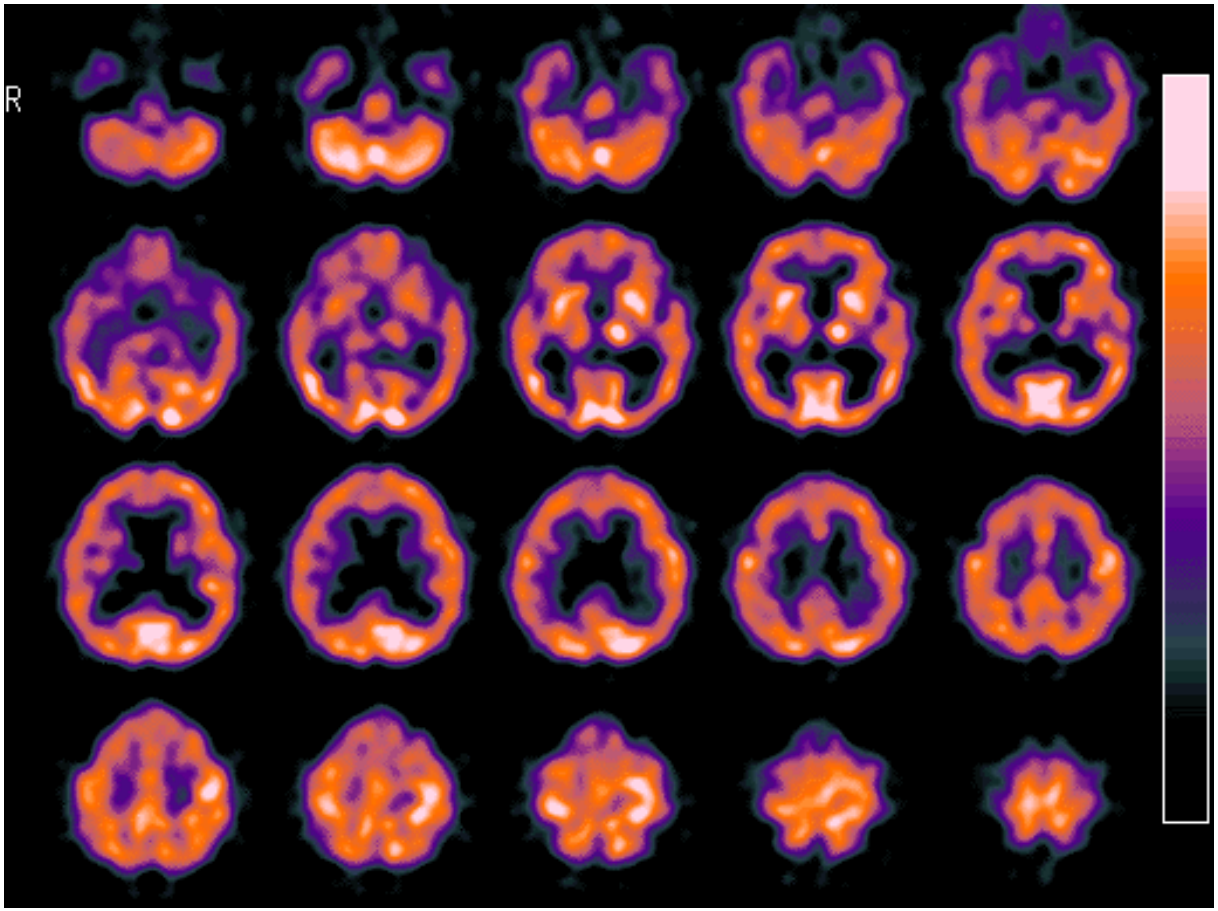
What do you see



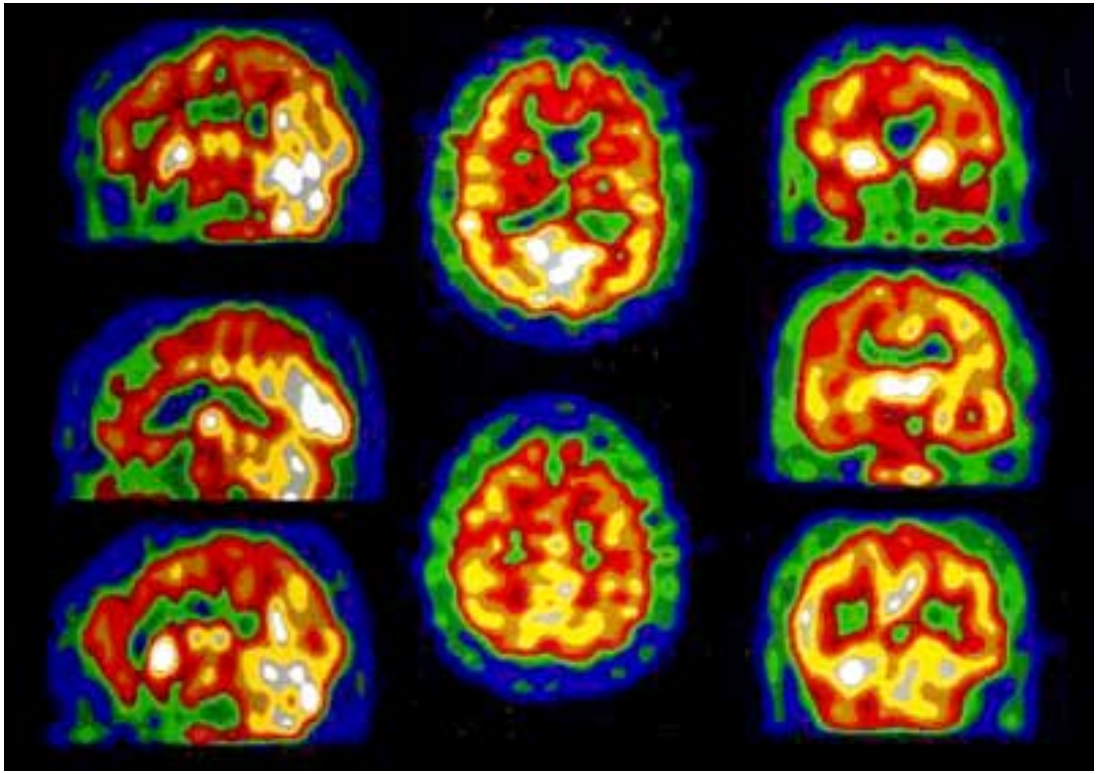
*Images are Spect scans showing blood flow through the brain, which can help identify types of dementia

Source: Professor John O'Brien & Alzheimer's Society

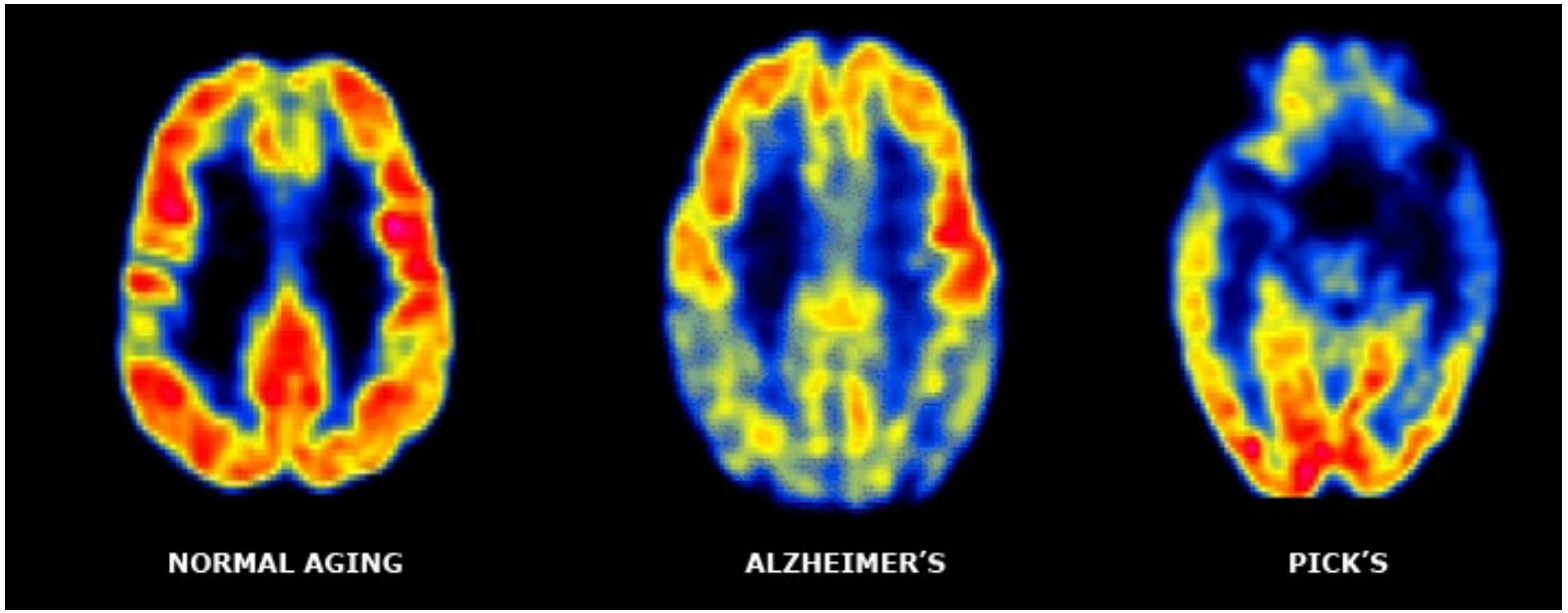
Early DAT



Pick's (fronto-temporal dementia)

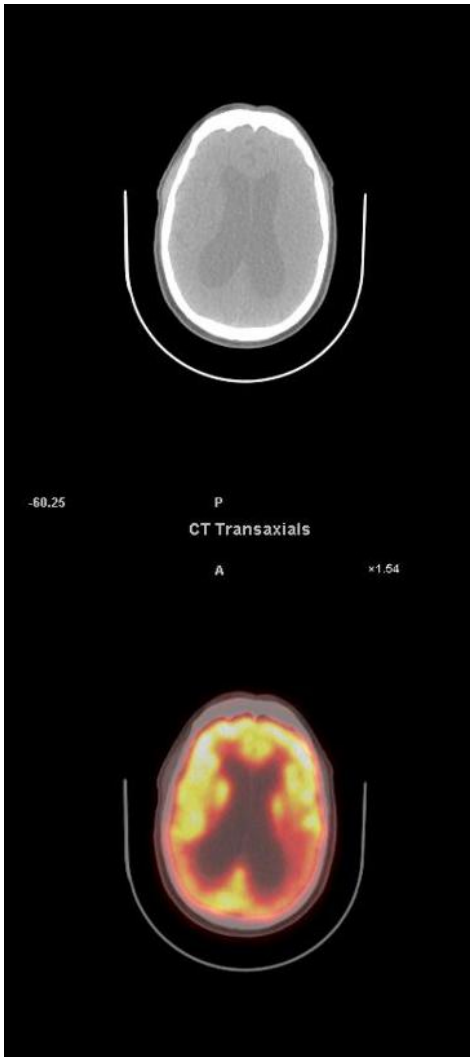


DAT vs Pick's

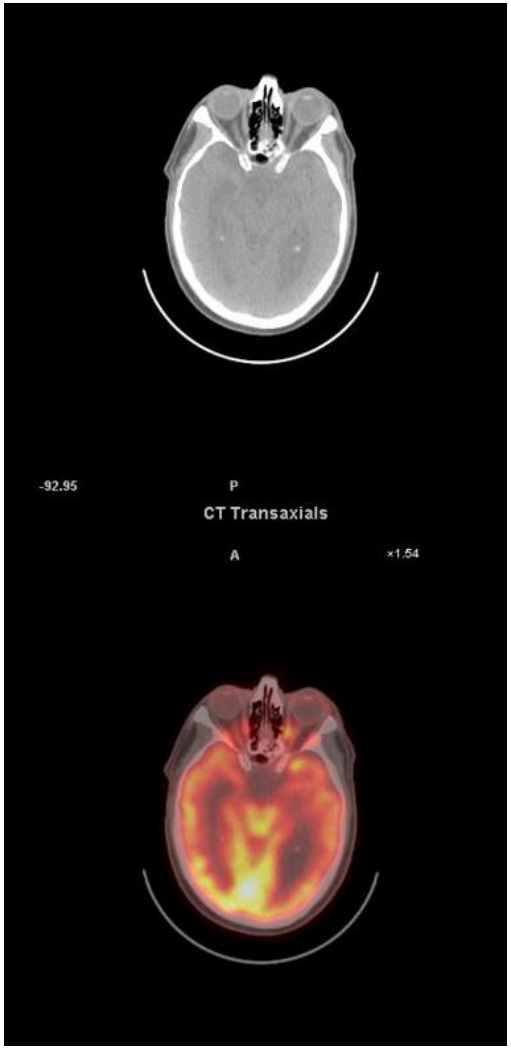


Patterns in AD

Parietal type



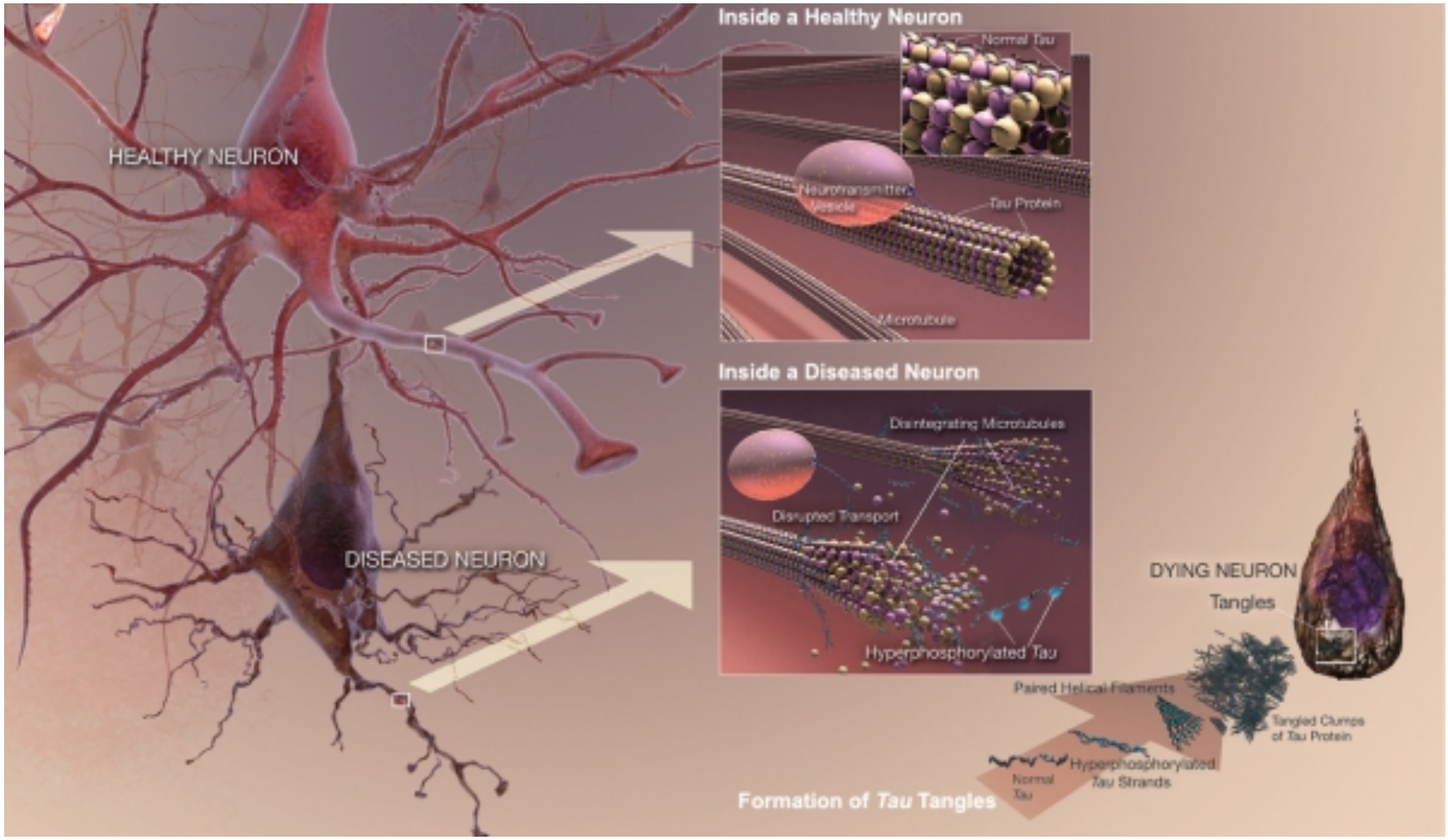
temporal type



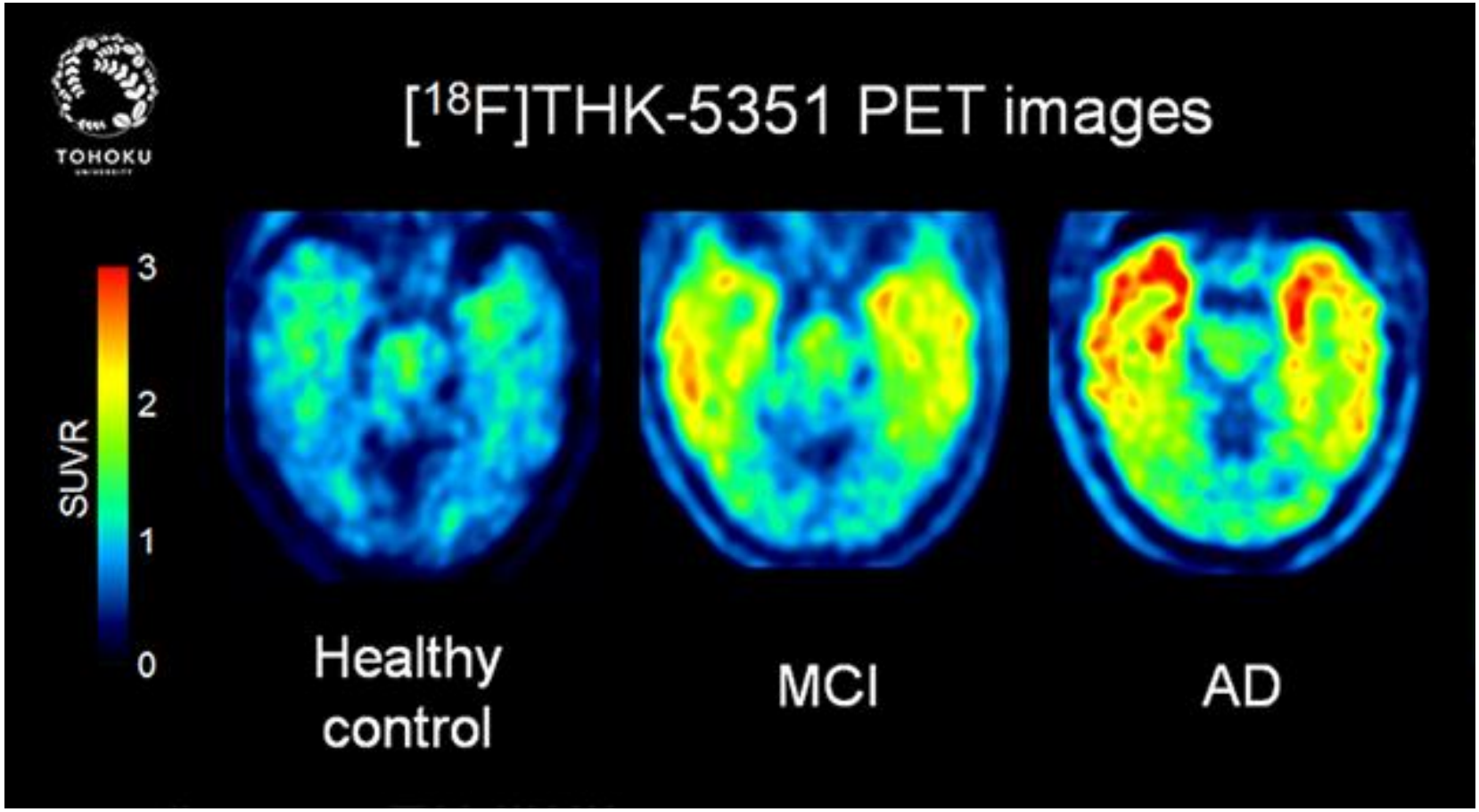
Mechanism of AD

- This is not clearly understood but knowledge beginning to increase
- First sign is presence of tau protein
- If tau persists then triggers laying down of beta amyloid sheets
- Beta amyloid results in neuro-fibrillary tangles-first irreversible step
- Then brain cell death

Tau a marker of damage



Tau imaging Tohoku, Japan



When do we see Tau

- Tau uptake in grey matter is non-specific
- Can be related to any damage
- Seen in those post brain trauma but can clear in 12-24 months
- Seen in young schzophrenics
- Seen in early Alzheimers

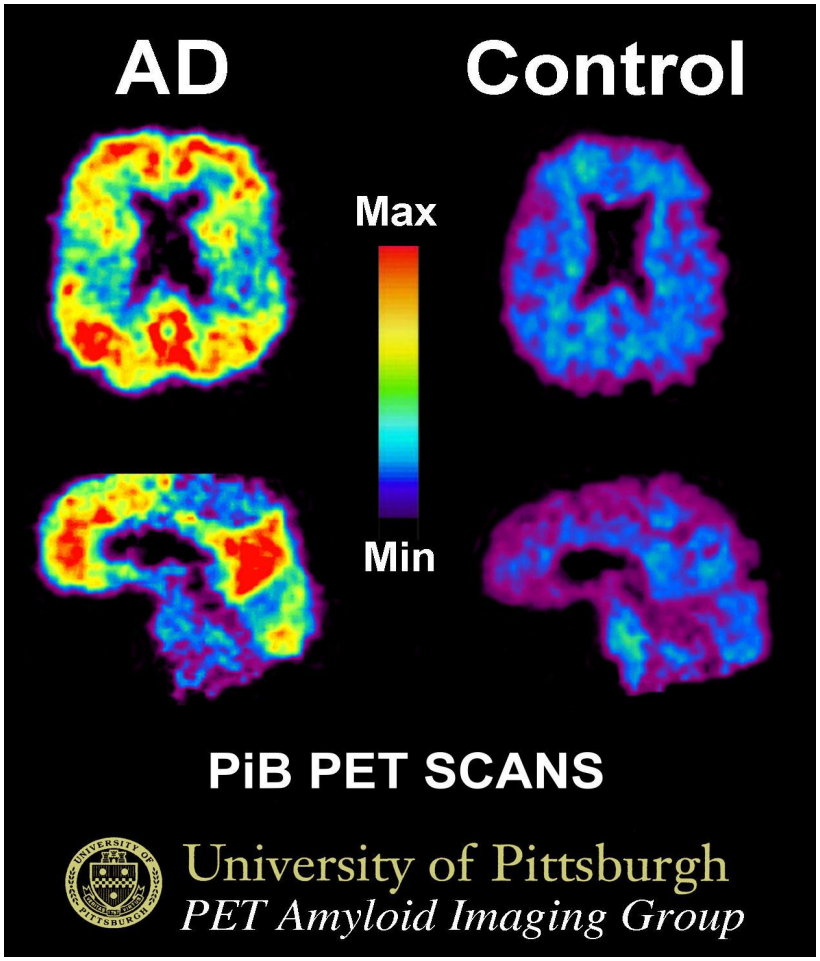
Beta amyloid imaging

- The next step is imaging beta amyloid
- However, we have beta-amyloid by 70
- So imaging restricted to those under 65 with early memory loss
- Negative study uptake in white matter, positive study uptake in grey matter of at least two lobes

Agents used

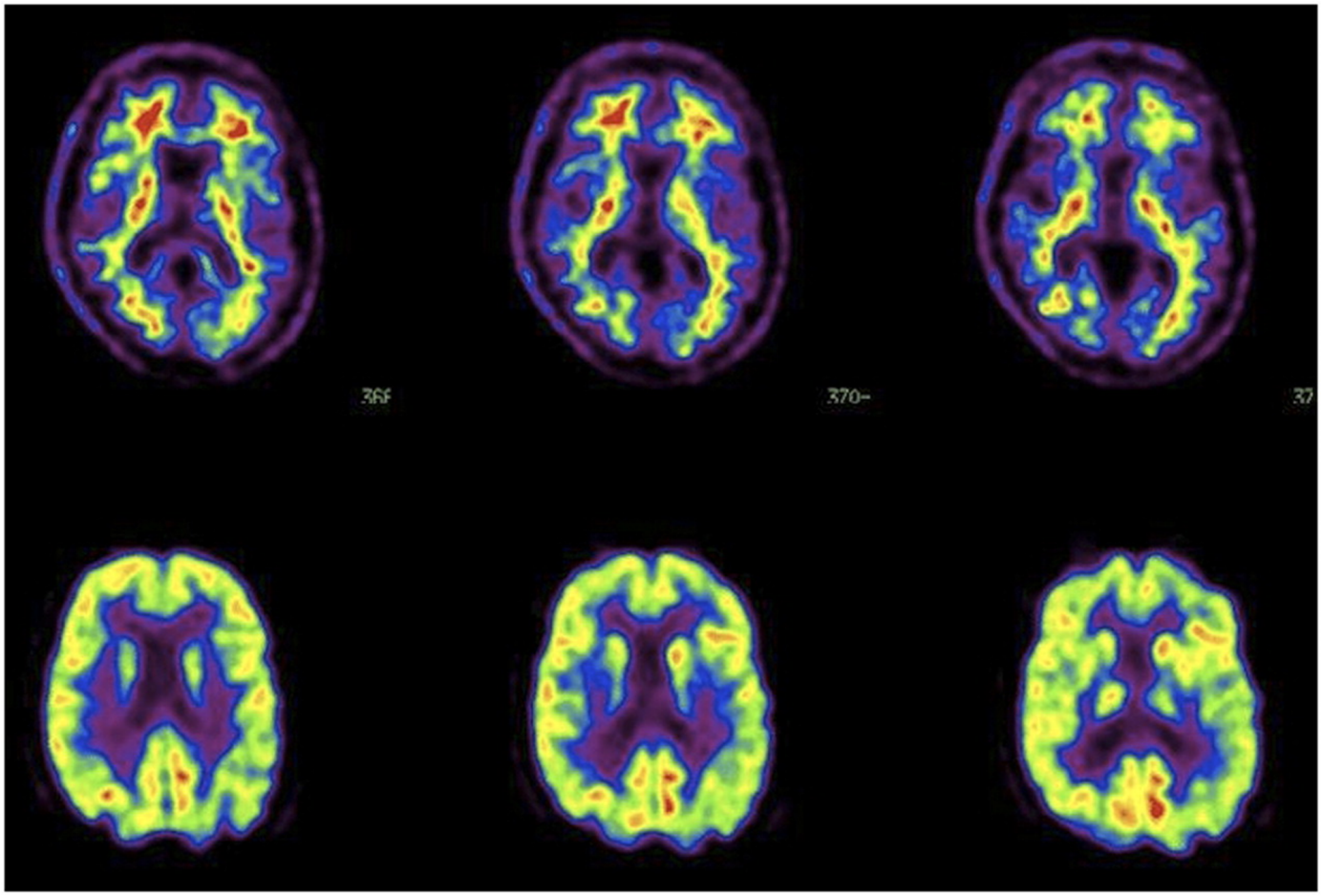
- C-11 PiB the Pittsburgh agent not widely used because of C-11 label
- F-18 Fluorbetapir the first commercial agent made by Lilly
- F-18 Fluorbetapen which is distributed through Siemens
- Sensitivity >90%, specificity 85% determined by imaging vs PM
- If cerebral atrophy does not work

C-11 PiB

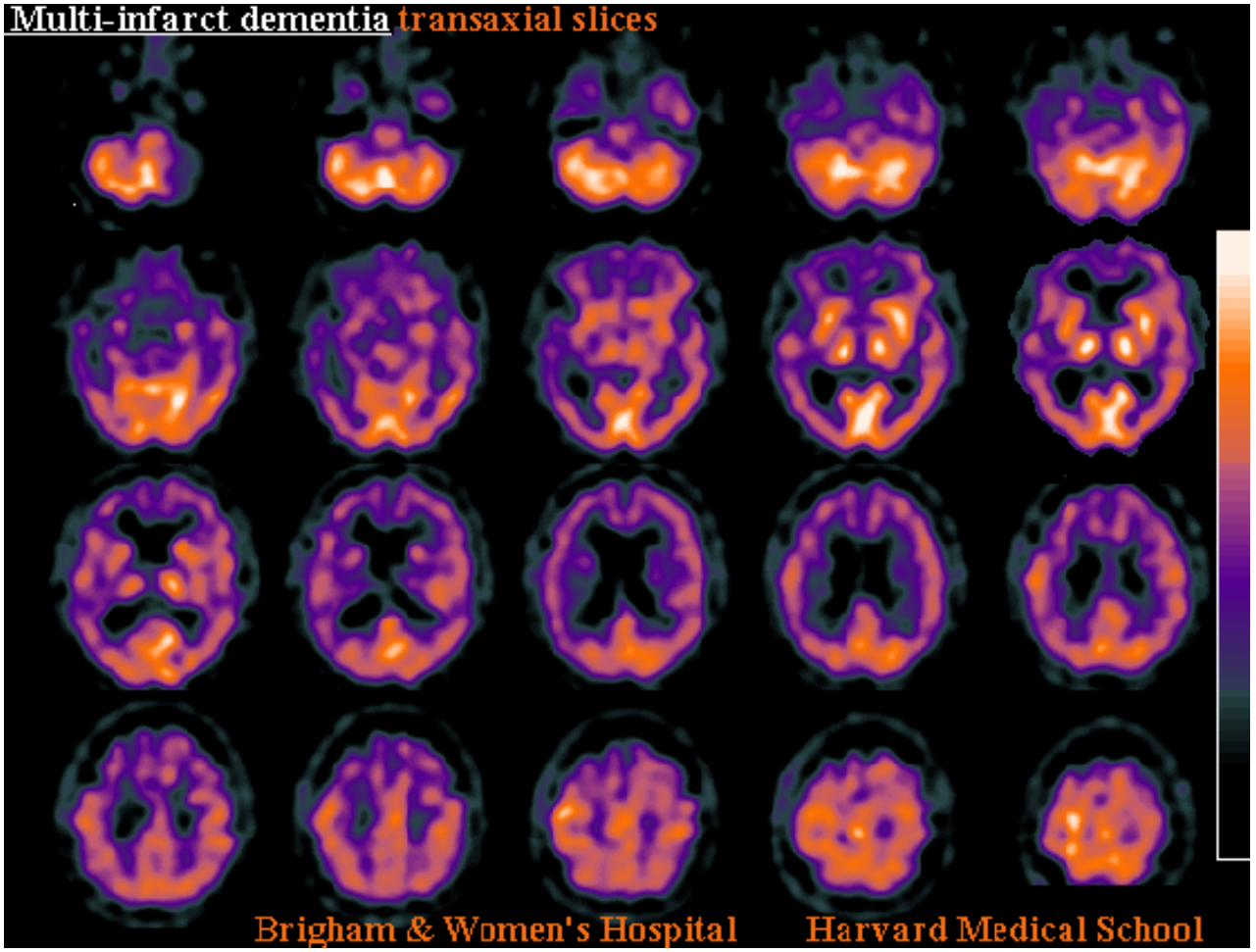

AD
Control
Max
Min
PiB PET SCANS
University of Pittsburgh
PET Amyloid Imaging Group

F-18 Flurobetapir

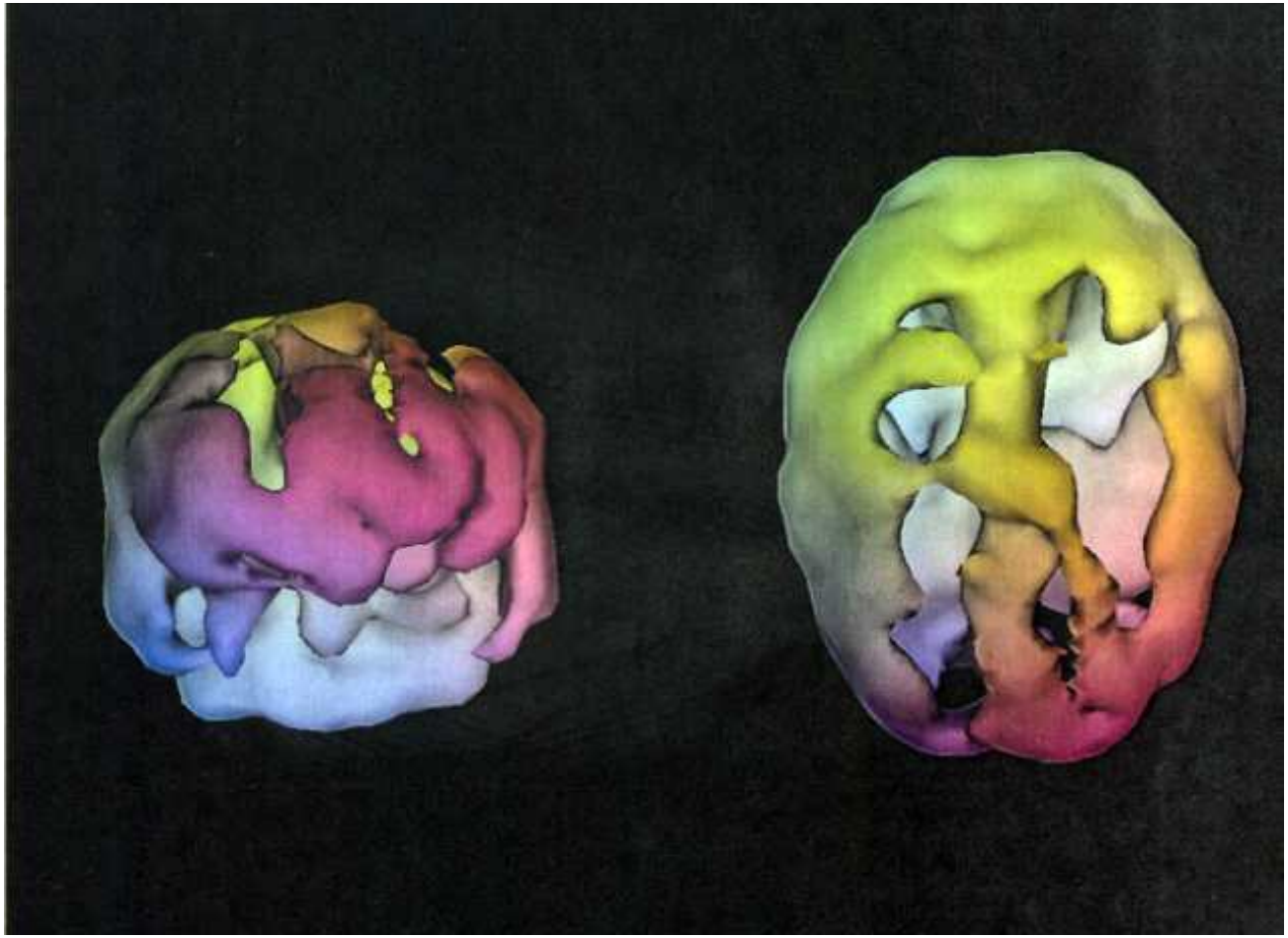
Note in negative study there is white matter uptake



Vascular dementia



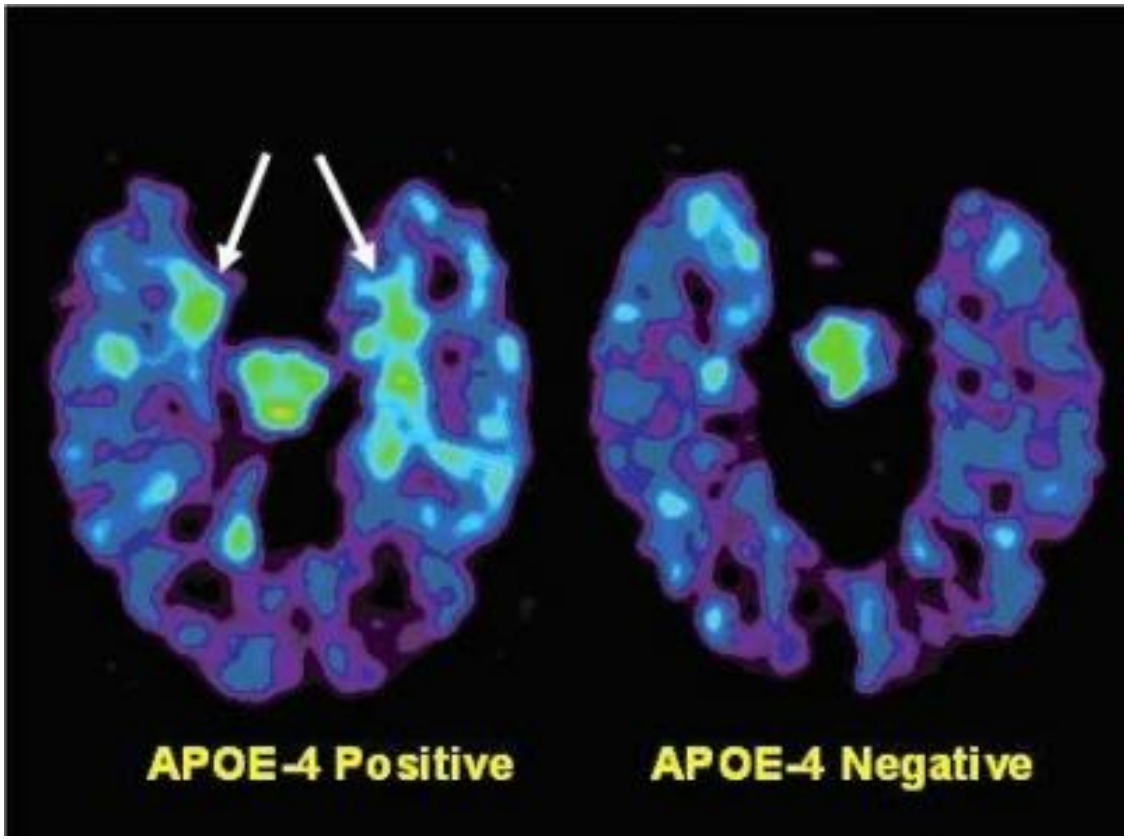
Vascular dementia



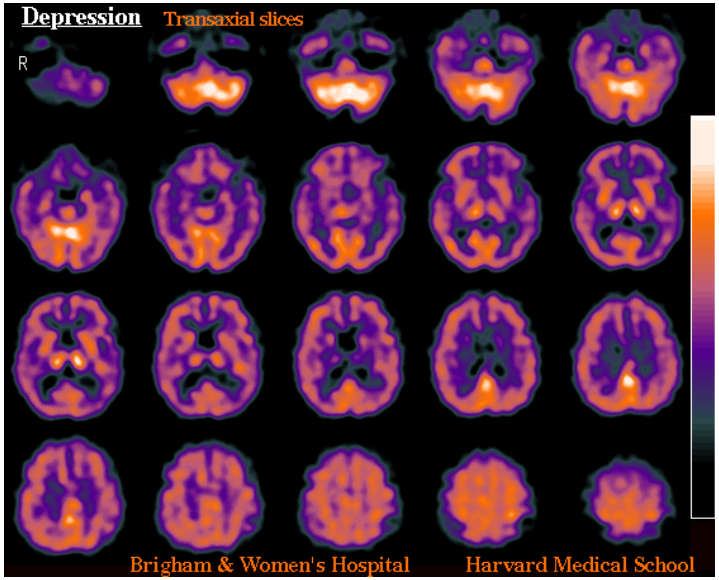
Identifying pathology directly

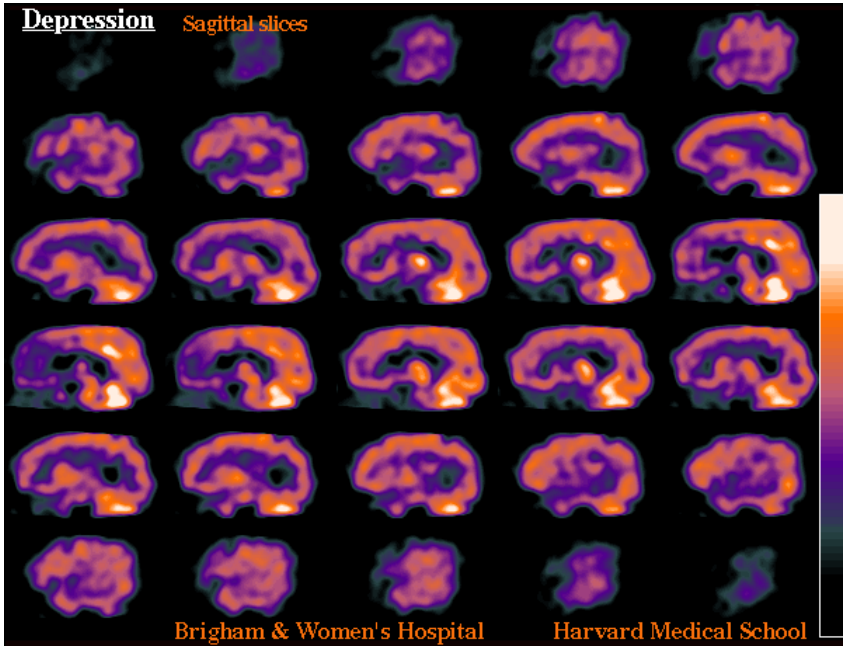
- Need ability to see directly at process causing DAT
- Related to deposition of neurotangular bundles
- These are plaques of cerebral amyloid (different from systemic amyloid)
- Coded for by the APOE-4 gene
- Imaged for the Pittsburg agent - F-18 FDDPD

F-18 FDDPD in memory loss



Excluding depression

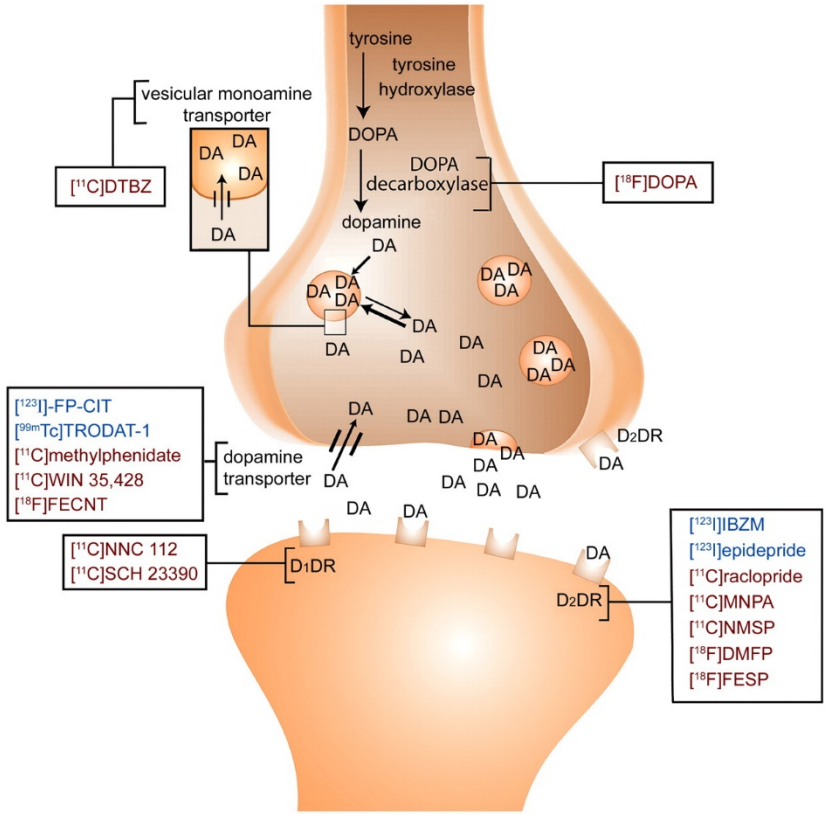




Looking at more complex dementias

- Lewy body dementia
- Cognitive loss with rigidity
- Complex disease
- May see reduced uptake in basal ganglia
- However have reduced uptake of I-123 ioflupane like Parkinsons
- May be confused with multi-system atrophy where you get dementia + Parkinsons + Sympathetic denervation

Imaging Parkinson's syndromes



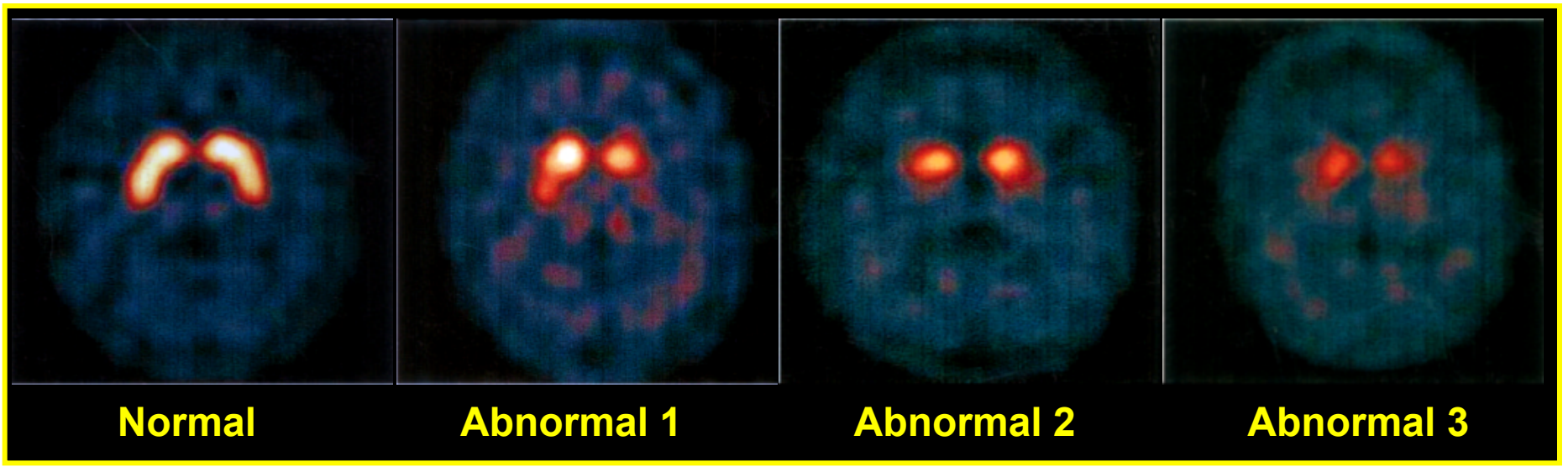
- Different methods evolved to look at basal ganglia function
- The only lisenced form is I-123 Iopflupane
- Pre-synaptic uptake so not affected by most anti-Parkinson's drugs

The Parkinson syndromes

- All involve destruction of the basal ganglia
- Parkinson's disease including that due to trauma
- Lewey body dementia
- Progressive supranuclei palsy
- Multi-system atrophy
- Last 3 sometimes called Parkinsons Plus

Diagnosis of Parkinson's disease

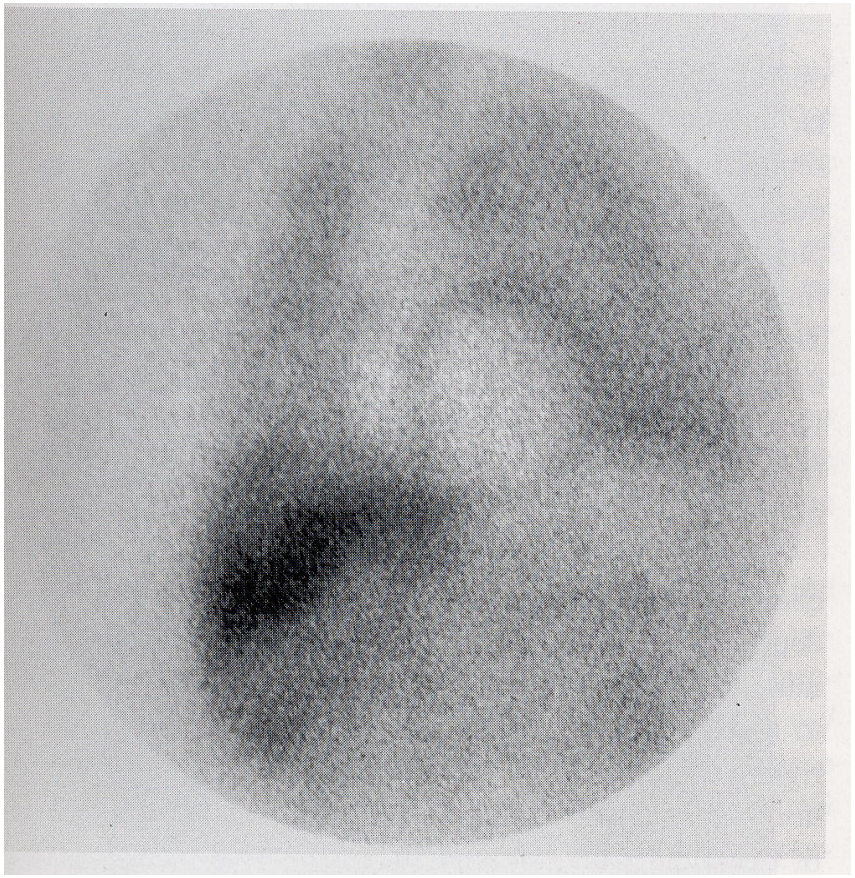
- Imaging with I-123 DAT scan
- rating according to the classification reported by Catafau et al.*



*Catafau A.M. et al 2004, 19:1175-82. Mov. Disord.

I-123 MIBG in MSA

- Method is to inject I-123 MIBG
- Image at 1& 4 hours
- Persistent lung uptake suggests denervation of the heart=MSA if not diabetic



Summary

- Nuclear medicine techniques provide subtle and accurate answers to the cause of cognitive impairment maybe we do do not do many tests because we do not want to know the answer?