Overview of neuropsychiatric symptoms in neurodegeneration

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Neuropsychiatric symptoms
Pose a major challenge for patients – and their carers

- Behavioural and psychological symptoms are most difficult symptoms for patients and caregivers to deal with. They can cause a great deal of distress.

“\textit{I can cope with the memory problems, but what I find very difficult is that my husband thinks I’m having an affair with the neighbour. He’s always suspicious that there’s someone else in the house at night. He gets agitated and hits me.”}

- Treating these symptoms can make a real difference to reduce stress for patients and their families and improve quality of life.

- Neurobiology for most symptoms poorly understood but there is progress on some fronts.
Consequences of neuropsychiatric symptoms

Major impact on patients, families, medical staff and economy

Wint & Cummings (2016) in Husain & Schott
Oxford Textbook of Cognitive Neurology & Dementia
Neuropsychiatric symptoms (NPS)
What are they?

- Aggression
- Agitation
- Anxiety
- Apathy
- Appetite / eating changes
- Delusions
- Depression or dysphoria
- Disinhibition
- Euphoria
- Hallucinations
- Irritability or lability
- Motor disturbance or stereotyped behaviours
  - Pacing, wandering, picking, rummaging
- Night-time behaviours and sleep disturbance

### Neuropsychiatric Inventory (NPI)

<table>
<thead>
<tr>
<th>Domain</th>
<th>N/A</th>
<th>Absent</th>
<th>Frequency</th>
<th>Severity</th>
<th>Frequency x Severity</th>
<th>Caregiver Distress</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Delusions</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
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</tr>
<tr>
<td>B. Hallucinations</td>
<td></td>
<td></td>
<td>1 2 3</td>
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<tr>
<td>C. Agitation/Aggression</td>
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<td>1 2 3</td>
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<tr>
<td>D. Depression/Dysphoria</td>
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<td>1 2 3</td>
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<tr>
<td>E. Anxiety</td>
<td></td>
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<td>1 2 3</td>
<td>1 2 3</td>
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<tr>
<td>F. Elation/Euphoria</td>
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<tr>
<td>G. Apathy/Indifference</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H. Disinhibition</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
<td></td>
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</tr>
<tr>
<td>I. Irritability/Lability</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J. Aberrant Motor Behavior</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL SCORE:</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
<td></td>
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</tr>
<tr>
<td>K. Sleep and Nighttime Behavior Disorders</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L. Appetite/Eating Changes</td>
<td></td>
<td></td>
<td>1 2 3</td>
<td>1 2 3</td>
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<td></td>
</tr>
</tbody>
</table>
Frequency of one or more NPS

Most patients suffer more than one or more neuropsychiatric symptom

Prevalence of neuropsychiatric symptoms

Cache County (Utah) study | N= 408 cases with dementia

The mean symptom severity among participants with an NPI score > 0 in each domain is presented in Table 3. The highest severity score at each assessment point was consistently for apathy. For most other items, mean severity was in the 2.0 to 4.0 range at most assessment points.

DISCUSSION

In this study of the longitudinal course of neuropsychiatric symptoms in dementia over a mean (and median) of 5 years, we found a trend for the point prevalence of nearly all symptoms to increase over time. Nevertheless, prevalence varied among individual symptoms. Apathy, depression, delusions overall were most common, while disinhibition and elation were least prevalent.
Prevalence of neuropsychiatric symptoms

European Alzheimer Disease Consortium | N=2354 cases with Alzheimer’s

Table 2. Mean NPI scores (severity × frequency: range = 0–12) and percentage of patients with symptoms

<table>
<thead>
<tr>
<th>NPI items</th>
<th>Mean</th>
<th>SD</th>
<th>Patients with symptom (score &gt;3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>%</td>
</tr>
<tr>
<td>Delusions</td>
<td>1.5 ± 2.8</td>
<td></td>
<td>19.4</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.7 ± 2.1</td>
<td></td>
<td>9.1</td>
</tr>
<tr>
<td>Agitation</td>
<td>2.3 ± 3.1</td>
<td></td>
<td>31.1</td>
</tr>
<tr>
<td>Depression</td>
<td>2.8 ± 3.4</td>
<td></td>
<td>36.7</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.7 ± 3.3</td>
<td></td>
<td>37.0</td>
</tr>
<tr>
<td>Euphoria</td>
<td>0.4 ± 1.4</td>
<td></td>
<td>4.9</td>
</tr>
<tr>
<td>Apathy</td>
<td>4.2 ± 3.8</td>
<td></td>
<td>55.2</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>0.8 ± 2.2</td>
<td></td>
<td>9.5</td>
</tr>
<tr>
<td>Irritability</td>
<td>2.4 ± 3.1</td>
<td></td>
<td>32.1</td>
</tr>
<tr>
<td>Aberrant motor behaviour</td>
<td>2.0 ± 3.4</td>
<td></td>
<td>27.5</td>
</tr>
<tr>
<td>Night-time behaviour disturbances</td>
<td>1.5 ± 2.9</td>
<td></td>
<td>19.5</td>
</tr>
<tr>
<td>Appetite and eating abnormalities</td>
<td>1.7 ± 3.2</td>
<td></td>
<td>21.8</td>
</tr>
</tbody>
</table>

Scores > 3 in a symptom considered to be clinically relevant

Prevalence of neuropsychiatric symptoms

European Alzheimer Disease Consortium | N=2354 cases with Alzheimer’s

Factor loading

<table>
<thead>
<tr>
<th></th>
<th>Factor 1: hyperactivity</th>
<th>Factor 2: psychosis</th>
<th>Factor 3: affective</th>
<th>Factor 4: apathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions</td>
<td>0.294</td>
<td>0.707</td>
<td>0.063</td>
<td>−0.018</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.134</td>
<td>0.808</td>
<td>0.054</td>
<td>−0.011</td>
</tr>
<tr>
<td>Agitation</td>
<td><strong>0.700</strong></td>
<td>0.112</td>
<td>0.274</td>
<td>0.036</td>
</tr>
<tr>
<td>Depression</td>
<td>0.069</td>
<td>0.052</td>
<td><strong>0.728</strong></td>
<td>0.206</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.154</td>
<td>0.141</td>
<td><strong>0.706</strong></td>
<td>0.023</td>
</tr>
<tr>
<td>Euphoria</td>
<td>(0.359)</td>
<td>0.049</td>
<td>−0.355</td>
<td>0.207</td>
</tr>
<tr>
<td>Apathy</td>
<td>0.121</td>
<td>−0.141</td>
<td>0.184</td>
<td><strong>0.629</strong></td>
</tr>
<tr>
<td>Disinhibition</td>
<td>0.682</td>
<td>0.139</td>
<td>−0.119</td>
<td>0.030</td>
</tr>
<tr>
<td>Irritability</td>
<td><strong>0.707</strong></td>
<td>0.093</td>
<td>0.278</td>
<td>0.026</td>
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<tr>
<td>Aberrant motor behaviour</td>
<td><strong>0.432</strong></td>
<td>0.222</td>
<td>−0.118</td>
<td>(0.412)</td>
</tr>
<tr>
<td>Night-time behaviour disturbances</td>
<td>−0.054</td>
<td><strong>0.510</strong></td>
<td>0.157</td>
<td>(0.431)</td>
</tr>
<tr>
<td>Appetite and eating abnormalities</td>
<td>0.000</td>
<td>0.105</td>
<td>−0.011</td>
<td><strong>0.705</strong></td>
</tr>
<tr>
<td>Eigenvalues</td>
<td>2.772</td>
<td>1.264</td>
<td>1.117</td>
<td>1.063</td>
</tr>
<tr>
<td>Variance, %</td>
<td>23.10</td>
<td>10.54</td>
<td>9.31</td>
<td>8.86</td>
</tr>
</tbody>
</table>

- Factor analysis demonstrated four factors that accounted for 52% of variance in data.
Caregiver burden

Systematic review | Total N=2835 cases with dementia

Symptoms that impact most on caregivers

- Irritability
- Agitation/aggression
- Sleep disturbance
- Anxiety
- Apathy
- Delusions

# Neuropsychiatric Inventory (NPI)

**Scoring Summary**

<table>
<thead>
<tr>
<th>CENTER</th>
<th>SCREENING</th>
<th>PATIENT</th>
<th>PATIENT INITIALS</th>
<th>VISIT DATE</th>
</tr>
</thead>
</table>

Please transcribe appropriate categories from the NPI Worksheet into the boxes provided.

- If symptoms of a domain did not apply, check the "N/A" box.
- If symptoms of a domain were absent, check the "0" box.
- If symptoms of a domain were present, check one score each for Frequency and Severity.
- Multiply Frequency score x Severity score and enter the product in the space provided.
- Total all Frequency x Severity scores and record the Total Score below.
- If symptoms of a domain were present, check one score for Distress; total all distress scores for a summary score.

<table>
<thead>
<tr>
<th>DOMAIN</th>
<th>N/A</th>
<th>ABSENT</th>
<th>FREQUENCY</th>
<th>SEVERITY</th>
<th>FREQUENCY X SEVERITY</th>
<th>CAREGIVER DISTRESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Delusions</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>B. Hallucinations</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>D. Depression/Dysphoria</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>E. Anxiety</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
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<td>F. Elation/Euphoria</td>
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<td>☐</td>
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<td>H. Disinhibition</td>
<td>☐</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>TOTAL SCORE:</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>☐</td>
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<td>☐</td>
</tr>
<tr>
<td>L. Appetite/Eating Changes</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</tbody>
</table>
NPI questions for apathy
If caregiver says Yes to screening question proceed to ask detailed questions

G. APATHY/INDIFFERENCE

Has the patient lost interest in the world around him/her? Has he/she lost interest in doing things or does he/she lack motivation for starting new activities? Is he/she more difficult to engage in conversation or in doing chores? Is the patient apathetic or indifferent?

☐ Yes (if yes, please proceed to subquestions)  ☐ No (if no, please proceed to next screening question)  ☐ N/A

1. Does the patient seem less spontaneous and less active than usual?  ☐ Yes  ☐ No
2. Is the patient less likely to initiate a conversation?  ☐ Yes  ☐ No
3. Is the patient less affectionate or lacking in emotions when compared to his/her usual self?  ☐ Yes  ☐ No
4. Does the patient contribute less to household chores?  ☐ Yes  ☐ No
5. Does the patient seem less interested in the activities and plans of others?  ☐ Yes  ☐ No
6. Has the patient lost interest in friends and family members?  ☐ Yes  ☐ No
7. Is the patient less enthusiastic about his/her usual interests?  ☐ Yes  ☐ No
8. Does the patient show any other signs that he/she doesn't care about doing new things?  ☐ Yes  ☐ No

If the screening question is confirmed, determine the frequency and severity of the apathy/indifference.
NPI questions for apathy

Then get them to rate frequency and severity, and level of distress to them

Frequency:

☐ 1. Rarely – less than once per week.
☐ 2. Sometimes – about once per week.
☐ 3. Often – several times per week but less than every day.
☐ 4. Very often – nearly always present.

Severity:

☐ 1. Mild – apathy is notable but produces little interference with daily routines; only mildly different from patient’s usual behavior; patient responds to suggestions to engage in activities.
☐ 2. Moderate – apathy is very evident; may be overcome by the caregiver with coaxing and encouragement; responds spontaneously only to powerful events such as visits from close relatives or family members.
☐ 3. Severe – apathy is very evident and usually fails to respond to any encouragement or external events.

Distress: How emotionally distressing do you find this behavior?

☐ 0. Not at all
☐ 1. Minimally (almost no change in work routine)
☐ 2. Mildly (almost no change in work routine but little time rebudgeting required)
☐ 3. Moderately (disrupts work routine, requires time rebudgeting)
☐ 4. Severely (disruptive, upsetting to staff and other residents, major time infringement)
☐ 5. Very Severely or Extremely (very disruptive, major source of distress for staff and other residents, requires time usually devoted to other residents or activities)
**NPI questions for disinhibition**

*Then get them to rate frequency and severity, and level of distress to them*

**H. DISINHIBITION**

Does the patient seem to act impulsively without thinking? Does he/she do or say things that are not usually done or said in public? Does he/she do things that are embarrassing to you or others?

- [ ] Yes (if yes, please proceed to subquestions)
- [ ] No (if no, please proceed to next screening question)
- [ ] N/A

1. Does the patient act impulsively without appearing to consider the consequences?  
   - [ ] Yes  
   - [ ] No

2. Does the patient talk to total strangers as if he/she knew them?  
   - [ ] Yes  
   - [ ] No

3. Does the patient say things to people that are insensitive or hurt their feelings?  
   - [ ] Yes  
   - [ ] No

4. Does the patient say crude things or make sexual remarks that he/she would not usually have said?  
   - [ ] Yes  
   - [ ] No

5. Does the patient talk openly about very personal or private matters not usually discussed in public?  
   - [ ] Yes  
   - [ ] No

6. Does the patient take liberties or touch or hug others in way that is out of character for him/her?  
   - [ ] Yes  
   - [ ] No

7. Does the patient show any other signs of loss of control of his/her impulses?  
   - [ ] Yes  
   - [ ] No

If the screening question is confirmed, determine the frequency and severity of the disinhibition.
Apathy and disinhibition can co-exist

An example from CADASIL*

* Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

Reyes et al (2013) Neurology
Apathy and disinhibition can co-exist
An example from CADASIL

<table>
<thead>
<tr>
<th>Behavioral disturbance</th>
<th>Cohort (n = 132)</th>
<th>Apathetic (n = 54)</th>
<th>Nonapathetic (n = 78)</th>
<th>p</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total NPI score, mean (SD)</td>
<td>15.3 (16.0)</td>
<td>29.0 (14.9)</td>
<td>5.8 (7.6)</td>
<td>&lt;0.0001</td>
<td>—</td>
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<tr>
<td>At least one behavioral</td>
<td>75 (99)</td>
<td>94.4 (51)</td>
<td>61.5 (48)</td>
<td>&lt;0.0001</td>
<td>—</td>
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<tr>
<td>disturbance, % (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression/dysphoria, % (n)</td>
<td>46.2 (61)</td>
<td>61.1 (33)</td>
<td>35.9 (28)</td>
<td>0.0048 0.02</td>
<td></td>
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<tr>
<td>Disturbed sleep, % (n)</td>
<td>44.7 (59)</td>
<td>64.8 (35)</td>
<td>30.8 (24)</td>
<td>0.0001 0.31</td>
<td></td>
</tr>
<tr>
<td>Irritability/lability, % (n)</td>
<td>43.1 (57)</td>
<td>64.8 (35)</td>
<td>28.2 (22)</td>
<td>&lt;0.0001 0.0003</td>
<td></td>
</tr>
<tr>
<td>Anxiety, % (n)</td>
<td>37.1 (49)</td>
<td>40.7 (22)</td>
<td>34.6 (27)</td>
<td>0.47 0.71</td>
<td></td>
</tr>
<tr>
<td>Apathy, % (n)</td>
<td>41.0 (54)</td>
<td>—</td>
<td>—</td>
<td>—    —</td>
<td></td>
</tr>
<tr>
<td>Agitation/aggression, % (n)</td>
<td>26.6 (35)</td>
<td>53.7 (29)</td>
<td>7.7 (6)</td>
<td>&lt;0.0001 &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Disturbed appetite, % (n)</td>
<td>16.0 (21)</td>
<td>31.5 (17)</td>
<td>5.1 (4)</td>
<td>&lt;0.0001 0.003</td>
<td></td>
</tr>
<tr>
<td>Disinhibition, % (n)</td>
<td>13.7 (18)</td>
<td>27.8 (15)</td>
<td>3.9 (3)</td>
<td>&lt;0.0001 0.008</td>
<td></td>
</tr>
<tr>
<td>Euphoria, % (n)</td>
<td>7.5 (10)</td>
<td>14.8 (8)</td>
<td>2.6 (2)</td>
<td>0.009 0.20</td>
<td></td>
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<tr>
<td>Aberrant motor behavior, % (n)</td>
<td>6.0 (8)</td>
<td>14.8 (8)</td>
<td>0.0 (0)</td>
<td>0.0005 0.0007</td>
<td></td>
</tr>
<tr>
<td>Delusion, % (n)</td>
<td>2.2 (3)</td>
<td>3.7 (2)</td>
<td>1.3 (1)</td>
<td>0.36 NA</td>
<td></td>
</tr>
<tr>
<td>Hallucination, % (n)</td>
<td>0.7 (1)</td>
<td>1.9 (1)</td>
<td>0.0 (0)</td>
<td>0.23 NA</td>
<td></td>
</tr>
</tbody>
</table>

132 cases from a multicentre study

Reyes et al (2013) Neurology
Dysexecutive syndrome
Both behavioural and cognitive changes occur


Alzheimer and Parkinson diseases, (4) initiation was predominantly affected in traumatic brain injury and multiple sclerosis, and (5) deduction was predominantly affected in stroke and traumatic brain injury. The differences persisted ($p < 0.03$, all) in the subgroup with loss of autonomy for initiation, generation, and planning (data not shown). This indicates that the pattern of cognitive but not behavioral dysexecutive syndrome was influenced by the underlying disease.

Discussion
This study proposed criteria for dysexecutive syndrome, gave an operational definition based on easily administered tests and questionnaires, and showed that they discriminated between patients and controls, with a higher frequency in patients with loss of autonomy, and that both behavioral and cognitive dysexecutive syndromes were independent predictors of loss of autonomy. In addition, it provided evidence for differing patterns of cognitive disorders according to the underlying disease.

This cooperative study has several limitations. It was a clinical study involving a large number of patients; the complete battery of tests and questionnaires therefore cannot be administered to all patients. A reliable informant was not available in all cases, precluding assessment of behavioral disorders and disability. However, the subgroups did not differ from the complete sample, and the reduction of sample size due to unavailable data did not result in type II error. This study deliberately included patients suffering from various diseases to be representative of clinical populations referred for cognitive assessment. In addition, this transnosological study overcomes numerous biases related to the study of a single disease, such as effects related to associated perceptuomotor deficits (eg, stroke), associated cognitive deficits (eg, memory deficit in Alzheimer disease), or the prominence of one site or type of lesions within the network subserving executive functions.

The transnosological study design led us to adopt a common criterion for loss of autonomy based on several severity scales. The loss of autonomy criterion was simple and was assisted by well-validated disability scales.

FIGURE 1: Frequency (%) of behavioral (upper part) and cognitive (lower part) dysexecutive disorders in patients and controls (A) and in patients (B) according to the presence of loss of autonomy.

FIGURE 2: Pattern (frequency %) of behavioral (left) and cognitive (right) disorders according to the disease. BI = brain injury; I = impairment.

Overlap with dysexecutive syndrome
Associated with both behavioural and cognitive deficits

# NPI-Q questionnaire for caregiver

*Rapid screening – without interview and no index of frequency*

<table>
<thead>
<tr>
<th>NPI-Q SUMMARY</th>
<th>No</th>
<th>Severity</th>
<th>Caregiver Distress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Agitation/Aggression</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Dysphoria/Depression</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Euphoria/Elation</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Apathy/Indifference</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Irritability/Lability</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Aberrant Motor</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Nighttime Behavior</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>Appetite/Eating</td>
<td>0</td>
<td>1 2 3</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cambridge Behavioural Inventory

Also rapid screening – without interview

Cambridge Behavioural Inventory Revised (CBI-R)

For the Carer

Your Name: _____________________________

Today’s date: / /

Patient’s name: _____________________________

Relationship to the patient: _____________________________

We would like to ask you a number of questions about various changes in the patient’s behaviour that you may have noticed. It is important that we obtain your view as it will help us in our assessment.

Please read the description of each problem carefully. Then circle the number under the heading “Frequency” that best describes the occurrence of the behavioural change.

Some of the everyday skill questions may not apply, if for instance the person you care for has never done the shopping. Please enter N/A (not applicable).

All questions apply to the patient’s behaviour OVER THE PAST MONTH.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Never</td>
<td>a few times per month</td>
<td>a few times per week</td>
<td>daily</td>
</tr>
</tbody>
</table>

Memory and Orientation

- Has poor day-to-day memory (e.g. about conversations, trips etc.)
  - FREQUENCY
  - 0 1 2 3 4
- Asks the same questions over and over again
  - 0 1 2 3 4
- Loses or misplaces things
  - 0 1 2 3 4
- Forgets the names of familiar people
  - 0 1 2 3 4
- Forgets the names of objects and things
  - 0 1 2 3 4
- Shows poor concentration when reading or watching television
  - 0 1 2 3 4
- Forgets what day it is
  - 0 1 2 3 4
- Becomes confused or muddled in unusual surroundings
  - 0 1 2 3 4

Everyday Skills

- Has difficulties using electrical appliances (e.g. TV, radio, cooker, washing machine)
  - 0 1 2 3 4
- Has difficulties writing (letters, Christmas cards, lists etc.)
  - 0 1 2 3 4
- Has difficulties using the telephone
  - 0 1 2 3 4
- Has difficulties making a hot drink (e.g. tea/coffee)
  - 0 1 2 3 4
- Has problems handling money or paying bills
  - 0 1 2 3 4

Self Care

- Has difficulties grooming self (e.g. shaving or putting on make-up)
  - 0 1 2 3 4
- Has difficulties dressing self
  - 0 1 2 3 4
- Has problems feeding self without assistance
  - 0 1 2 3 4
- Has problems bathing or showering self
  - 0 1 2 3 4

Abnormal Behaviour

- Finds humour or laughs at things others do not find funny
  - 0 1 2 3 4
- Has temper outbursts
  - 0 1 2 3 4
- Is uncooperative when asked to do something
  - 0 1 2 3 4
- Shows socially embarrassing behaviour
  - 0 1 2 3 4
- Makes tactless or suggestive remarks
  - 0 1 2 3 4
- Acts impulsively without thinking
  - 0 1 2 3 4

Cambridge Behavioural Inventory Revised (CBI-R)

<table>
<thead>
<tr>
<th>Mood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cries</td>
</tr>
<tr>
<td>Appears sad or depressed</td>
</tr>
<tr>
<td>Is very restless or agitated</td>
</tr>
<tr>
<td>Is very irritable</td>
</tr>
</tbody>
</table>

Beliefs

- Sees things that are not really there (visual hallucinations)
  - 0 1 2 3 4
- Hears voices that are not really there (auditory hallucinations)
  - 0 1 2 3 4
- Has odd or bizarre ideas that cannot be true
  - 0 1 2 3 4

Eating Habits

- Prefers sweet foods more than before
  - 0 1 2 3 4
- Wants to eat the same foods repeatedly
  - 0 1 2 3 4
- Her/his appetite is greater, s/he eats more than before
  - 0 1 2 3 4
- Table manners are declining e.g. stuffing food into mouth
  - 0 1 2 3 4

Sleep

- Sleep is disturbed at night
  - 0 1 2 3 4
- Sleeps more by day than before (cat naps etc.)
  - 0 1 2 3 4

Stereotypic and Motor Behaviours

- Is rigid and fixed in her/his ideas and opinions
  - 0 1 2 3 4
- Develops routines from which s/he can not easily be discouraged e.g. wanting to eat or go for walks at fixed times
  - 0 1 2 3 4
- Clock watches or appears pre-occupied with time
  - 0 1 2 3 4
- Repeatedly uses the same expression or catch phrase
  - 0 1 2 3 4

Motivation

- Shows less enthusiasm for his or her usual interests
  - 0 1 2 3 4
- Shows little interest in doing new things
  - 0 1 2 3 4
- Fails to maintain motivation to keep in contact with friends or family
  - 0 1 2 3 4
- Appears indifferent to the worries and concerns of family members
  - 0 1 2 3 4
- Shows reduced affection
  - 0 1 2 3 4

Any other comments:

10/03/2008 © John R Hodges
Cambridge Behavioural Inventory

Also rapid screening – without interview

Examples

<table>
<thead>
<tr>
<th>Abnormal Behaviour</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finds humour or laughs at things others do not find funny</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Makes tactless or suggestive remarks</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Motivation</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Take the history properly

*If you don’t ask you won’t know. It will save you time in the long run.*

- Listen to the patient. *Take me through your day*
- But also see the caregiver alone to obtain independent, collateral history
- Otherwise lots of things will remain unsaid and you won’t know full context
- If information is not forthcoming, probe gently about how things are:
  - *Are there any new stresses at home or work for the caregiver?*
  - *What about family, financial or domestic concerns?*
  - *Have there been any changes in medication or compliance?*
  - *Sleep disturbance?*
  - *Mood?*
  - *False beliefs?*
  - *Altered, inappropriate behaviour?*
## Take the history properly

*If you want, use the screening questions of NPI to act as prompts*

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delusions</strong> Does the patient have false beliefs, such as thinking that</td>
<td></td>
</tr>
<tr>
<td>others are stealing from him/her or planning to harm him/her in some way?</td>
<td></td>
</tr>
<tr>
<td><strong>Hallucinations</strong> Does the patient have hallucinations such as false visions or voices? Does he or she seem to hear or see things that are not present?</td>
<td></td>
</tr>
<tr>
<td><strong>Agitation/Aggression</strong> Is the patient resistive to help from others at times, or hard to handle?</td>
<td></td>
</tr>
<tr>
<td><strong>Depression/Dysphoria</strong> Does the patient seem sad or say that he/she is depressed?</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety</strong> Does the patient become upset when separated from you? Does he/she have any other signs of nervousness such as shortness of breath, sighing, being unable to relax, or feeling excessively tense?</td>
<td></td>
</tr>
</tbody>
</table>
# Take the history properly

*If you want, use the screening questions of NPI to act as prompts*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elation/Euphoria</strong></td>
<td>Does the patient appear to feel too good or act excessively happy?</td>
</tr>
<tr>
<td><strong>Apathy/Indifference</strong></td>
<td>Does the patient seem less interested in his/her usual activities or in the activities and plans of others?</td>
</tr>
<tr>
<td><strong>Disinhibition</strong></td>
<td>Does the patient seem to act impulsively, for example, talking to strangers as if he/she knows them, or saying things that may hurt people's feelings?</td>
</tr>
<tr>
<td><strong>Irritability/Lability</strong></td>
<td>Is the patient impatient and cranky? Does he/she have difficulty coping with delays or waiting for planned activities?</td>
</tr>
<tr>
<td><strong>Motor Disturbance</strong></td>
<td>Does the patient engage in repetitive activities such as pacing around the house, handling buttons, wrapping string, or doing other things repeatedly?</td>
</tr>
</tbody>
</table>
Don’t just reach for the prescription pad

*Drug treatments are not often effective and may not be the solution*
DICE Approach to the patient

Describe Investigate Create Evaluate

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DICE Approach to the patient

D: Describe the problem

- Contextualize and characterize the behavior (e.g. patient hit care giver while bathing at home) through discussion with the key informant (care giver or proxy)
- Determine whether there are immediate concerns about safety or risk

Kales, Gitlin & Lyketsos (2015) BMJ
DICE Approach to the patient

**D**: Describe the problem

- Contextualize and characterize the behavior (e.g., patient hit care giver while bathing at home) through discussion with the key informant (care giver or proxy)
- Determine whether there are immediate concerns about safety or risk

---

**SAFETY RISK**

Consider psychotropic drug use out of concern for harm/risk and to allow for full description of behavior

---

**NO SAFETY RISK**
DICE Approach to the patient

I: Investigate the problem

- Examine possible underlying causes of behavior (see figure 3)
  - Patient factors
  - Care giver factors
  - Environmental contribution

Kales, Gitlin & Lyketsos (2015) BMJ
DICE Approach to the patient

Modifiable causes of behavioral and psychological symptoms

- Unmet needs (hunger, thirst, pain)
- Acute medical problems (including drug related side effects and interactions)
- Sensory deficits (hearing, vision)

1/3 patients in one study had undetected illness

- Overstimulating or understimulating
- Unsafe
- Lack of activity
- Lack of established routines

- Care giver stress, burden, depression
- Lack of education about dementia and BPSD
- Communication issues
- Mismatch of expectations and dementia severity

Kales, Gitlin & Lyketsos (2015) BMJ
DICE Approach to the patient

I: Investigate the problem

INVESTIGATE

- Examine possible underlying causes of behavior (see figure 3)
  - Patient factors
  - Care giver factors
  - Environmental contribution

SAFETY RISK

Consider psychotropic drug use out of concern for harm/risk and to allow for full investigation of behavior

Kales, Gitlin & Lyketsos (2015) BMJ
DICE Approach to the patient

C: Create and implement a treatment plan

CREATE
- Collaborate with care giver and treatment team to create and implement a treatment plan to manage the most distressing symptoms
- Key interventions to
  - Patient
  - Care giver
  - Environment
  (see table 1)

Presence of depression, psychosis, or aggression with risk?
**DICE Approach to the patient**

**C: Create and implement a treatment plan**

<table>
<thead>
<tr>
<th>Modifiable factor</th>
<th>Intervention example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Unmet needs                               | • Make sure the person with dementia is getting enough sleep and rest  
• Deal with fear, hunger, toilet needs  |
| Acute medical problems                     | Talk to the person’s doctor about whether symptoms could have physical (e.g., urinary tract infection or pain) causes or be the result of a drug interaction or side effect |
| Sensory deficits                          | Encourage use of eyeglasses or hearing aids; have vision and hearing assessed                                                                    |
| **CARE GIVER**                            |                                                                                                                                                    |
| Care giver stress, burden, depression      | Care givers need to care for themselves by exercising regularly, getting help with care responsibilities, attending their own doctor’s appointments, and using stress reduction techniques |
| Education                                 | Understand that behaviors are not intentional or “on purpose” but are the consequence of a brain disease                                              |
| Communication                             | • Use a calm voice  
• Do not use open ended questions  
• Keep it simple – do not over explain or discuss what events will be happening in the future  
• Limit the number of choice offered |
| **ENVIRONMENT**                           |                                                                                                                                                    |
| Overstimulating or understimulating...    | Regulate the amount of stimulation in the home by decluttering the environment, limiting the number of people in the home, and reducing noise by turning off radios and television sets |
| Unsafe environment                        | Make sure the person does not have access to anything (e.g., sharp objects) that could cause harm to themselves or others                                |
| Lack of activity                          | • Keep the person engaged in activities that match interests and capabilities  
• Relax the rules – there is no right or wrong way to perform an activity if the person is safe |
| Lack of structure or established routines  | • Establish daily routines  
• Changing the time, location, or sequence of dialy activities can trigger outbursts  
• Allow enough time for activities  
• Trying to rush activities can also trigger behaviors |

Kales, Gitlin & Lyketsos (2015) *BMJ*
# DICE Approach to the patient

## C: Create and implement a treatment plan

<table>
<thead>
<tr>
<th>Modifiable factor</th>
<th>Intervention example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT</strong></td>
<td></td>
</tr>
<tr>
<td>Unmet needs</td>
<td>• Make sure the person with dementia is getting enough sleep and rest</td>
</tr>
<tr>
<td></td>
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---

Kales, Gitlin & Lyketsos (2015) *BMJ*
**DICE Approach to the patient**

**C: Create and implement a treatment plan**

<table>
<thead>
<tr>
<th>CARE GIVER</th>
<th>CARE GIVER stress, burden, depression</th>
<th>Education</th>
<th>Communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Care giver stress, burden, depression</td>
<td>Care givers need to care for themselves by exercising regularly, getting help with care responsibilities, attending their own doctor’s appointments, and using stress reduction techniques</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
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<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- Non-pharmacological approaches with strongest evidence base are those that involve family caregiver interventions, e.g. training given to caregivers by occupational therapists to customize activity based on patient’s current & previous interests and cognitive & physical abilities.

Kales, Gitlin & Lyketsos (2015) *BMJ*
2. aggression

Aggressive behavior may be verbal (shouting, name calling) or physical (hitting, pushing). It’s important to try to understand what is causing the anger, as it can occur suddenly with no apparent reason or can result from a frustrating situation.

How to respond:

Rule out pain as the cause of the behavior
Pain can cause a person with dementia to act aggressively.

Try to identify the immediate cause
Think about what happened right before, which may have triggered the behavior.

Focus on feelings, not facts
Look for the feelings behind the words or actions.

Try not to get upset
Be positive and reassuring. Speak slowly in a soft tone.

Limit distractions
Examine the person’s surroundings and adapt them to avoid other similar situations.

Try a relaxing activity
Use music, massage or exercise to help soothe the person.
10 COMMON SIGNS OF CAREGIVER STRESS

1. Denial about the disease and its effect on the person who has been diagnosed.
   *I know Mom is going to get better.*

2. Anger at the person with Alzheimer’s or frustration that he or she can’t do the things they used to be able to do.
   *He knows how to get dressed — he’s just being stubborn.*

3. Social withdrawal from friends and activities that used to make you feel good.
   *I don’t care about visiting with the neighbors anymore.*

4. Anxiety about the future and facing another day.
   *What happens when he needs more care than I can provide?*

5. Depression that breaks your spirit and affects your ability to cope.
   *I just don’t care anymore.*

6. Exhaustion that makes it nearly impossible to complete necessary daily tasks.
   *I’m too tired for this.*

7. Sleeplessness caused by a never-ending list of concerns.
   *What if she wanders out of the house or falls and hurts herself?*
### DICE Approach to the patient

C: *Create and implement a treatment plan*

#### ENVIRONMENT

<table>
<thead>
<tr>
<th>Issue</th>
<th>Suggestions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overstimulating or understimulating environment</td>
<td>Regulate the amount of stimulation in the home by decluttering the environment, limiting the number of people in the home, and reducing noise by turning off radios and television sets.</td>
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<td>Unsafe environment</td>
<td>Make sure the person does not have access to anything (e.g. sharp objects) that could cause harm to themselves or others.</td>
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DICE Approach to the patient

C: Create and implement a treatment plan

CREATE

- Collaborate with caregiver and treatment team to create and implement a treatment plan to manage the most distressing symptoms
- Key interventions to
  - Patient
  - Care giver
  - Environment
  (see table 1)

Presence of depression, psychosis, or aggression with risk?

Consider psychotropic drug use as a first line strategy

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DICE Approach to the patient

E: Evaluate the effects of treatment plan

EVALUATE

- Were the interventions effective?
- If psychotropic drugs were used, evaluate for adverse effects, symptom persistence, and responsiveness to other interventions

Kales, Gitlin & Lyketsos (2015) BMJ
DICE Approach to the patient

**E: Evaluate the effects of treatment plan**

- **EVALUATE.**
  - Were the interventions effective?
  - If psychotropic drugs were used, evaluate for adverse effects, symptom persistence, and responsiveness to other interventions

- **NO**
  - Determine whether interventions were implemented
  - Problem solve with care giver and team
  - Revise recommendations

Kales, Gitlin & Lyketsos (2015) *BMJ*
DICE Approach to the patient

E: Evaluate the effects of treatment plan

EVALUATE
- Were the interventions effective?
- If psychotropic drugs were used, evaluate for adverse effects, symptom persistence, and responsiveness to other interventions

YES

Continue to monitor for the emergence of new behaviors

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Drug treatments

Only when really necessary

- **Antidepressants**
  - Tricyclics have limited benefit and potential risks
  - SSRIs: variable data. Citalopram may be effective for agitation

- **Antipsychotics**
  - Variable and poor evidence of efficacy
  - Adverse events including increased mortality for both conventional and atypical antipsychotics, but perhaps less for quetiapine

- **Cholinesterase inhibitors and memantine**
  - Small but significant effects on neuropsychiatric symptoms

- **Benzodiazepines**
  - Evidence lacking for neuropsychiatric symptoms

- **Mood stabilizers**
  - Some evidence for use of low dose carbamazepine

**New drugs:** e.g. Pimavanserin
<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose (daily)</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>5 - 20 mg</td>
<td>Dry mouth, falls, headache, GI symptoms, sedation, sexual dysfunction</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>5 - 40 mg</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>25 - 100 mg</td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>25 - 300 mg</td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>2.5 - 10 mg</td>
<td>Cerebrovascular events, death, extrapyramidal symptoms, falls, metabolic syndrome, malignant syndrome, QTc prolongation, sedation, sexual dysfunction</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>2.5 - 10 mg</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.25 - 2 mg</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25 - 200 mg</td>
<td></td>
</tr>
<tr>
<td><strong>Cholinesterase inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil</td>
<td>5 - 10 mg</td>
<td></td>
</tr>
<tr>
<td>Galantamine</td>
<td>4 - 24 mg</td>
<td>Bradycardia, confusion, GI symptoms, sedation</td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>1.5 - 12 mg or 4.6- to 9.5-mg patch</td>
<td></td>
</tr>
<tr>
<td><strong>Memantine</strong></td>
<td>7 - 28 mg</td>
<td>Confusion, sedation</td>
</tr>
<tr>
<td><strong>Mood stabilizers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>100 - 400 mg</td>
<td>Confusion, falls, hyperammonemia, liver dysfunction, sedation, thrombocytopenia</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>125 - 1000 mg</td>
<td></td>
</tr>
</tbody>
</table>
Case 1

- 62 yr old active man with Parkinson’s disease
- Anxious about his condition
- Worried that his wife has met someone else
- Agitated
- Checking where she goes, which websites she visits and her emails

**Interview with her alone**

- She denies these claims
- Increasingly frustrated by his behaviour
- Seeking more time to do things for herself

- Question her further to see if there is a safety risk
DICE Approach to the patient

Modifiable causes of behavioural and psychological symptoms

- Unmet needs (hunger, thirst, pain)
- Acute medical problems (including drug related side effects and interactions)
- Sensory deficits (hearing, vision)

- Overstimulating or understimulating
- Unsafe
- Lack of activity
- Lack of established routines

- Care giver stress, burden, depression
- Lack of education about dementia and BPSD
- Communication issues
- Mismatch of expectations and dementia severity

Kales, Gitlin & Lyketsos (2015) BMJ
Case 2

- 70 yr old man with Alzheimer’s disease
- New onset anger outbursts in a man who was usually very calm
- Verbally aggressive to his wife
- Agitated

**Interview with her alone**

- Unaware of trigger factors
- Enquiry about home circumstances reveals his driving license has been revoked
- Wants to drive to social club to meet friends
Case 3
Summary

Neuropsychiatric symptoms have a major impact

- Almost all patients with dementia suffer one or more
- Taking the history properly is vital – including from carer
- Approach to the problem requires careful evaluation – of patient, caregiver and environment
- DICE (Describe, Investigate, Create, Evaluate) may be helpful
- Think twice before using drugs
- Are there non-pharmacological approaches that might work?