Management of Behavioral Symptoms in Dementia
Principles & Case Vignettes

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Disclosures: none
Outline du jour

- Magnitude of the problem
- Definitions & descriptions
- Evaluation
- Treatments
- Case vignettes
What’s in a Name?

- Behavioral & psychological sx$s
- Non-cognitive sx$s
- Neuropsychiatric sx$s
- “Agitation”
BPSD are the Norm!

Five-year period prevalence of NPI symptoms (NPI>0)

Cache County study
Steinberg IJGP 2008

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
<th>baseline=408</th>
<th>1.5 years=236</th>
<th>3.0 years=106</th>
<th>4.1 years=61</th>
<th>5.3 years=36</th>
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<td>Delusions</td>
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<td>Hallucinations</td>
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<td>Agitation/Aggression</td>
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<td>Anxiety</td>
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<td>Disinhibition</td>
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<td>Irritability/Lability</td>
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<td>Aberrant Motor</td>
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<td>NPI total</td>
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</table>
BPSD are not good

- Greater ADL impairment
- Worse QoL
- Earlier institutionalization
- Higher caregiver burden
- $10K/year additional costs
- More rapid decline
- Accelerated mortality
IPA Provisional Research Diagnostic Criteria: “agitation with cognitive impairment”

- cognitive impairment or dementia
- observed or inferred emotional distress
  - excessive motor activity
  - verbal aggression
  - physical aggression
- excess disability beyond cognitive impairment alone
- not due solely to another psychiatric disorder
An approach to nosology

- Affective
  - depressive
  - manic
- Psychotic
- Anxiety
- Apathy
- Sleep

- Agitation
  - verbal
  - physical
  - wandering
  - toward self
  - toward objects
  - toward others
BPSD Epi

- up to 95% during course of dementia
  - most common: apathy, depression, agitation/aggression
- 43–59% during MCI
  - most common: depression, apathy, irritability
BPSD Characteristics

- >40% have multiple sxss
- often intermittent/persistent
- ~65% have sxss over 2 years
- association with dementia stage
  - shorter: hallucinations, disinhibition, euphoria
  - longer: apathy, aberrant motor, agitation
Agitation

- Often stage-specific
- Includes
  - verbal/physical aggression
  - repetitive/hyperactive talk, vocalizations, behaviors
  - disinhibition / inappropriate talk or actions
- ↑ disability, distress, injury, NH placement
Evaluating BPSD 1

- Routine surveillance
- ABCs: Antecedents, Behavior, Consequences
Evaluating BPSD 2: DICE
expert panel JAGS 2014

- Describe
- Investigate
- Create
- Evaluate
Evaluating BPSD 3

- Psychiatric diagnoses
  - delirium?
- Other medical diagnoses
- Role of pain / sensory impairments
- Meds
  - CNS drugs!
  - anticholinergics
  - withdrawals
  - interactions
Create a plan

- Collaboration: us, caregiver, patient
- Respond to modifiable factors
- Behavioral/environmental approaches generally 1\textsuperscript{st} approach
Evaluate the plan

- was it implemented?
- consequences of intervention
- ongoing monitoring over time
- is psychotropic med needed?
- is it still needed?
Treatments Overview

- Non-medication options promising but only short-term data
- Hard (+/− costly) to implement
- Meds have been disappointing
- Many have failed to show efficacy
- Some have had safety concerns
Non-pharm approaches 1

- Limit expectations
- Define from ABCs / D & I
- Limit damage / prevent risk
- Remove triggers
- Calm reassurance or distraction
- Address unmet needs
- Positive reinforcement
Non-pharm approaches 2

- activities schedule
- music therapy
- sensory interventions (eg, massage)
- person-centered communication skills training for caregivers
- maybe
  - pet therapy
  - aromatherapy
Pharm: Overview

- no drugs with FDA indications
- use after non-pharm, except
  - major depression
  - psychosis with harm potential
  - aggression with risk to self/others
Antipsychotics

- Meta-analysis in psychosis & agitation
  - modest effects
  - significant side effects

- Modest dose haloperidol (1–2 mg/d) ↓ psychosis ~60%

- 2nd generations suggest modest efficacy
  - clearest efficacy for risperidone, aripiprazole
  - ↑ CVAs, mortality
<table>
<thead>
<tr>
<th>Source</th>
<th>Dose, mg/d</th>
<th>Standardized Mean Difference (95% CI)</th>
<th>Favors Placebo</th>
<th>Favors Treatment</th>
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<tr>
<td><strong>Aripiprazole</strong></td>
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<tr>
<td>Mintzer et al,(^{14}) 2007</td>
<td>2, 5, 10</td>
<td>0.16 (0.05 to 0.37)</td>
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<td>De Deyn et al,(^{16}) 2003(^{a})</td>
<td>10 (mean)</td>
<td>0.06 (0.21 to 0.34)</td>
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<td>Streim et al,(^{15}) 2004 and Streim et al,(^{15}) 2006</td>
<td>8.6 (mean)</td>
<td>0.36 (0.11 to 0.61)</td>
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<tr>
<td><strong>Subtotal</strong></td>
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<td>0.20 (0.04 to 0.35)</td>
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<tr>
<td><strong>Olanzapine</strong></td>
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<td>De Deyn et al,(^{18}) 2004</td>
<td>1, 2.5, 5, 7.5</td>
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<td>Deberdt et al,(^{23}) 2005</td>
<td>5.2 (mean)</td>
<td>-0.02 (-0.27 to 0.23)</td>
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<td>Schneider et al,(^{52}) 2006 and Sultzer et al,(^{26}) 2008</td>
<td>5.5 (mean)</td>
<td>0.15 (-0.11 to 0.40)</td>
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<td>Street et al,(^{17}) 2000</td>
<td>5, 10, 15</td>
<td>0.30 (-0.03 to 0.63)</td>
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<td>0.12 (0 to 0.25)</td>
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<td><strong>Quetiapine</strong></td>
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<td>Schneider et al,(^{52}) 2006 and Sultzer et al,(^{26}) 2008</td>
<td>56.5 (mean)</td>
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<td>Tariot et al,(^{29}) 2002(^{3}) and Tariot et al,(^{48}) 2006</td>
<td>97 (median)</td>
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<td>Zhong et al,(^{54}) 2004 and Zhong et al,(^{39}) 2007</td>
<td>100, 120, 200</td>
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<td><strong>Risperidone</strong></td>
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<td>Brodaty et al,(^{31}) 2003 and Brodaty et al,(^{55}) 2005</td>
<td>0.95 (mean)</td>
<td>0.46 (0.23 to 0.69)</td>
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<tr>
<td>Deberdt et al,(^{23}) 2005</td>
<td>1 (mean)</td>
<td>-0.13 (-0.38 to 0.12)</td>
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<td>De Deyn et al,(^{30}) 1999</td>
<td>1.1 (mean)</td>
<td>0.12 (-0.14 to 0.36)</td>
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<td>Katz et al,(^{32}) 1999</td>
<td>0.5, 1.2</td>
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<td>Mintzer et al,(^{48}) 2006</td>
<td>1.03 (mean)</td>
<td>-0.01 (-0.21 to 0.18)</td>
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<td>Schneider et al,(^{52}) 2006 and Sultzer et al,(^{26}) 2008</td>
<td>1 (mean)</td>
<td>0.40 (0.13 to 0.68)</td>
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<td><strong>Subtotal</strong></td>
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<td>0.19 (0 to 0.38)</td>
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## Divalproex / Carbamazepine

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<tr>
<th>Study</th>
<th>Sample Description</th>
<th>Treatment</th>
<th>Outcome Measures</th>
<th>Duration</th>
<th>Comparison</th>
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<tr>
<td>Tariot P 2001</td>
<td>172 dementia nursing home and secondary mania</td>
<td>Valproate 20-30mg/kg/d</td>
<td>BRMS, CMAI, CGI</td>
<td>6 weeks</td>
<td>DVS=PBO</td>
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<td>Porsteinsson A 2001</td>
<td>56 nursing home dementia &amp; agitation</td>
<td>Valproate individualized vs. PBO</td>
<td>BPRS-agitation</td>
<td>6 weeks</td>
<td>DVS&gt;PBO ?</td>
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<td>Sival RC 2002</td>
<td>42 dementia hospitalized</td>
<td>Valproate</td>
<td>SADS-9 target aggression</td>
<td>3 weeks</td>
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<td>Tariot P 2005</td>
<td>153 nursing home pAD with agitation</td>
<td>Valproate target 750/d vs. placebo</td>
<td>BPRS, CMAI</td>
<td>6 weeks</td>
<td>DVS=PBO</td>
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<td>Hermann N 2007</td>
<td>14 AD—MMSE below 10</td>
<td>Valproate</td>
<td>NPI, CMAI</td>
<td>6 weeks</td>
<td>DVS&lt;PBO</td>
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<td>Tariot PN 1994</td>
<td>25 nursing home dementia</td>
<td>Carbamazepine modal 300mg/d vs. PBO</td>
<td>BPRS, CGIC</td>
<td>5+5 weeks</td>
<td>CRB&gt;PBO</td>
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<td>Cooney C 1996</td>
<td>6 AD outpatients</td>
<td>Carbamazepine up to 600mg/d vs. PBO</td>
<td>RAGE-agression</td>
<td>8 weeks</td>
<td>CRB&gt;PBO</td>
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<td>Tariot PN 1998</td>
<td>51 nursing home dementia</td>
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<td>BPRS, CGIC</td>
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<td>CRB&gt;PBO</td>
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<td>Olin JT 2001</td>
<td>21 AD failed antipsychotics</td>
<td>Carbamazepine</td>
<td>CGIC, BPRS</td>
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<td>CRB&gt;PBO</td>
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<td>Study</td>
<td>Population</td>
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<td>Primary Outcome</td>
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<td>Lawlor BA 1994</td>
<td>10 AD with agitation</td>
<td>Trazodone vs. Buspirone vs. PBO</td>
<td>BPRS DMAS</td>
<td>12 weeks</td>
<td>TRA&gt;PBO</td>
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<td>Auchus AP 1997</td>
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<td>Teri L 2001</td>
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<td>Lanctot K 2002</td>
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<td>Pollock BG 2002</td>
<td>85 hospital dementia</td>
<td>Citalopram vs. perphenzine vs. PBO</td>
<td>NBRS</td>
<td>17 days</td>
<td>CIT&gt;PBO</td>
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<td>Finkel SI 2004</td>
<td>24 pAD outpatients</td>
<td>Sertraline (24) vs. PBO (120) after open donepezil</td>
<td>NPI CGI-I</td>
<td>8 weeks then 12 weeks</td>
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<td>Sultzer DL 1997</td>
<td>28 dementia</td>
<td>Trazodone vs. haloperidol</td>
<td>Agitation</td>
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<td>Gaber S 2001</td>
<td>23 nursing home dementia and agitation</td>
<td>Sertraline vs. haloperidol</td>
<td>CMAI</td>
<td>10 weeks</td>
<td>SER=HAL</td>
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<td>Pollock B 2007</td>
<td>103 hospitalized, moderate+ NPS</td>
<td>Citalopram vs. risperidone</td>
<td>Neurobehavior Rating Scale (NBRS)</td>
<td>12 weeks</td>
<td>CIT=RIS in efficacy but CIT&gt;RIS in tolerability</td>
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other drug classes

- BDZs: beware!
- Lithium: beware!
- Buspirone: ?
- Stimulants: beware
- Cholinesterase inhibitors: +/-
- Memantine: ? delays onset of aggressive behaviors
case vignettes
Patient 1

- 76 y/o female, admitted to NH 2 months ago
- AD, now “early severe”
- admitted d/t anxiety, irritability, aggression toward husband
more hx

PMH: spinal stenosis, chronic neuropathic pain, HTN, hyperchol, DJD

remote h/o “mood d/o” tx’d with TCAs, haloperidol

SH: married, 2 adult children, former secretary
Assessment

- PE: LE weakness/dysesthesias, gait impaired, bilateral palmomentals
- MMSE 7/30, limited communication, no psychosis, intermittent psychomotor restlessness
- insomnia; impulsive aggression w/o clear triggers
Medications

- amitriptyline 50 mg qhs
- donepezil 5 mg qd
- memantine 10 mg bid
- lorazepam 0.5 mg IM prn agitation
- metoprolol, simvastatin, ASA 81 mg, APAP
Patient 2

- 63 y/o male LTC resident referred for exhibitionism, masturbation, sexual advances toward residents/staff, combative with care, insomnia, cross-dressing
- Urinating in flower pots
- Wanders aimlessly, rummages
- Staff apprehensive, feels he is manipulative
more hx

- Dx FTD (? Pick’s)
- PMH: TBI 30 years ago, GERD, glucose intolerance
- h/o brief EtOH abuse
- no PH of problematic sexual behavior
- married, former forensic psychologist
assessment 1

- MMSE 13
- very distractible
- severe psychomotor restlessness
- executive dysfxn
- expressive language deficit
- no delusions/halluc
- no insight
assessment II

- bilateral palmomental, grasp, root reflexes
- paratonia bilaterally
- mild bilateral cogwheel rigidity, resting tremor
- routine labs wnl
medications

- risperidone 1.5 mg qhs
- omeprazole 20 mg qd
- lorazepam 1 mg bid & 0.5 mg bid prn agitation
Patient 3

- 84 y/o married male, referred by NH for psychotherapy to adjust to stroke disability

- Right hemisphere CVA 7 months earlier, since then:
  - Emotional lability (tearful, irritable, anxious)
  - Intermittent helplessness / hopelessness
  - Insomnia
  - Wandering (into street)
  - Cognitive deficits (exec dysfxn, visuospatial, language and attention relatively preserved)

- PMH – CVA as above, MRI also showed right thalamic infarcts; atrial fibrillation; BPH; DJD s/p TKRs

- SH – retired foreman; obtained college degree in his late 40s. Widowed x 1, 2nd wife very supportive, takes him on o/n passes, despite his accusations otherwise
Exam

- MSE – depressed and irritable, ruminative about desire to leave NH, 19/30 on MMSE. Poor insight – “no” when asked if his CVA left him paralyzed in any way.

- Neuro – dense left hemiplegia. Needed reminders to tend to his left. Right–left disorientation, limited recognition of left UE, double simultaneous extinction in left UE.