Behavioural change

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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.

“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.
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 Symptoms Overview

#### What are they?

- Aggression
- Agitation
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- Apathy
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#### Neuropsychiatric Symptoms

<table>
<thead>
<tr>
<th>Domain</th>
<th>N/A</th>
<th>Amount</th>
<th>Frequency</th>
<th>Severity</th>
<th>Frequency Severity</th>
<th>Caregiver</th>
</tr>
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<tbody>
<tr>
<td>A. Delusions</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
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<td>no</td>
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<tr>
<td>B. Hallucinations</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>C. Agitation/Agegression</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>D. Depression/Dysphoria</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>E. Anxiety</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>F. Elation/Euphoria</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
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<tr>
<td>G. Apathy/Indifference</td>
<td>no</td>
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<td>no</td>
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<td>no</td>
</tr>
<tr>
<td>H. Grunt/Blunt</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
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<tr>
<td>I. Irritability/Lability</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
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<tr>
<td>J. Wandering/Motor Behavior</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td><strong>TOTAL SCOR</strong></td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

- **TOTAL SCOR**

### Neuropsychiatric Symptoms

For symptoms of a domain were present, check one score for Frequency and Severity.

Multiply Frequency score x Severity score and enter the product in the space provided.

If symptoms of a domain did not apply, check the "N/A" box.

For example, if symptoms of a domain were present, check one score for Distress; total all distress scores for a domain.

### Neuropsychiatric Symptoms

- **A.** Delusions
- **B.** Hallucinations
- **C.** Agitation/Agegression
- **D.** Depression/Dysphoria
- **E.** Anxiety
- **F.** Elation/Euphoria
- **G.** Apathy/Indifference
- **H.** Grunt/Blunt
- **I.** Irritability/Lability
- **J.** Wandering/Motor Behavior

- **TOTAL SCOR**

### Neuropsychiatric Symptoms

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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*
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...
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 and SD</th>
<th>Patients with symptom (score &gt;3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Delusions</td>
<td>1.5 ± 2.8</td>
<td>19.4</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>0.7 ± 2.1</td>
<td>9.1</td>
</tr>
<tr>
<td>Agitation</td>
<td>2.3 ± 3.1</td>
<td>31.1</td>
</tr>
<tr>
<td>Depression</td>
<td>2.8 ± 3.4</td>
<td>36.7</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.7 ± 3.3</td>
<td>37.0</td>
</tr>
<tr>
<td>Euphoria</td>
<td>0.4 ± 1.4</td>
<td>4.9</td>
</tr>
<tr>
<td>Apathy</td>
<td>4.2 ± 3.8</td>
<td>55.2</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>0.8 ± 2.2</td>
<td>9.5</td>
</tr>
<tr>
<td>Irritability</td>
<td>2.4 ± 3.1</td>
<td>32.1</td>
</tr>
<tr>
<td>Aberrant motor behaviour</td>
<td>2.0 ± 3.4</td>
<td>27.5</td>
</tr>
<tr>
<td>Night-time behaviour</td>
<td>1.5 ± 2.9</td>
<td>19.5</td>
</tr>
<tr>
<td>Appetite and eating</td>
<td>1.7 ± 3.2</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 analysis demonstrated four factors that accounted for 52% of variance in data

<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>0.700</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>0.728</td>
<td>0.206</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.154</td>
<td>0.141</td>
<td>0.706</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>
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<tr>
<td>Apathy</td>
<td>0.121</td>
<td>-0.141</td>
<td>0.184</td>
<td>0.629</td>
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<tr>
<td>Disinhibition</td>
<td>0.682</td>
<td>0.139</td>
<td>-0.119</td>
<td>0.090</td>
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<tr>
<td>Irritability</td>
<td>0.707</td>
<td>0.093</td>
<td>0.278</td>
<td>0.026</td>
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<tr>
<td>Aberrant motor behaviour</td>
<td>0.432</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>0.510</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>0.705</td>
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<tr>
<td>Eigenvalues</td>
<td>2.772</td>
<td>1.264</td>
<td>1.117</td>
<td>1.063</td>
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<tr>
<td>Variance, %</td>
<td>23.10</td>
<td>10.54</td>
<td>9.31</td>
<td>8.86</td>
</tr>
</tbody>
</table>

Italics indicate factor loading ≥ 0.40. Parentheses indicate factor loading just below criterion ≥ 0.40.
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)

Developed by Jeff Cummings | Downloadable from npitest.net

<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>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. Hallucinations</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. Agitation/Aggression</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
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<tr>
<td>D. Depression/Dysphoria</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Anxiety</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Elation/Euphoria</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G. Apathy/Indifference</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H. Disinhibition</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I. Irritability/Lability</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J. Aberrant Motor Behavior</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
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<td>TOTAL SCORE:</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>K. Sleep and Nighttime</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
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<tr>
<td>Behavior Disorders</td>
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<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
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<tr>
<td>L. Appetite/Eating Changes</td>
<td></td>
<td></td>
<td>0 1 2 3 4</td>
<td>1 2 3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NPI questions for disinhibition

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

H. DISINHIBITION (NA)

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 a 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.
Cambridge Behavioural Inventory Revised (CBI-R)

**For the Carer**

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 views 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.

**Patient’s name: _____________________________ Relationship to the patient: ___________________________**

Please circle the number that best describes the patient’s behaviour that you may have noticed.

**Today’s date: / / **

It is important that we obtain your view as it will help us track the patient’s behavioural change.

Thank you for your time.

**_html_**

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### Memory and Orientation

- Has poor day-to-day memory (e.g., about consultations, trips etc.): 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
- Shows poor concentration when reading or watching television: 0 1 2 3 4
- Forget what day it is: 0 1 2 3 4
- Becomes confused or muddled: 0 1 2 3 4

### Everyday Skills

- Has difficulties writing (letters, Christmas cards, lists etc.): 0 1 2 3 4
- Has difficulties making a hot drink (e.g., tea/coffee): 0 1 2 3 4
- Has difficulties using electrical appliances (e.g., TV, radio, cooker, washing machines): 0 1 2 3 4
- Has difficulties grooming self (e.g., shaving or putting on makeup): 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

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**Cambridge Behavioural Inventory Revised (CBI-R)**

**Patient’s name: _____________________________ Relationship to the patient: ___________________________**

Please circle the number under the heading “FREQUENCY” that best describes the occurrence of the behavioral change.

Your Name: _____________________________ Today’s date: / / **

0: Never 1: a few times per month 2: a few times per week 3: daily 4: constantly

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<tr>
<td>Has difficulties grooming self (e.g., shaving or putting on makeup)</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

---

**Any other comments:**

---

12

(C) John R Hodges 2008
Cambridge Behavioural Inventory
*Rapid screening – without interview – completed by an informant*

**Examples**

<table>
<thead>
<tr>
<th>Abnormal Behaviour</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finds humour or laughs at things others do not find funny</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Has temper outbursts</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Is uncooperative when asked to do something</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows socially embarrassing behaviour</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Makes tactless or suggestive remarks</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Acts impulsively without thinking</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Motivation</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shows less enthusiasm for his or her usual interests</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows little interest in doing new things</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Fails to maintain motivation to keep in contact with friends or family</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Appears indifferent to the worries and concerns of family members</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shows reduced affection</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>
**Taking the history properly**

*Requires information from patient and informant | Screening questions of NPI can act as prompts*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions</td>
<td>Does the patient have false beliefs, such as thinking that others are stealing from him/her or planning to harm him/her in some way?</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>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>
</tr>
<tr>
<td>Agitation/Aggression</td>
<td>Is the patient resistive to help from others at times, or hard to handle?</td>
</tr>
<tr>
<td>Depression/Dysphoria</td>
<td>Does the patient seem sad or say that he/she is depressed?</td>
</tr>
<tr>
<td>Anxiety</td>
<td>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>
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Taking the history properly

*Requires information from patient and informant | Screening questions of NPI can act as prompts*

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<tr>
<td><strong>Elation/Euphoria</strong></td>
<td>Does the patient appear to feel too good or act excessively happy?</td>
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<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>
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<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>
Behavioural change is the defining feature of bvFTD

Diagnostic criteria for behavioural variant frontotemporal dementia

Possible bvFTD
Three of the features (A–F) must be present; symptoms should occur repeatedly, not just as a single instance:
A Early (3 years) behavioural disinhibition
B Early (3 years) apathy or inertia
C Early (3 years) loss of sympathy or empathy
D Early (3 years) perseverative, stereotyped, or compulsive/ritualistic behaviour
E Hyperorality and dietary changes
F Neuropsychological profile: executive function deficits with relative sparing of memory and visuospatial functions

Probable bvFTD
All the following criteria must be present to meet diagnosis:
A Meets criteria for possible bvFTD
B Significant functional decline
C Imaging results consistent with bvFTD (frontal and/or anterior temporal atrophy on CT or MRI or frontal hypoperfusion or hypometabolism on SPECT or PET)

Definite bvFTD
Criteria A and either B or C must be present to meet diagnosis:
A Meets criteria for possible or probable bvFTD
B Histopathological evidence of FTLD on biopsy at post mortem
C Presence of a known pathogenic mutation

Exclusion criteria for bvFTD
Criteria A and B must both be answered negatively; criterion C can be positive for possible bvFTD but must be negative for probable bvFTD:
A Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders
B Behavioural disturbance is better accounted for by a psychiatric diagnosis
C Biomarkers strongly indicative of Alzheimer’s disease or other neurodegenerative process
Behavioral variant frontotemporal dementia

Is one of the three types of frontotemporal dementia (FTD)

<table>
<thead>
<tr>
<th>Behavioral-Dysexecutive FTD</th>
<th>Progressive Nonfluent Aphasia</th>
<th>Semantic Dementia</th>
</tr>
</thead>
</table>

**Clinical Features**
- Change in personality and behavior that results in impairment in social interpersonal conduct, with emotional blunting, loss of insight, and the absence of prominent anterograde amnesia.
- Prominent difficulty with expressive speech characterized by nonfluency, speech hesitancy, word-finding difficulty, labored speech, apraxia of speech, phonemic paraphasias, and agrammatism; the absence of prominent anterograde amnesia.
- Prominent loss of vocabulary and anomia affecting expressive speech and impairment of comprehension of word meaning in the context of fluent speech production; the absence of prominent anterograde amnesia.

**Neuropsychological features consistent with diagnosis**
- Prominent executive deficits; relatively preserved learning and delayed recall; relatively preserved visuospatial functions.
- Prominent deficits in spontaneous speech; deficits in verbal fluency and naming; relatively preserved learning and delayed recall; relatively preserved visuospatial functions.
- Prominent anomia and impaired semantic knowledge; relatively preserved learning and delayed recall; relatively preserved visuospatial functions.

**Structural Imaging features consistent with diagnosis**
- Focal asymmetric or symmetric cortical atrophy of the anterior temporal and/or prefrontal regions.
- Focal cortical atrophy of anterior temporal lobe or prefrontal regions greater left than right.

**Functional Imaging features consistent with diagnosis**
- Focal asymmetric or symmetric frontal and/or temporal hypoperfusion.
- Focal frontal and/or temporal hypoperfusion, left greater than right.
**Behavioural change is the defining feature of bvFTD**

*Diagnostic criteria for behavioural variant frontotemporal dementia*

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<td>E  Hyperorality and dietary changes</td>
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<td>F  Neuropsychological profile: executive function deficits with relative sparing of memory and visuospatial functions</td>
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*Loss of empathy can be a key feature – not captured by Neuropsychiatric Inventory*
What is empathy?
Different definitions for different investigators

- One perspective distinguishes between emotional and cognitive empathy
- The emotional and cognitive responses of an individual to the experiences of others

- **Emotional empathy**: capacity to experience affective reactions to the observed experiences of others or share a “fellow feeling”
- **Cognitive empathy**: capacity to engage in the cognitive process of adopting another’s psychological point of view
Empathic concern is one measure of emotional empathy

*Assessed by the Interpersonal Reactivity Index*

- Rate on a 5-interval scale how these statements describe you: A [Does not describe me well].....through to E [Very well]

- I often have tender, concerned feelings for people less fortunate than me
- Sometimes I don't feel very sorry for other people when they are having problems
- When I see someone being taken advantage of, I feel kind of protective towards them
- Other people's misfortunes do not usually disturb me a great deal
- When I see someone being treated unfairly, I sometimes don't feel very much pity for them
- I am often quite touched by things that I see happen
- I would describe myself as a pretty soft-hearted person
Perspective taking is one measure of cognitive empathy
Assessed by the Interpersonal Reactivity Index

- Rate on a 5-interval scale how these statements describe you: A [Does not describe me well].....through to E [Very well]

- I sometimes find it difficult to see things from the "other guy's" point of view
- I try to look at everybody's side of a disagreement before I make a decision
- I sometimes try to understand my friends better by imagining how things look from their perspective
- If I'm sure I'm right about something, I don't waste much time listening to other people's arguments
- Before criticizing somebody, I try to imagine how I would feel if I were in their place
- I believe that there are two sides to every question and try to look at them both.
- When I'm upset at someone, I usually try to "put myself in his shoes" for a while
Emotional and cognitive empathy are dissociable

In patients with focal brain lesions

Empathic concern

Perspective taking

Shamay-Tsoory et al (2009) Brain
Altered empathy in FTD

Associated with atrophy in a right hemisphere system | temporal pole, insula and medial frontal regions

Based on Interpersonal Reactivity Index but using informants’ assessments of patients’ behaviour
An FTD syndrome associated with right temporal atrophy

In a pattern which is close to a ‘mirror image’ of semantic dementia patients

A frontotemporal dementia syndrome associated with striking right temporal lobe atrophy and

- Prosopagnosia
- Topographical disorientation
- Disinhibition
- Apathy
- Loss of empathy
- Hyper-religiosity
- Aggression
Behavioral change can be feature of dysexecutive syndrome

Dysexecutive syndrome associated with both behavioural and cognitive deficits
Is behavioural change accounted for by cognitive deficits?

In other words, is the *behavioural change* in the dysexecutive syndrome simply attributable to the deficits in *cognitive control* measured – and operationally defined – by performance on neuropsychological or experimental tasks?

Theoretically, what might we need to make a claim to the contrary?

Let’s examine empathy
Can deficits in *empathy* be explained by deficits in *cognitive control* processes?
Empathy in bvFTD assessed using an experimental task

*Empathy for pain task probes intentionality and empathic concern (plus other measures)*

**FIGURE 1** | (A) Examples of the visual stimuli used for each category. The durations of the first, second, and third picture were 1000, 200, and 1000 ms, respectively.
(B) Examples of the questions designed to assess different empathy aspects. Each question was answered using a computer-based visual analog scale.
Empathic concern not explained by executive function deficit

But intentionality (Was action performed on purpose?) could be accounted for by executive impairments
Empathic concern in bvFTD related to orbitofrontal cortex

Atrophy here relates to lower scores of empathic concern
Management of behavioural change

_How can it be treated?_
Drug treatments are often not effective

*Although they sometimes have to be used as a last resort or for safety of patient, carer or public*

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.
The DICE approach

Step 1: Describe

The first step is to elicit a thorough description of the symptoms by accurately characterizing the symptoms and the context in which they occur through discussion with the care giver and the person with dementia (if possible).

This description should include consideration of possible "describe, investigate, create, and evaluate." The DICE approach assumes that a problem BPSD has been identified and brought to the provider’s attention (fig 2). We have designed DICE to be used by any health professional and to work well within a team care setting that facilitates coordination among the implementation of medical, pharmacological, and non-pharmacologic strategies.

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**DICE Approach to the patient**

D: Describe the problem

**DESCRIBE**

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

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

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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 description of behavior

NO SAFETY RISK

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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)

1/3 patients in one study had undetected illness

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

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

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

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

<table>
<thead>
<tr>
<th>CREATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Collaborate with care giver and treatment team to create and implement a treatment plan to manage the most distressing symptoms</td>
</tr>
<tr>
<td>- Key interventions to</td>
</tr>
<tr>
<td>- Patient</td>
</tr>
<tr>
<td>- Care giver</td>
</tr>
<tr>
<td>- Environment</td>
</tr>
<tr>
<td>(see table 1)</td>
</tr>
</tbody>
</table>

Presence of depression, psychosis, or aggression with risk?

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

---

Kales, Gitlin & Lyketsos (2015) *BMI*
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>
<td>• Deal with fear, hunger, toilet needs</td>
</tr>
<tr>
<td>Acute medical problems</td>
<td>Talk to the person’s doctor about whether symptoms could have physical cause (e.g., urinary tract infection or pain) causes or be the result of a drug interaction or side effect</td>
</tr>
<tr>
<td>Sensory deficits</td>
<td>Encourage use of eyeglasses or hearing aids; have vision and hearing assessed</td>
</tr>
<tr>
<td><strong>CARE GIVER</strong></td>
<td></td>
</tr>
<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>
<td>Education</td>
<td>Understand that behaviors are not intentional or “on purpose” but are the consequence of a brain disease</td>
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<td>Communication</td>
<td>• Use a calm voice</td>
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<td>• Do not use open ended questions</td>
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<td>• Keep it simple – do not over explain or discuss what events will be happening in the future</td>
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<td>• Limit the number of choice offered</td>
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<td><strong>ENVIRONMENT</strong></td>
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</tr>
<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>
</tr>
<tr>
<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>
</tr>
<tr>
<td>Lack of activity</td>
<td>• Keep the person engaged in activities that match interests and capabilities</td>
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<td></td>
<td>• Relax the rules – there is no right or wrong way to perform an activity if the person is safe</td>
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<td>Lack of structure or established routines</td>
<td>• Establish daily routines</td>
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<tr>
<td></td>
<td>• Changing the time, location, or sequence of daily activities can trigger outbreaks</td>
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Kales, Gitlin & Lyketsos (2015) BMJ
**DICE Approach to the patient**

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

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

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| Communication | • Use a calm voice  
• Do not use open ended questions  
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• Limit the number of choice offered |

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.
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**

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*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

**If 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

---

Kales, Gitlin & Lyketsos (2015) *BMJ*
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>
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<th>Medication</th>
<th>Dose (daily)</th>
<th>Adverse effects</th>
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<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>Antipsychotics</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, neuroleptic 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>Cholinesterase inhibitors</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 4.5- to 9.5-mg patch</td>
<td></td>
</tr>
<tr>
<td>Memantine</td>
<td>7 - 28 mg</td>
<td>Confusion, sedation</td>
</tr>
<tr>
<td>Mood stabilizers</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>
Reading

Core text is available online on SOLO

- For overview of neuropsychiatric symptoms: Chapter 19
- See also separate reading list