Structure of talk
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• Part (i) – The relationship of Parkinson’s disease and dementia
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• Part (i) – The relationship of Parkinson’s disease and dementia

• Part (ii) - Dopamine imaging in drug-induced movement disorder
Structure of talk

• Part (i) – The relationship of Parkinson’s disease and dementia

• Part (ii) - Dopamine imaging in drug-induced movement disorder

• Part (iii) - Dopamine imaging in dementia with Lewy bodies
Part (i): The relationship of Parkinson’s disease and dementia
Lewy Body Disorders
Lewy Body Disorders

• Idiopathic Parkinson’s disease
Lewy Body Disorders

• Idiopathic Parkinson’s disease
  – Lewy body dementia (< 1 year)
  – Parkinson’s dementia disease (> 1 year)
Lewy Body Disorders

• Idiopathic Parkinson’s disease
  – Lewy body dementia (< 1 year)
  – Parkinson’s dementia disease (> 1 year)

• Lewy body dementia
  – Following parkinsonian symptoms
  – Cognitive presentation
Parkinson’s disease and Lewy Body dementia

- 40~80% of PD patients develop clinical dementia
- Others may have cognitive problems without meeting clinical criteria for dementia
- ~75% of DLB patients will develop Parkinsonian features

McKeith IG, Lancet Neurology 2004; 3: 19-28
$^{123}$I-FP-CIT
Lewy Body Disorders
(DaTSCAN®)
DaTSCAN

• D – Dopamine

• a – active

• T – Transporter

NOT Dementia of the Alzheimer’s Type
DaTSCAN logistics

• Intravenous injection of 185mBq of $^{123}$I-FP-CIT

• 3 hour delay before imaging

• Open scanner – 30 minutes supine, ‘not like MRI’

• Medication
Normal DaTSCAN
Caudate

Putamen

Globus pallidus
$^{123}$I-FP-CIT (DaTSCAN)
$^{18}$F-DOPA

$^{123}$I-FP-CIT (DaTSCAN)
$^{18}$F-DOPA

$^{123}$I-FP-CIT (DaTSCAN)

$^{123}$IBZM
Normal DaTscan
Caudate nuclei
Abnormal DaTscan
FC (49) ♀

- Right hand tremor
- Action and ? Rest
- ? Essential tremor  ?? Parkinson’s disease
MB 55♀

- Reduced movement right hand
- Right sided tremor ?rest
- ? PD
CB (54) ♀

- Bradykinesia and clumsy right arm for two years
- Poor response to dopamine agonist
- ?? Parkinson’s Disease
Note – clinical symptoms on right only
Part (ii)
Dopamine Imaging in Suspected Drug Induced Movement Disorder
A Potential Role of the DaTSCAN in Suspected Drug Induced Movement Disorder
Drug induced Parkinsonism

- Anti-psychotics may cause parkinsonian symptoms due to D2 receptor blockade
Drug induced Parkinsonism

- Anti-psychotics may cause parkinsonian symptoms due to D2 receptor blockade

- Clinical question: Are the symptoms drug induced (due to D2 blockade) or reflect true dopamine deficient Parkinson’s disease?
The $^{18}$F-DOPA or DaTSCAN provides a measure of the pre-synaptic dopamine terminals.
Anti-psychotics blockade some of the D2 receptors

The $^{18}$F-DOPA or DaTSCAN provides a measure of the presynaptic dopamine terminals
JB (70) ♀

- Bradykinesia – upper limbs – 1 yr
- Risperidone (an anti-psychotic) stopped 8 months previously
- ? PD  ? Drug induced movement disorder
AW (70) ♂

- Extrapyramidal rigidity
- On prochlorperazine (anti-psychotic)
- Right upper limb bradykinesia and tremor
- ? Drug induced movement disorder or underlying PD
Drug induced movement disorder or underlying Parkinson’s disease?

In drug induced movement disorder medications that blockade the D2 receptors, which are largely located on the POST-synaptic membrane, will give a NORMAL DaTSCAN.
Frequency of drug induced movement disorder

- Aberdeen prevalence study - 18%
  - Neurologists/GPs
  
  Mutch WJ et al., BMJ 1986; 292: 534-536
Frequency of drug induced movement disorder

- Aberdeen prevalence study - 18%
  - Neurologists/GPs
    Mutch WJ et al., BMJ 1986; 292: 534-536

- Geriatric clinic, Edinburgh - 51%
  - Similar symptoms to IPD
  - Only 2/3 resolved within 9 months
    Stephen PJ et al., Lancet 1984; ii: 1082-1083
D$_2$ receptor damage can last up to 18/12
Part (iii): Dopamine Imaging in Cognitive Disorders
Types of dementia

- Alzheimer’s - 60%
- Vascular - 20%
- Dementia of the Lewy body type (DLB) - 20%
- Fronto-temporal - 1%
Features of Lewy Body dementia

- Many similarities to Alzheimer’s plus core features
  - Visual hallucinations more common
  - Fluctuating cognitive state
  - Features of Parkinsonism
Features of Lewy Body dementia

• Many similarities to Alzheimer’s plus core features
  • Visual hallucinations more common
  • Fluctuating cognitive state
  • Features of Parkinsonism

Two core features – probable DLB

McKeith IG et al Neurology 1996; 47: 1113-1124
Normal DaTscan: Control or Alzheimer’s disease
Abnormal DaTscan: DLB (PD/PDD)
CH (78) ♂

- 3 year history – gradual features
- Disorientated, language and counting difficulties
- Visual hallucinations
  - Shouting at cats and dogs in the greenhouse
  - Someone dressing in wife’s clothes, but not the wife

?Dementia with Lewy Bodies  ??Alzheimer’s
Note – no Parkinsonian features
PP (78) ♂

- Visual hallucinations
- Cognitive impairment - memory, language
- MMSE 24/30
- Stooped posture
- Equivocal Parkinsonism

?Dementia with Lewy Bodies  ?Alzheimer’s disease
Clinical importance of differential diagnosis of DLB vs AD
Clinical importance of differential diagnosis of DLB vs AD

• Differential response to cholinergic therapy
Clinical importance of differential diagnosis of DLB vs AD

• Differential response to cholinergic therapy

• High incidence of adverse side effects to antipsychotics/neuroleptics in DLB patients
Clinical importance of differential diagnosis of DLB vs AD

• Differential response to cholinergic therapy

• High incidence of adverse side effects to antipsychotics/neuroleptics in DLB patients

• Approx 80% of patients may experience a parkinsonian crisis, this will be life-threatening in one-half.

McKeith IG et al, BMJ 1992; 305: 673-678
$^{18}$F-DOPA

$^{123}$I-FP-CIT (DaTSCAN)
Lewy bodies destroy the pre-synaptic terminals
Anti-psychotic medication blockades the post-synaptic receptors.

Lewy bodies destroy the pre-synaptic terminals.
Neurology versus psychiatry – the therapeutic dilemma
Neurology versus psychiatry – the therapeutic dilemma

Neurologist aims to preserve motor function
Neurology versus psychiatry – the therapeutic dilemma

Neurologist aims to preserve motor function

Psychiatrist aims to prevent psychosis
Therapeutic implications

• Typical and atypical anti-psychotics (neuroleptics) are indicated in AD, FTD, VaD

• In DLB acetylcholinesterase inhibitors are the first-line treatment for psychotic symptoms
Critical clinical studies with $^{123}$I-FP-CIT

- O’Brien JT 2004 - IPD, PDD, DLB, and AD,
- European multi-centre study – DLB, AD, VaD
- Solitary post-mortem study
Results

• For DLB vs AD:
  – Sensitivity for DLB - 78%  (78%)
  – Specificity for non-DLB - 94%  (90%)

O’Brien JT, Arch Neurol 2004; 61: 919-925
McKeith I, Lancet Neurol 2007; 6: 305-313
Prospective post-mortem study

- Initial clinical diagnosis based on established criteria
- $^{123}$I-FP-CIT (DaTSCAN)
- Regular clinical follow-up
- Post-mortem (40% prevalence of DLB)

Walker Z et al. JNNP 2002
Costa DC et al Mov Disord 2003
Walker Z et al. Austria. October 2004
Walker Z et al JNNP 2007
Clinical and imaging accuracy with autopsy gold-standard - prospective

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Conclusions from $^{123}$I-FP-CIT trials

- Concordance of ~80% between image findings and clinical criteria.

- Concordance of ~95% between image findings and histopathology.
“.........highlights shortcomings in the accuracy of the clinical diagnostic criteria”

Walker Z et al, 2002
Quotes by authors

“…….highlights shortcomings in the accuracy of the clinical diagnostic criteria”

“The incorporation of the results of functional imaging of the striatum into diagnostic criteria would greatly improve the diagnosis of DLB during life”

Walker Z et al, 2002
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Two core features – probable DLB

McKeith IG et al Neurology 1996; 47: 1113-1124
Revised clinical criteria for DLB - 2005

• ONE CORE + ONE SUGGESTIVE = PROBABLE DLB
Revised clinical criteria for DLB - 2005

• ONE CORE + ONE SUGGESTIVE
  = PROBABLE DLB

• Suggestive features
  • Abnormal $^{123}$I-FP-CIT or $^{18}$F-DOPA
  • Severe neuroleptic sensitivity
  • REM sleep behavioural disorder

DW (77) ♂

- **Clinical details**
  Mild cognitive impairment, executive dysfunction, occasional confusional episodes (?TIA’s)

- **Differential clinical diagnosis**
  ? VaD, ? DLB, ?? AD
• Post-mortem showed moderately severe Lewy bodies, grade II Braak, and mild vascular brain disease.

• A significant number of dementia cases exhibit mixed pathologies.

• The marked fluctuations of DLB can mimic vascular events and delirium.
The potential effect of a DaTSCAN on patient management in dementia

- Anti-psychotic sensitivity
- Cholinergic response
- Dopaminergic response
- Patient/carer awareness
- Confident management

DLB patient: hallucinating with Parkinsonian features

AD patient: hallucinating with ‘extra-pyramidal Features’
Conclusions: imaging in DLB/PD
Conclusions: imaging in DLB

$^{123}$I-FP-CIT or $^{18}$F-DOPA is normal in drug induced movement disorder
Conclusions: imaging in DLB

- $^{123}$I-FP-CIT or $^{18}$F-DOPA is normal in drug induced movement disorder

- $^{123}$I-FP-CIT or $^{18}$F-DOPA ~ 90-95% accuracy in suspected DLB
Conclusions: imaging in DLB

- $^{123}$I-FP-CIT or $^{18}$F-DOPA is normal in drug induced movement disorder

- $^{123}$I-FP-CIT or $^{18}$F-DOPA ~ 90-95% accuracy in suspected DLB

- NICE recommends $^{123}$I-FP-CIT or $^{18}$F-DOPA in DLB
The End