At the Diagnostic Crossroads of Behavior and Cognition

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Why do we get consulted?

• Behavioral disturbance

  • Capacity evaluation: medical “non-compliance”, ability to live alone, ability to refuse care, drive

  • Late onset depression (1st episode after age 65)

  • Longstanding mood/psychotic disorder now medically complex and to help with polypharmacy
**Objectives**

- Describe the prevalence of most likely causes of behavior change at different ages
- Discern the clinical importance of function over diagnosis
- Explain that new onset behavior change in the absence of medical illness is most often a sign of dementia in older adults
- Give examples that a DSM-V diagnosis can and should be used to guide care, but that functional status should drive treatment planning

**Lots of overlap**

Other contributors: delirium, substance use

- Dementia (neurodegenerative vs. TBI)
- Chronic psychiatric illness
- Behavioral disturbance
What are “behaviors?”

Dictionary: observable activity; aggregate of responses to internal or external stimuli
- Can extrapolate to “unmet need”

- Alzheimer's Association includes: aggression, agitation, confusion, depression, suspicion, hallucinations, sundowning, repetition, wandering

ABC’s of behavior

- Antecedent
- Behavior
- Consequences

- What exactly happens before, during and after? Is there a pattern?
Unmet needs

- Boredom
- Comfort: pain, hunger, thirst, constipation, fatigue
- Response to change in environment
- Acute medical illness (is the change sudden?)
- Medication side effects/interactions

  *Is the patient declining in general? Is it time for a more structured environment? to revisit goals of care?*

What do we think?

Mr. A is coming in today for “behaviors…”

I hope I have a longer appointment!

Will he need placement? Where will we find a bed?

His poor wife – she can’t take another thing
How to sort it out?

- Past psych hx?
- Known dementia?
- What is specific behavior (s)?
- New, old, same, worse?
- Does it place pt. and /or caregiver at risk of harm?
- Is it distressing? To whom – pt. or others?

Apathy: Dementia vs. depression
Mr. A

- 71 years old, married
- CC: “not interested in anything anymore”; wife’s cc: “won’t get off the couch”
- Wife states he is lazy now, only does things when “nagged”

PHQ-9 = 12 (mod depression)
MOCA = 25 (mild range)

Further interview and history….

Version 1 Mr. A

- HX depression and PTSD, two remote past hospitalizations for SI
- Generally healthy – no current meds
- 7th grade education
- Recently retired from landscape business
- Never had any hobbies
- Mood subjectively no better or worse than usual
- Stopped antidepressants “a few years ago” didn’t find them helpful
- Pays bills reliably, drives without incident and helps take care of grandkids
Version 2 Mr. A

- No psychiatric history
- PMH: obesity, DM and had MI 2 years ago; 7 meds
- College grad
- Working part-time as admin manager of small business, boss recently encouraged him to cut back
- Dropped out of rotary club and relinquished his HOA presidency this year “I've already given enough”
- Wife takes care of bills – “for last several years – because I’m tired of doing them”

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Version 1 – diagnostic thinking

- Probable scenario is that Veteran has chronic depression, may benefit from medication /other EBP interventions
- He is also newly retired with limited interests and education and may be bored
- +/- dementia onset

- Treatment recs:
  - Discuss goals of care and preferences for treatment; SSRI plus/psychotherapies for depression
  - Encourage lifestyle changes to increase socialization, structure and purposeful activity
  - Healthy brain habits
  - Repeat cognitive testing in 6 months to assess for possible dementia component

Version 2 Mr. A

- No psychiatric history
- PMH: obesity, DM and had MI 2 years ago; 7 meds
- College grad
- Working part-time as admin manager of small business, boss recently encouraged him to cut back
- Dropped out of rotary club and relinquished his HOA presidency this year “I’ve already given enough”
- Wife takes care of bills – “for last several years – because I’m tired of doing them”
Version 2 – diagnostic thinking

- Probable scenario is that Veteran has vascular dementia
- He has vascular risk factors, large cognitive reserve and current apathy; also withdrawing from activities that require complex thinking and executive function (IADL’s)
- +/- depression; likelihood of response to meds is low

- Treatment recs:
  - Discuss goals of care and preferences for treatment; CHEI could have modest efficacy given mild-mod stage
  - Education to pt./family on dementia; set expectations
  - Encourage lifestyle changes to increase socialization, structure and purposeful activity
  - Healthy brain habits – particular attention to vascular health
  - Repeat cognitive testing in 6 months

Apathy:  Depression, Dementia or both?

- Apathy is the most common neuropsychiatric behavior with dementia (up to 75% of patients with AD)

- Higher levels of apathy associated with greater cognitive impairment, more comorbidities, older age, and more impaired ability to perform ADLs

- Apathy at baseline in patients with AD is a significant predictor for more rapid decline in functional status
Pseudodementia reconsidered

- Among treated people with late-life depression, even if cognitive symptoms remit, the risk of progressive dementia in the ensuing years as high as 60%.

- Antidepressant trials in AD dementia do not show improvement of cognitive symptoms and have produced disappointing results about antidepressant efficacy in general.


Do Antidepressants work for depression in patients with dementia?

- Previously mixed studies and an inconclusive Cochrane review
  - Depression in Alzheimer Disease Study (DIADS) assessed Sertraline (SSRI) in 44 patients and found small benefit to treatment
  - DIADS-2 (Sertraline for the treatment of depression in Alzheimer’s disease, 2010) compared 67 patients on sertraline to 64 on placebo and found no benefit at 12 or 24 weeks
  - Systematic review and meta-analysis of 6 studies: evidence equivocal
Depression of Dementia

- Banerjee, Lancet 2011; 378: 403–11
  - Largest trial to date: 208 people with AD and depression
  - No difference at 13 or 39 weeks in sertraline (∼100mg) or mirtazapine (∼30mg) compared with placebo – all improved
  - Adverse reactions/dropouts: sertraline > mirtazapine > placebo
  - Confirms previous negative trials (sertraline, TCA’s)

“Because of the absence of benefit compared with placebo and increased risk of adverse events, the present practice of use of these antidepressants, with usual care, for first-line treatment of depression in Alzheimer’s disease should be reconsidered.”

Agitation: delirium vs. dementia
Ms. S

- 83 years old, single
- CC: “loud neighbors – and the police won’t do anything about them– said I needed to get seen”
- Friend states she calls the police at least weekly

PHQ-9 = 6 (mild depression)
MOCA = 18 (mod range)

Further interview and history….

Version 1 Ms. S

- HX schizophrenia and medication non-adherence
- Smoker and poor self-care – can’t remember what meds she takes but endorses HTN
- HS grad and has lived alone whole life, no family
- Wet cough and elevated BP on physical exam
- Mood “fine” subjectively – looks disheveled, distracted, but is logical and calm; states neighbors are new and she hears them selling drugs from their house (police say house is vacant)
- In Section 8 housing with a payee, has never driven
Version 2 Ms. S

• Past psych hx – remote depression in 20’s
• Lives in supportive retirement community
• HS grad and widowed in last year
• Mild CHF and MD, on 4 meds, stable
• Mood “frustrated” subjectively – looks disheveled, distracted, but is logical and calm; states neighbors are new and she is worried they are selling drugs from their house (police say house is vacant)
• Friends say she has slowly become more unlike herself in last few years and describe her as paranoid and more isolative

Version 1 – diagnostic thinking

• Probable scenario is that she has psychosis r/t med non-adherence now made worse by dementia
• Delirium must also be considered given likelihood of poor overall health, cough and HTN
• +/- kernels of truth abut neighbors

• Treatment recs:
  • Full medical evaluation – correct treatable problems
  • Resume/consider antipsychotic
  • OT assessment and more info on neighbors
  • May reflect grave disability?
Version 2 – diagnostic thinking

• Probable scenario is that she has psychosis r/t dementia
• Delirium must also be considered given CHF and MD
• Age, slow onset and paranoia (as predominant psychotic sx) consistent with dementia +/- depression

• Treatment recs:
  • Full medical evaluation – address treatable conditions
  • Psychoeducation about dementia to pt., caregivers, community – rally any potential supports

  • May reflect grave disability?

Do antipsychotics work?
CATIE-AD TRIAL
Schneider et al, NEJM October 12, 2006

• Average age 78, average MMSE 15; required agitation, psychosis or aggression
• Most required ALF or NH level of care
• RCT to Olanzapine (mean dose 5.5 mg) Risperidone (1.0 mg), Quetiapine (56.5mg) or placebo
• 82% stopped meds – on average in 5-8 weeks
• NO clinical difference between groups
• Authors concluded: “Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer’s disease.”
Black box warning
(now for all antipsychotics)

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 times to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared with a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature.

Antipsychotics linked to AKI

Atypical Antipsychotic Drugs and the Risk for Acute Kidney Injury and Other Adverse Outcomes in Older Adults: A Population-Based Cohort Study

Y. Joseph Hwang, MSc; Stephanie N. Dixon, PhD; Jeffrey P. Reiss, MD, MSc; Ron Wald, MD, MPH; Chirag R. Parikh, MD, PhD; Sonja Gandhi, BSc; Salimah Z. Shariff, PhD; Neesh Pannu, MD, SM; Danielle M. Nash, MSc; Faisal Rehman, MD; and Amit X. Garg, MD, PhD Ann Intern Med. 2014;161(4):242-248. doi:10.7326/M13-2796

- relative risk [RR]: 1.73
- Quetiapine, olanzapine, risperidone
- For hospitalization related to AKI in first 90 days of use
### Receptor affinities

**TABLE 1. RELATIVE RECEPTOR AFFINITIES OF ATYPICAL ANTIPSYCHOTIC DRUGS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>D₁</th>
<th>D₂</th>
<th>D₃</th>
<th>D₄</th>
<th>α₁</th>
<th>α₂</th>
<th>H₁</th>
<th>ACh</th>
<th>5-HT₁</th>
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<th>5-HT₁₀</th>
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<tr>
<td>Clozapine</td>
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<td>Risperidone</td>
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</table>

Dopamine receptors: (D₁, D₂, D₃, D₄) 5-HT receptors: (5-HT₁, 5-HT₂, 5-HT₁₀) Acetylcholine (ACh). +++ very high affinity, ++ high affinity, + moderate affinity, ! low affinity, — negligible affinity. Table adapted from: Ameis S, Paramore I, Marder E. Curr Pharm Des. 2004;10:2285-2217.

### Common sense about prescribing antipsychotics in late life

It is hard to justify (especially in court) using a medication that:

* Does **NOT** have an FDA indication for dementia
* Shows **no clear benefit**
* Has many unfavorable side effects
* Increases the risk of adverse events and death
Trajectory of disease

- Chronic schizophrenia: typically steady with periodic episodes of psychosis and return to baseline; SMI can be associated with executive dysfunction and cognitive slowing over time

- Dementia: degenerative and progressive with periodic behavioral manifestations that change over time and continual decline of overall function

- MDD plus PTSD plus TBI plus toxic exposures plus vascular disease plus recent cancer plus family stressors...???

Final common pathway = symptom

Behavioral disturbance
How to sort it out?

- Past psych hx?
- Known dementia?
- What is specific behavior (s)?
- New, old, same, worse?
- Does it place pt. and/or caregiver at risk of harm?
- Is it distressing? To whom – pt. or others?

Henry
Summary

• Attempt diagnostic clarification
• Address safety issues (potential violence and/or self care)
• Optimize general medical care
• Identify potentially treatable target sx.
• Focus on unmet needs
• Determine goals of care and facilitate strategy

• REPEAT
Measures of success

- Communicating realistic expectations about medications and prognosis
- Eliciting and honoring goals of care – help make plan
- Actively contributing to safe transitions and delirium prevention
Positive aging – University of Wisconsin Institute on Aging -- Carol Ryff PhD

• Redefining “well being” by discerning “eudaimonic” from “hedonic” formulations [PURPOSE vs. HAPPINESS]

• EUDAEMONIA – personal happiness according to the greeks… meaning “human flourishing”; highest human good; lit. “having a good indwelling spirit” –
• In moral philosophy it refers to having right actions that result in well – being
• Activity of the soul in accord with virtue
• Core aspects of being human

• Having PURPOSE protects BRAINS and HEALTH

Ryff's model of psychological well-being
MIDUS study – midlife in the US

- Started in 1995 with 7000 respondents aged 25-85 – still going!
- First to link psychosocial and behavioral factors to health
- Identified factors that promote positive health and resilience

- PURPOSE (and well-being) PWB predicts morbidity and mortality – PWB moderates expected decline in satisfaction with chronic illness, shortens recovery from illness

- AND protects against AD and MCI

www.midus.wisc.edu

What is well-being based on Eudaimonia?

- Having positive relationships
- Feeling good about yourself
- Looking forward to the future
- Feeling engaged in work, fun and community
- Being active
Lighten UP

- 8 week group CBT sessions – 90 minutes
- FOCUS is on **well-being** and identifying obstacles to it, including principles of stopping automatic negative thoughts and savoring the positive
- Decreased depression, loneliness
- Increased health behaviors
- Positively impacted inflammatory markers

- Implications are huge and proactive

*Friedman et al., 2015 Aging and Mental Health*