BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS IN DEMENTIA
Unmet needs

What might be your behavioural response to this experience?
Content

• Definition – What are BPSD?
• Prevalence – How common are they?
• Aetiological considerations and prevention
• Assessment – Bio-psycho-social approach; Rating scales
• Management – what works and what doesn’t? What are the risks of treatments?
• Prognosis
BPSD = Neuropsychiatric symptoms = Challenging behaviours

**Behavioural**
- Aggression
- Agitation
- Apathy
- Wandering / Restlessness
- Hoarding
- Screaming
- Sexual Disinhibition
- Changes in sleep and appetite

**Psychological**
- Anxiety
- Depression
- Psychosis
Syndrome approach to Classification

Hyperactivity
- Agitation
- Aggression
- Disinhibition
- Irritability

Affective
- Depression
- Anxiety

Psychosis
- Hallucinations
- Delusions

Apathy
- Apathy
- Eating behaviours
TRUE or FALSE?

Neuropsychiatric symptoms in dementia are nearly universal.
Prevalence estimates

- **Cache County Study (1999)** population based study
  - 61% of those with dementia had had 1 or more neuropsychiatric symptom (based on the NPI) in the month prior to interview
  - Apathy, depression, agitation and aggression were the most common symptoms reported
  - Those with Alzheimer’s disease: 23% had delusions (most commonly misidentification and jealousy delusions), 13% had hallucinations (80% visual vs 20% auditory)

- **Maryland Assisted Living Study (2004)** residents in nursing homes based study
  - 83% of residents with dementia had neuropsychiatric symptoms (based on NPI).
Influence of the Dementia Subtype

Neuropsychiatric manifestations are embedded in some diagnostic criteria:

- **Frontotemporal dementia (FTD)**
  - gradual and insidious decline in social functioning and regulation of personal conduct; emotional blunting; stereotypic behaviours

- **Semantic Dementia**
  - Compulsive behaviours

- **Lewy Body Dementia**
  - 76% experience visual hallucinations

- **Parkinson’s disease dementia**
  - 54% experience visual hallucinations
Pathophysiology 1 – Agitation and Aggression

Possible underlying neurobiology:

- Glutamatergic system disrupted by formation of neurofibrillary tangles in frontal and cingulate cortices (Tekin et al 2001) resulting in exaggerated response to triggers
Pathophysiology 2 – Depression

• Recurrence of depression
• Emotional reaction to cognitive deficits
• Cerebrovascular damage
• Direct consequence of neurodegenerative process
  • Noradrenergic neuronal loss in locus coeruleus and serotonergic neuronal loss in dorsal raphe nucleus (Forstl et al, 1992)
### Pathophysiology 3 - Psychosis

<table>
<thead>
<tr>
<th>Delusions</th>
<th>Hallucinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Common, especially in early stages and in those who are older (Leroi et al, 2003)</td>
<td>• Associated with lower choline acetyltransferase levels in parietal and temporal lobes (Perry et al, 1990)</td>
</tr>
<tr>
<td>• Associated with presence of neurofibrillary tangles, and with frontal hypoperfusion (Cummings, 2000)</td>
<td>• Note: Relative efficacy of CEIs in treating hallucinations in dementia</td>
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</tbody>
</table>
Pathophysiology 4 - Apathy

- Most common BPSD and stable across several dementia subtypes (AD, VaD, DLB, FTD)
- Can be prodrome of AD
- Lesion along the frontal-subcortical network
  - Mesiofrontal circuit – lack of drive
  - Dorsolateral frontal cortex-loss of goal-directed behaviour
BUT......PINCH ME

- Pain
- Infection
- Nutrition
- Constipation
- Hydration
- Medication
- Environment
Pain is Common, Missed and Increases Suffering

- **40 – 83%** of residents in nursing homes are affected by pain.

- Pain is **under-reported** and **under-treated** in older people, even more so in people with dementia.

- Pain is the **highest** issue affecting **quality of life**.
Pain Perception in the Elderly

Pain tolerance

Pain severity

Increased pain threshold i.e. reduced sensitivity to mild pain

Less ‘flexible’ pain system

Increased vulnerability to severe and persistent pain
Why do people with dementia have pain?
Prevention of BPSD

- Show respect to the person with dementia
- Maximise communication
- Prevent pain
- Engage in meaningful personalised activity
- Encourage choice and independence
- Ensure persons fundamental needs are met
Assessment

Initial questions to ask:

- Is it really a problem?
- Who is it that finds the behaviour problematic?
- Are there external factors that are challenging to the person with dementia?
- Is the behaviour compromising the safety of the person or others?
What Information do you need

- What is the person’s previous behaviour and personality
- What has changed – nature, degree and frequency?
- When did it change?
- What are the triggers?
- Understand the biopsychosocial context – i.e. Rule out PAIN, DELIRIUM, ENVIRONNMENTAL and INTERPERSONAL FACTORS
- What has been tried to date?
Management: Psychosocial approaches first line

- Personalised activities with social interaction
- 40-45% Placebo response in RCTs – suggests that **good clinical practice** provides clinically meaningful benefit
A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia

Gill Livingston, Lynsey Kelly, Elanor Lewis-Holmes, Gianluca Baio, Stephen Morris, Nishma Patel, Rumana Z Omar, Cornelius Katona and Claudia Cooper
<table>
<thead>
<tr>
<th>No Evidence</th>
<th>Some Evidence</th>
<th>Best Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light therapy</td>
<td>Training family carers</td>
<td>Activities (whilst they are in place)</td>
</tr>
<tr>
<td>Aromatherapy</td>
<td>Music therapy without protocol</td>
<td>Music therapy following a protocol</td>
</tr>
<tr>
<td>Home-like care</td>
<td>Exercise</td>
<td>Sensory interventions (involving touch at least) – benefit even for severe agitation</td>
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<tr>
<td></td>
<td>Staff training without supervision</td>
<td>Training staff in PCC/Communication skills <em>with supervision</em></td>
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<tr>
<td></td>
<td>Environmental intervention</td>
<td>Dementia Care Mapping (even for severe agitation; sustained benefits)</td>
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<td></td>
<td>Pet therapy</td>
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<td></td>
<td>Cognitive stimulation and validation</td>
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Management

Medications in the treatment of BPSD – Worth the risk?
2 Recent Systematic Reviews

Other reviews include:
- Gauthier et al 2002
- Gauthier et al 2005
- Gauthier et al 2008
- Schneider et al 2006
- Ballard and Waite 2006

BUT:
- Not many studies
- Not many well-designed studies
- Evidence-base remains slim

REVIEW

Pharmacological treatments for neuropsychiatric symptoms of dementia in long-term care: a systematic review

Dallas P. Seitz,1 Sudeep S. Gill,2 Nathan Herrmann,3,4 Sarah Brisbin,1 Mark J. Rapoport,3,4 Jenna Rines,1 Kimberley Wilson,5 Ken Le Clair1 and David K. Conn3,6

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2 Division of Geriatric Medicine, Queen’s University, Kingston, Ontario, Canada
3 Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada
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5 Canadian Coalition for Seniors’ Mental Health, Toronto, Ontario, Canada
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JNPP Online First, published on May 29, 2014 as 10.1136/jnnp-2014-308112

RESEARCH PAPER

Pharmacological treatment of neuropsychiatric symptoms in Alzheimer’s disease: a systematic review and meta-analysis

Jun Wang,1 Jin-Tai Yu,1,2 Hui-Fu Wang,2 Xiang-Fei Meng,1 Chong Wang,1 Chen-Chen Tan,1 Lan Tan1,2
# Pharmacological Rx of BPSD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Evidence</th>
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</table>
| **Cholinesterase inhibitors** | • Modest benefit on NPI  
• Especially apathy, depression and anxiety but NOT agitation  
• ? Especially galantamine (Wang et al, 2014) |
| **Memantine**           | • Modest benefit for agitation/aggression, delusions and disinhibition (Gauthier et al 2005 and 2008)  
• Wang et al – favours but not statistically significant |
| **Antipsychotics**      | • Most studied medications for BPSD Rx  
• Risperidone 1-2mg daily: modest benefit on aggression, more limited benefit for psychosis. No benefit from quetiapine (Schneider et al, 2006)  
• Small benefits for risperidone, olanzapine and aripiprazole (Seitz et al, 2013)  
• Small benefits of olanzapine and aripiprazole (Wang et al, 2014) |
### Pharmacological Rx of BPSD

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<th>Medication</th>
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<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td>• Modest benefit of citalopram 30mg but QTc prolongation - CitAD (Porsteinsson et al, 2014)</td>
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<tr>
<td></td>
<td>• No benefit of antidepressants (Seitz and Wang)</td>
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<tr>
<td><strong>Anticonvulsants</strong></td>
<td>• Small single study support for carbamazepine (Seitz et al, 2013)</td>
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<tr>
<td></td>
<td>• No benefit of valproate (Seitz) and <em>clinical worsening</em> (Wang et al, 2014)</td>
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<tr>
<td><strong>Others</strong></td>
<td>Single small study support for:</td>
</tr>
<tr>
<td></td>
<td>• Oestrogen</td>
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<td></td>
<td>• Cyproterone acetate</td>
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<td>• Propranolol</td>
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<td>• Prazosin</td>
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<tr>
<td><strong>Pain relief</strong></td>
<td>• Improvements in agitation after stepped treatment with analgesics (Husebo et al 2011; Corbett et al 2012)</td>
</tr>
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</table>
Antipsychotic in Dementia – Considerable Risk of Adverse Events

- Antipsychotics increase the risk of death (1% attributable risk over 12 weeks of Rx)

- And risk of cerebrovascular events increased 3 fold

- And somnolence, falls, and fall-related injuries including hip fractures

- They also accelerate cognitive and functional decline

- Other problems: EPSE, peripheral oedema, DVT/PE, prolonged QTc, chest infections
Antipsychotics in Dementia

Licensed use

• Risperidone only for use in dementia for up to 6 weeks in patients with severe aggression (causing risk or severe distress, which has not responded to other treatments)

Guidelines

• NICE and American Psychiatric Association (APA) recommend:
  • Atypical antipsychotic treatment for maximum of 12 weeks, except in exceptional circumstances
Prognosis

- BPSD in early stages of dementia predict a worse outcome

- Most BPSD will stop after 4 weeks without any pharmacological treatment

- Long term prescriptions of antipsychotics can be discontinued without a detrimental effect on Neuropsychiatric symptoms (Declercq et al 2013)