Mental health disorders in Parkinson’s disease

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Birmingham Movement Disorders Course 2016
## The problems

| Early        | • Anxiety  
|              | • Depression  
|              | • Apathy  
| Middle       | • Psychosis  
|              | • Impulsive behaviours  
|              | • DAWS  
| Late         | • Mild cognitive impairment  
|              | • Dementia  

Anxiety and depression

• Very common in PD
• May precede the motor symptoms by several years
• First depressive illness in midlife increases odds ratio for PD by 3 fold
Screening for anxiety and depression

• Ask and look
Screening for anxiety and depression

• Ask and look
• “Do you feel cheerful and relaxed?”
Screening for anxiety and depression

• Ask and look
• “Do you feel cheerful and relaxed?”
• Pay attention to reaction of spouse
Screening for anxiety and depression

• With anxiety, ask about specific situations and times when anxiety occurs

• With depression, ask about mood and anhedonia
Treatment of anxiety and depression

• Many studies showing benefit of antidepressants and CBT for depression

• Fewer studies in anxiety, some evidence for antidepressants and CBT, probably not pregabalin
## Depression treatment trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Number</th>
<th>Duration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devos, 2008</td>
<td>48</td>
<td>4</td>
<td>Desimipramine &gt; placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Citalopram = placebo</td>
</tr>
<tr>
<td>Menza, 2009</td>
<td>52</td>
<td>8</td>
<td>Nortriptyline &gt; placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Paroxetine = placebo</td>
</tr>
<tr>
<td>Richard, 2012</td>
<td>115</td>
<td>12</td>
<td>Paroxetine &gt; placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Venlafaxine &gt; placebo</td>
</tr>
<tr>
<td>Dobkin, 2011</td>
<td>80</td>
<td>10</td>
<td>CBT &gt; monitoring</td>
</tr>
</tbody>
</table>
SAD - PD

The graph shows the mean change in HAM-D scores for three groups: Placebo, Paroxetine, and Venlafaxine. The x-axis represents the week, and the y-axis represents the mean change in HAM-D scores. The Placebo group shows a gradual decrease in scores, while the Paroxetine and Venlafaxine groups show a more pronounced and rapid decrease in scores, with Venlafaxine having the highest reduction in scores.
CBT for depression in PD
Apathy

• Again may be prodromal
• Often associated with depression or dementia, but may occur without either (perhaps 20% of patients)
• Associated with impairments in frontal-executive function
• Perhaps reflects reduced frontal dopamine
• Hard to treat
Apathy

- Regular routine of activities
- Cheerful spouse
- One small RCT suggests rivastigmine is helpful
- Brief/small studies suggesting potential role for dopaminergic treatments, noradrenergic antidepressants and amantadine
- May be made worse by STN DBS
Two main problems with too much dopamine

• Psychosis

• Impulse control disorders

• Dopamine agonist withdrawal syndrome (DAWS)
Psychosis

• Mack et al, 2011
  – N = 250 PD community clinics
  – 26% any psychotic symptom
  – ½ mild, associated with depression
  – ½ significant delusions or hallucinations
Visual hallucinations
Hallucinations

• Can happen to any patient with excessive treatment
Hallucinations

• Can happen to any patient with excessive treatment
• Much more likely in older/cognitively-impaired
Hallucinations

• Can happen to any patient with excessive treatment
• Much more likely in older/cognitively-impaired
• More likely with depression, visual impairment or intercurrent illness
Hallucinations

- Can happen to any patient with excessive treatment
- Much more likely in older/cognitively-impaired
- More likely with depression, visual impairment or intercurrent illness
- May be associated illusions of presence, auditory or sensory hallucinations, delusions
Hallucinations

- Reduce latest PD drug if possible
- Treat associated problems
- Cholinesterase inhibitors
- Quetiapine (25 - 200 mg at night)
- Clozapine (through registered pharmacy)
Hallucinations

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• Treat associated problems
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• 5HT drugs?
Pimavanserin (5HT$_{2A}$ inverse agonist)

Cummings et al, Lancet 2013
Impulse control behaviours

• All characterised by an urge, which is hard to control, to perform repeatedly an action which is usually at best transiently pleasurable and which has risky or adverse consequences
Impulse control behaviours
Impulse control behaviours

- Different high-risk group
- Young at onset of PD
- Male > female*
- On dopamine agonists*
- History of alcohol or drug misuse (or FH)
- Other impulsive behaviours
- Depression
Prevalence

- Dopamine dysregulation 3% in specialist clinics
- Gambling 2-8% (14% of those on agonists)
- Hypersexuality 3-4%
- Binge eating 4%
- Excessive spending 5-6%
- Punding (widely defined) 14%
Prevalence

- Any ICB about 20%
ICB: prevention

- Warn patients, especially high-risk groups
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- Ask about alcohol, gambling, hobbies
ICB: prevention

• Warn patients, especially high-risk groups
• Ask about alcohol, gambling, hobbies
• Ask about anxiety and depression
ICB: prevention

- Warn patients, especially high-risk groups
- Ask about alcohol, gambling, hobbies
- Ask about anxiety and depression

- Try to negotiate lower treatment goals in high-risk individuals
ICB: screening

• Routinely ask and record
• Especially in patients with perfect motor control (or dyskinesia), and in patients with erratic attendance, and in patients with depression
ICB: management

• Reduce PD medication where possible
  – especially dopamine agonists, with compensatory levodopa if necessary
ICB: management

• Reduce PD medication where possible
• Practical measures
  – Handing over control of medication, credit cards, computer; blocking software; support groups
ICB: management

- Reduce PD medication where possible
- Practical measures
- Antipsychotics do not seem to work
ICB: management

- Reduce PD medication where possible
- Practical measures
- Antipsychotics do not seem to work
- STN DBS
  - Several small series now, showing benefit for gambling and over-medicating
  - One report of failure due to compulsive fiddling with wires
• Often more than one eg punding and dysregulation

• Excessive ventral striatal dopamine release in response to visual cues

• Excessive ventral striatal activity in response to visual cues, gambling tasks etc

• ‘Buzz’ from placing the bet, regardless of outcome

• Imbalance between effort/risk and reward
Dopamine agonist withdrawal syndrome (DAWS)

- Described in patients coming off agonists rapidly for ICD
- Anxiety, depression, sweating, cravings
- Not clear if it is a distinct entity
Mild cognitive symptoms

• Mild frontal-executive dysfunction
  – Dopaminergic
  – Not necessarily progressing to dementia
Mild cognitive symptoms

- Mild frontal-executive dysfunction
  - Dopaminergic
  - Not necessarily progressing to dementia

- Memory/language/visuospatial impairment

- Drowsiness and visual hallucinations
  - Usually progress to dementia
Cambridge studies

• Incident cohort
• 17% dementia after 5 years

• Baseline risk factors:
  – Age 72 years +
  – Reduced semantic fluency
  – Imperfect pentagons
  – Tau H1/H1 haplotype
Dementia

• Main unsolved problem in PD
• Primary target for neuroprotection

• Prevalence after 10 years 65-80%
Pathology
Risk factors for dementia in PD

- PD
- Age > 75 years
- Postural instability-gait disorder phenotype > mixed phenotype >> tremor phenotype
- Depression
- REM sleep behaviour disorder
- Other risk factors for dementia

- Tau polymorphisms
The start of dementia in PD

- Cognitive symptoms
- Drowsiness
- Visual hallucinations
- Episodes of delirium
Cognitive symptoms

• Inattention
• Memory
• Language
• Visuospatial
• More frontal than Alzheimer’s
• More visuospatial than Alzheimer’s
Cognitive fluctuations

• Hour by hour
• Day by day
• Episodes of confusion

• Attention
• Drowsiness
• Staring into space
Investigation

• Acute confusion:
  – Rule out infection and metabolic upset

• CT head
  – Cerebrovascular disease
  – Subdural haematoma
Treatment

• Cholinesterase inhibitors
  – Good for hallucinations
  – Quite good for fluctuations
  – Sometimes help baseline cognition

• Agitation, anorexia and diarrhoea
• Rivastigmine/galantamine > donepezil
• Rolinski et al, Cochrane review 2012
Treatment

• Cholinesterase inhibitors

• Higher-than-licensed doses of cholinesterase inhibitors?

• Memantine
Other approaches

- Improve vision and lighting
- Withdraw aggravating PD drugs
- Atypical neuroleptics
- Consider depression
- Improve sleep
Prognosis

- Gradual decline
- Benefit of drug treatment wanes
- Very high carer burden
- Marked reduction in life expectancy
Prevention

- Exercise
- Social engagement
- Control vascular risk factors
THE
VILLAGER'S
FRIEND AND PHYSICIAN;
or,
A FAMILIAR ADDRESS
 ON THE
PRESERVATION OF HEALTH,
AND THE
REMOVAL OF DISEASE, ON ITS FIRST APPEARANCE,
supposed to be delivered by a Village Physician;
WITH CONSIDERATIONS ON
THE TREATMENT OF CHILDREN, ON SOBRIETY,
INDUSTRY, &c.
Intended for the Promotion of Domestic Happiness.

By JAMES PARKINSON.

SECOND EDITION.

LONDON:
Printed by C. Whittlestone,
and sold by H. Dymond, Paternoster Row.

1793.
[Price One Shilling]
Prevention

• Exercise
• Social engagement
• Control vascular risk factors
• Cognitive training?
• Neuroprotection?
Exenatide

- Glucagon-like peptide-1 (GLP1) agonist
Exenatide

**Figure 3**
Change from baseline in the Mattis DRS-2 score by study visit. Data represent mean ± SEM.
Summary

• Think of Parkinson’s disease as a psychiatric disease with some motor features

• Look out for anxiety, depression, apathy and impulse control disorders

• The big challenge is dementia