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 can 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 unpleasant
- 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 interictal imaging
Subtraction imaging

- **Ideal method**
- **Give 350MBq Tc-99m HMPAO**
- **Image for 30 minutes**
- **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 epilepsy 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
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 deterioration 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 stabilized 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

[18F]THK-5351 PET images

Healthy control | MCI | AD
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 schizophrenics
- 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
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 FDDDPD 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 licensed 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.*

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 not want to know the answer?