Causality Matters: Preventing and Mitigating Behavioral and Psychological Symptoms of Dementia

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What are the Behavioral and Psychological Symptoms of Dementia (BPSD)?

Sources: Robheru, 2004; McShane, International Psychogeriatrics, 2000
### Evidence for Current Pharmacological Treatments

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Evidence from Randomized Controlled Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics</td>
<td>No evidence for behavioral improvement with conventional APs. Atypical antipsychotics appear to improve behaviors like agitation in a modest way (effect size 0.13)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>No evidence for behavioral improvement with older antidepressants. Mixed evidence for depression with newer antidepressants. Preliminary evidence for the treatment of agitation (citalopram).</td>
</tr>
<tr>
<td>Mood Stabilizers</td>
<td>No evidence for valproic acid and derivatives. Some evidence that carbamazepine is helpful for agitation.</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>No evidence for behavioral improvement.</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>No evidence for behavioral improvement except for in Parkinson’s disease dementia.</td>
</tr>
<tr>
<td>Memantine</td>
<td>No evidence for behavioral improvement.</td>
</tr>
</tbody>
</table>


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*Impact of the CMS National Partnership to Improve Dementia Care on Use of Antipsychotics and Other Psychotropics in Long-Term Care in the U.S.: 2009-2014*

Maust, Kim, Chiang, Kales, In Submission
### Evidence for Current Ecobiopsychosocial Treatments

<table>
<thead>
<tr>
<th>Type of Intervention</th>
<th>Evidence from Randomized Controlled Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensory stimulation</strong> (music, dance, acupressure, aromatherapy, etc)</td>
<td>Music therapy appears effective in reducing behaviors (agitation, aggression). However the evidence is limited by heterogeneity/variability of interventions.</td>
</tr>
<tr>
<td><strong>Cognitive/emotion-oriented interventions</strong> (cognitive stimulation, reminiscence, validation, simulated presence, etc)</td>
<td>Many methodological limitations. Convincing evidence lacking.</td>
</tr>
<tr>
<td><strong>Behavior-management therapies</strong></td>
<td>Effectiveness found for formal caregiver training; dementia mapping in residential care; and techniques to improve communication skills. Some evidence for multicomponent multidisciplinary approaches in nursing homes. Family caregiver training effect size estimated at 0.34.</td>
</tr>
<tr>
<td><strong>Other (exercise, animal-assisted therapy, etc)</strong></td>
<td>No convincing effect.</td>
</tr>
</tbody>
</table>


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### Current Real-World “Assessment” of Behavioral and Psychological Symptoms of Dementia

![Diagram](image)

- Agitation

- Psychotropic medication
  - Antipsychotic
  - Mood stabilizer
  - Benzodiazepine
Evidence for causality for specific BPSD

- Kolanowski et al, Nursing Outlook, In Press.

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Evidence for causality</th>
</tr>
</thead>
</table>
| Aggression | **PLWD**: male gender; lower functional status; sadness; premorbid personality  
**Caregiver**: caregiver burden |
| Agitation | **PLWD**: younger age; younger age of onset; male gender; Alzheimer’s dementia; dementia severity; pain; boredom; premorbid personality  
**Caregiver**: communication  
**Environment**: lack of stimulation or activity |
| Apathy | **PLWD**: BvFTD; dementia severity; presence of other BPSD; neuroanatomical changes; genetic factors  
**Environment**: lack of stimulation or activity |
| Depression | **PLWD**: female gender; lower level of education; younger age of onset; genetic factors; brain changes; type of dementia; cerebrovascular disease; premorbid personality; severity of functional impairment  
**Caregiver**: caregiver burden |
| Psychosis | **PLWD**: neuropathological changes in the brain; dementia severity; greater functional and cognitive impairment; genetic factors |
Summary

• Current real-world treatment of BPSD is often impressionistic (agitation=antipsychotic)

• Need to consider BPSD with equal precision as in medical symptoms (shortness of breath analogy)

• To do so, we need to fully consider causality
  • Is agitation caused by:
    • Pain?
    • An overstimulating environment?
    • Communication issues with a caregiver?

• Such approaches also have utility to improve the precision of treatment trials
Recommendations

1. Policy needs to be informed by research data showing that focusing on a single medication class may not be the most effective way to improve treatment of BPSD
   a. Unintended consequences of shifts to other (less efficacious classes)
   b. No evidence that National Partnership has increased use of effective non-pharmacologic strategies

2. More research is needed on the determinants of BPSD so that treatments can be better tailored to potentially modify those factors

3. Future research needs to take into account the impact of patient, caregiver and environmental factors on BPSD
   a. Combination pharmacologic and non-pharmacologic strategies
   b. Approaches like DICE ahead of randomization in pharmacologic trials to decrease heterogeneity (e.g. separate out agitation from pain or other modifiable causes)