Mental Health Problems in Dementia

Understanding the combination of preexisting psychiatric illness and dementia
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Disclosures

• Speaker’s Bureau for Forest (Viibryd)

Previously on Speaker’s Bureaus for:
AstraZeneca (Seroquel XR)
Lilly (Cymbalta, Zyprexa, Differential Diagnosis)
Phizer (Pristiq)

• I will be mentioning “off-label” uses of medications.
• I have not “friended” any Pharmaceutical companies on Facebook
More individuals with chronic mental illnesses are surviving to be seniors

- Schizophrenia
- Major Depression
- Bipolar Illness
- Anxiety illnesses (including PTSD and OCD)
How seniors differ from younger adults

As we age:

– We have less lean muscle mass
– We have a larger percentage of fat
– We metabolize drugs at a slower rate
How seniors differ from younger adults

– Our cognitive reserve drops, and we are more sensitive to insults that cause confusion (Delirium)
– Our dopamine system loses neurons. This lessens our *drive*, and makes us more sensitive to extra-pyramidal and Parkinsonian symptoms or side effects
– Our balance becomes less secure
– Our bone thinning increases (Worse balance + Thinner bones = Trouble)
How to approach people with chronic mental illness who have dementia

• The same way we approach anyone else; get to know them, find their strengths, identify things to like and respect about them, and enjoy those things. Be aware of their problems and difficulties.
Schizophrenia
Successful Aging

Defined as the absence of disability accompanied by high levels of physical, cognitive, and social functioning
– One in five (20%) of the general senior population
– One in fifty (2%) of seniors with schizophrenia
Frequency

- Between 0.1% and 0.3% of seniors have Schizophrenia (the rate of Schizophrenia worldwide is 1%)

- Middle aged persons with Schizophrenia are 4 times more likely to be in nursing homes when compared to age-matched peers without mental illness

- In spite of the above, 85% of older people with Schizophrenia live in the community
What is the course of Schizophrenia in seniors?

• Less impact from positive symptoms (hallucinations and delusions) with age
• More “verbal underproductivity”
• More cognitive decline (“neurodevelopmental”, not degenerative)
What is the course of Schizophrenia in seniors?

• Continued impact of co-morbid illnesses (i.e., diabetes, smoking related illnesses). This is a preview (foreshadowing)

• Prolactin increase from neuroleptics may lead to more bone demineralization (and thinner bones are already a problem)
Seniors with Schizophrenia

- As cognition worsens and speech production decreases, patients may have less insight about their illnesses and symptoms, and less ability to report symptoms
Seniors with Schizophrenia

- Caregivers need to assume more of a proactive role in anticipating the needs of our patients.
- What kind of wheel gets the grease? We need to “squeak up” for our patients or family members.
Social Functioning in Seniors with Schizophrenia

- Social functioning is more tied to cognitive status than it is to the positive or negative symptoms of schizophrenia
Schizophrenia

Why does dementia so often accompany Schizophrenia in seniors?

A. Dementia Praecox (the ongoing cognitive problems from Schizophrenia)

B. Many co-morbidities of Schizophrenia are risk factors for a dementia
Co-Morbidities in Schizophrenia: Medical

• The most common medical co-morbidities in Schizophrenia and Bipolar Illness are the illnesses most commonly seen in the general senior population.
Co-Morbidities in Schizophrenia: Medical

• Medical co-morbidities seen more frequently in Schizophrenia than in the general population include:
  – Diabetes: 1.5 to twice the risk
  – Metabolic Syndrome: 3 times the risk
  – Arrhythmia: 1.5 times the risk
  – Syncope: 4 times the risk
  – Heart Failure: 1.7 times the risk
  – Stroke: 2 times the risk
  – TIAs: 2.6 times the risk
Co-Morbidities in Schizophrenia
Medical (continued)

– Hypothyroidism: 2.6 times the risk
– COPD 1.9 times the risk
– Hepatitis C: 7 times the risk
– Nicotine dependence: 2.8 times the risk
– Obesity: 40-60% of people with Schizophrenia
Co-Morbidities in Schizophrenia: Psychiatric

– Alcoholism and substance abuse: 47%
– Depression: 50%
– Panic disorder: 15%
– PTSD: 29%
– OCD: 23%
– The rate of “GAD” is also quoted as high
Co-morbidities

• Many, if not most, of these conditions are not recognized. If they are recognized, they may be undertreated, or they might not be treated at all.

• Co-morbid conditions worsen over time, adding to the total illness burden, adding to problems accessing care and affecting mobility and other disabilities.
Risk Factors for Vascular Dementia and/or Alzheimer’s disease

• Hypertension
• Hyperlipidemia
• Diabetes
• Smoking
• Depression
• Head Injury
Risk Factors for Vascular Dementia and/or Alzheimer’s disease

- Alcoholism
- Genotype (ApoE4)
- Chemical exposure (such as organo-phosphates)
- Lower educational level
- Oxidative stress
- Inflammation
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<th>Schizophrenia Co-morbidities</th>
<th>Dementia risk Factors</th>
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Therefore:

• People with Schizophrenia are at a lot of risk for developing cognitive loss – both from the Schizophrenia itself, and from the co-morbid illnesses that are risk factors for other dementias.

• Treatments exist to slow down and delay progression of Alzheimer’s disease and other dementias. These are Acetylcholinesterase (Cholinesterase) Inhibitors (Donepezil (Aricept), Rivastigmine (Exelon), Galantamine (Razadyne)) - and the Glutamate affecting med, Memantine (Namenda)

• These medications are under-used in patients with mental illness (including Schizophrenia) who have Alzheimer’s Disease or Vascular Dementia
Altered perceptions (hallucinations, delusions, false beliefs) in schizophrenia and dementia are usually different in nature, have different causes, and are approached and treated differently.
Schizophrenia vs. Dementia

- **Schizophrenia**
  - Psychotic symptoms are consistent with past symptoms
  - Hallucinations more likely to be auditory
  - Slower progression (after age 65, 1 MMSE point/year)
  - Psychotic symptoms are dopamine related and neuroleptics are likely to be effective

- **Dementia**
  - Psychotic symptoms are different than past symptoms
  - Hallucinations more likely to be visual
  - Faster progression (2-3 MMSE points/year)
  - Psychotic symptoms are not likely to be dopamine related and neuroleptics are unlikely to be effective
Schizophrenia vs. Dementia

• Compared to Alzheimer’s Disease patients, patients with Schizophrenia demonstrated worse performance on naming and tests of constructional praxis, and better on tests of delayed recall.
Constructional Praxis

This is a task which requires three dimensional manipulation. Adults may prefer to attempt to assemble things that come “Assembly Required” using guesswork or give it to someone else to put together. Constructional praxis makes it much harder to transfer from a two dimensional design to three dimensional project.
Schizophrenia (and other mental illnesses) and Aging

• Cognitions may worsen from several causes
• Co-morbid illnesses and their complications may worsen over time
• Side effects of medications may worsen due to brain changes and metabolic changes – dosages may need adjustment
• Falls are a risk
Agitation in People with Schizophrenia and Dementia

• Treating Schizophrenia symptoms are a legitimate role for neuroleptics
• Agitation from schizophrenia looks like past schizophrenia symptoms (i.e. auditory hallucinations, recurrent delusions)
• Agitation from dementia shows newer symptoms (i.e. visual hallucinations)
• As a person with schizophrenia ages, positive symptoms decrease, negative and cognitive symptoms increase, and sensitivity to EPSE and Parkinson’s like symptoms increases
If the Agitation is due to Dementia in People with Schizophrenia and Dementia

- Try to decrease anticholinergic meds, stop benzos
- Use the Cholinesterase Inhibitors and Memantine
- Try to encourage using glasses, hearing aids, or correcting visual problems if present
- Use medications to decrease anxiety about the hallucinations or delusions (gabapentin, buspirone)
- Consider neuroleptics carefully. Avoid them if able. These symptoms *may be* “dopamine related” and respond, or they may not be. Warning to follow
- Theory: improve thinking, and the hallucinations will lessen
Neuroleptics: The Mortality Warning
Increased Mortality in Elderly Patients with Dementia-Related Psychosis

- 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 antipsychotics, revealed a risk of death in drug-treated patients of between 1.6 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 to 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 or sudden death) or infectious (eg, pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patient is not clear. This Neuroleptic is not approved for the treatment of patients with dementia-related psychosis.

(Class warning from a product insert)
Possible Mechanisms of Neuroleptic Related Increased Mortality in Dementia

- Aspiration secondary to EPSE affecting swallowing.
- Falls from Parkinsonianism.
- Falls from postural dizziness.
- Cardiovascular from prolonged QT interval.
- Ion channel disruptions (K+, Ca++) secondary to Dopamine D2 blockade (possible cause of prolonged QT).
- Sicker people may be prescribed neuroleptics for agitation that becomes “unmanageable” as they are dying.
- Death secondary to blood clots (a newly recognized potential side effect from neuroleptics).
- “All cause mortality” is greater from the “typicals” than from the “atypicals” (Liperoti, 2009)
What “The Warning” does NOT say:

• “On-label” use of neuroleptics for treating Schizophrenia and Mood Illness does not carry “the warning”, and may be lifesaving.

• In spite of the above, risks of prescribing neuroleptics “on-label” do exist and we should use lowest doses possible. Most of the proposed mechanisms of increased mortality listed on the previous slide are not limited to dementia patients or “off-label” situations.

• Use of the older “typical” neuroleptics is as dangerous, or worse, than use of newer neuroleptics (Liperoti, 2009).
Specific Agitation: Restlessness

• Look for physical causes
• Lower or remove neuroleptics, or look for less parkinsonian neuroleptics
• Treat with medications for Parkinson’s disease
  – Sinemet (Carbidopa-Levodopa). Start with 10/100 three times/day. Watch for hypersexuality.
  – Requip (Ropinirole). Start with 0.25 mg. 3 times/day
  – Mirapex (Pramipexole). Start with 0.125mg. 3 times/day

Consider Hydroxazine/Vistaril as a PRN
Schizophrenia and Dementia

• Individuals with Schizophrenia have many risk factors for dementia

• Treat both if present
  – Treat Schizophrenia symptoms with lowest possible dose neuroleptics
  – Treat Dementia with cholinesterase inhibitors and memantine, and by reducing anticholinergic load
  – Tailor the neuroleptics to the side effects the patient is most sensitive to (EPSE, hypotension, sedation).
Agitation in Schizophrenia and Dementia

The answer to agitation may be less neuroleptic, *not more*. Other meds for agitation, as well as behavioral techniques, may serve everyone better.

Visual hallucinations are more likely to be a product of visual problems plus cognitive loss, not “dopamine-related psychosis” from the Schizophrenia
Treating the Schizophrenia

• Neuroleptic doses may need to be decreased with age and more sensitivity to Parkinson’s disease.

• Tailor the neuroleptic to the physical side effects your patient is most prone to.

• Be aware that agitation and restlessness might be from neuroleptics, dementia, or medical illness and adjust care accordingly.
Depression
Depression and Dementia

• Depression and Dementia frequently co-exist
• Depression itself may be a risk factor for Dementia
• Look for the “classic” depression symptoms of sad mood, tearfulness, sleep changes, appetite changes, suicidal comments
• Isolating in your room may and decreased conversations/interactions may be from Dementia, not depression.
Treating Depression in Dementia

• Antidepressants may be helpful, but remember to use low doses, and watch for agitation side effects of antidepressants:
  
  A. Mania or hypomania
     (sexual inappropriateness, insomnia, intrusiveness, increased speech production, irritability)
  
  B. Serotonin-related agitation (may look like other deliriums)

Avoid tricyclic antidepressants such as Elavil/Amitriptyline due to cognitive and cardiac effects
Treating Depression in Dementia

- Look for co-morbid pain
- Screen for Bipolar personal or family history before you start antidepressants
- Use low doses of antidepressants
- I frequently use dual action meds, and frequently use Mirtazapine
- If pain is present I will look at using Cymbalta, Pristiq, or Effexor (dual action agents)
- Avoid TCAs due to anticholinergic and alpha blocking side effects
- Monitor, monitor, monitor
Antidepressants, Seniors, and New Onset Mania

It is common for a senior to live for 70 years without a mood episode, and then to lose spouse, health, home, and memory all within a brief period of time. They develop their “first ever” depressive episode. Antidepressants are started appropriately (along with psychotherapy if cognitions allow), but one or two months later they are intrusive, insomniac, irritable, hyperverbal, and hypersexual. They are admitted to me with “agitation in dementia”, often after a trial of increasing the antidepressant.
Bipolar Illness

• Untreated bipolar illness may worsen in Seniors – not “burn out”

• Mania in Seniors presents with more confusion, and irritability.
Bipolar Illness and Dementia

• More individuals with bipolar illness are living to become seniors, and concurrent dementia can occur.
Bipolar Illness and Dementia

• Symptoms of bipolar Illness can be “depression”, or the manic or hypomanic symptoms of:
  • Confusion
  • Decreased sleep
  • Increased speech production
  • Irritability
  • Increased motor activity
  • Intrusiveness
  • Impulsiveness
  • Sexual Inappropriateness/Hypersexuality
Co-morbidities in Bipolar Illness

• Medical illnesses that are more common in Bipolar Illness include:
  – Diabetes (5-17%)
  – COPD (6%)
  – Hypertension (10-35%)
  – HIV (2.8%)
  – Hepatitis C (1.9-5.9%)
  – Obesity (35%)
Psychiatric Co-Morbidities Seen in Bipolar Illness

- ADHD (10-20%)
- Alcohol Abuse 46%
- Substance Abuse 41%
- Generalized Anxiety Disorder 11-42%
- Obsessive Compulsive Disorder 3-39%
- Panic disorder 7-33%
- Phobias 10-26%
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- Hypertension
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- Smoking
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Risk Factors for Vascular Dementia and/or Alzheimer’s disease

- Alcoholism
- Genotype (ApoE4)
- Chemical exposure (such as organophosphates)
- Lower educational level
- Oxidative stress
- Inflammation
Dementia and Bipolar Illness

Bipolar Illness Co-morbidities

Diabetes (5-17%)
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**Hypertension (10-35%)**
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Dementia Risk Factors

- Alcoholism
  - Genotype (ApoE4)
  - Chemical exposure
  - Lower educational level
  - Oxidative stress
  - Inflammation
- Hypertension
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- Smoking
- Depression
- Head Injury
Specific Agitation: Sexual Inappropriateness

• Differential Diagnosis:
  – Hypomania or mania
  – Disinhibition
  – Perpetrators grown old
  – From Parkinsonian’s treatment medications (i.e., Sinemet)
Sexual Inappropriateness: Mania or Hypomania

• This may be a part of the brain degeneration (i.e., a manic behavior pattern develops).

• Stop the antidepressant if present.

• Treat the syndrome: mood levelers, newer antipsychotics (as secondary option).
Sexual inappropriateness: Disinhibition

- Hormonal therapy – Provera (or other).

Side effects include changes in fat distribution, increased risk of breast cancer.
Sexual inappropriateness: Perpetrators Grown Old

• Provera (or other hormonal therapy)
Anxiety and Dementia

• Anxiety can come from dementia, for example a person might not be sure what is happening, not be able to remember sources of security.
• Cognitive approaches that patients use to manage anxiety may be unavailable in the context of a dementia
Anxiety in Dementia

• Reassurance might be of help to a person for only a short time interval, and frequent reassurance may be needed.
Anxiety in Dementia

Pharmacological treatment of anxiety changes with aging:

• Benzodiazepines (i.e., Ativan) become dangerous to seniors, causing falls and poorer memory

• Antidepressants may cause agitation from serotonin reuptake or from hypomania, and lower doses will be needed

• Treatments such as gabapentin, buspirone, and ‘alpha” adrenergic blockers might be more useful
Treating the Agitation in Dementia
Meds to Treat Agitation: The Literature & Clinical Experience

• Valproic Acid
• Gabapentin
• Alpha Blockers and Agonists
• Buspirone
• Carbamazepine & Oxcarbazepine
• Trazodone
• Antidepressants
• Melatonin
• Neuroleptics (more to follow).
Valproic Acid (Depakene or Depakote)

- Mixed reviews in the literature. Most papers note that the side effects limit usefulness
  - I find it helpful for mood related agitation, or aggression.
  - I believe the studies dosed it too high. My experience with lower doses is more positive.
  - Use Sprinkles for people who can’t swallow or hate pills, start 125mg. three times/day.
  - Use “DR” form for those who can take pills, use either Sprinkles or DR form in the pm for sundowners.
  - Use “ER” form for those who can swallow and are agitated throughout the day, start with 250mg. or 500mg.
  - Watch for decreased appetite or liver problems. Excessive sedation may be from high ammonia levels.
  - Check Valproate levels for toxicity. Low blood levels are ok if the patient is doing well.
  - Some movement disorders/Parkinsonian syndromes can develop
Gabapentin (Neurontin)

• Most studies and reports are positive (note: this med has a history of being falsely promoted for off label uses, and some of the literature is suspect in my view)
  – I use this for anxiety or pain related agitation.
  – Start with liquid, 50mg. three times/day with meals.
  – It can build up rapidly if the kidneys do not work. It is kidney metabolized.
  – Watch for sleepiness and edema (10%).
Alpha 2 Agonists/Alpha 1 Blockers: Guanfacine (Tenex) and Prazosin (Minipress)

• Most literature reports are positive
• The theory is that enhanced behavioral reactions to centrally released norepinephrine occurs in Alzheimer’s Disease (Wang, 2009)
• Start with 1mg. of either medication daily, and increase the dose every few days (if in the hospital) or weekly (if in the nursing home).
• Propranolol (Beta Blocker) or Clonidine (Catapres) may also be useful
• Watch for low blood pressure, low pulse, or dizziness.
• I use these for aggression primarily
Buspirone (Buspar)

- Most literature reports are positive (mixed results)
- Start with 5mg. two or three times daily
- Watch for sedation, EPSE
- I use this for anxiety-related agitation
Carbamazepine

- Good literature reports
- Start with 100mg. twice daily
- Drug-drug interactions limit its use – I always need to look them up.
- I use this for mood-related agitation, pain-related agitation, or aggression
- Watch for low sodium (6% in seniors), sedation, serious skin reactions, and loss of white blood cells
- Check blood levels (for toxicity) and CBC, low blood levels are ok if the patient is doing well
- To avoid drug-drug interactions, I often use Oxcarbazepine (Trileptal) starting at 75mg. twice daily. Only a little literature support exists (one or two studies).
Daytime Trazodone

- Few articles exist, *all of the ones that I found were positive.*
- May calm some anxious or aggressive people.
- Watch for sedation.
- Watch for manic or hypomanic reactions, red eyes/stuffy nose, priapism (yup, even in seniors).
- It compared equally to Haldol in one study, and better than buspirone in another study (for what that is worth!).
Antidepressants

• Good literature support.
• Useful for anxiety or depression related agitation.
• Start with low doses.
• Due to the problems that patients with dementia have with insomnia and “the dwindles”, my “secret weapon” is Mirtazapine (Remeron).
• Dual action meds (Duloxetine/Cymbalta; Desvenlafaxine/Pristiq; possibly Venlafaxine/Effexor) may help with co-morbid pain syndromes.
• Watch for serotonin-related agitation or manic reactions. Nursing home staff may not recognize agitation as being caused by a manic reaction.
Antidepressants, Seniors, and New Onset Mania

It is common for a senior to live for 70 years without a mood episode, and then to lose spouse, health, home, and memory all within a brief period of time. They develop their “first ever” depressive episode. Antidepressants are started appropriately (along with psychotherapy if cognitions allow), but one or two months later they are intrusive, insomniac, irritable, hypervocal, and hypersexual. They are admitted to me with “agitation in dementia”, often after a trial of increasing the antidepressant.
Melatonin

• Mixed literature support (Of 4 randomized controlled studies, 2 were positive. Of 5 “case studies”, all showed improvement.

• Main use is 3mg. – 9mg. at bedtime

• Used for sundowning, and insomnia

• Rozerem (Ramelteon) also works on the melatonin receptor
Parkinson’s Disease or Syndromes

- Look for symptoms of shuffling gait, decreased arm swing, restlessness (“Doctor, order a med, the patient keeps trying to stand up!”), cogwheeling
- In my practice, restlessness is due to parkinsonian’s, pain, or bladder retention
- May be caused by neuroleptics, Compazine (Prochlorperazine), Reglan (Metoclopramide), antidepressants, Buspar (Buspirone), other meds, or idiopathic
- Treat with Sinemet (Carbidopa/Levodopa), Mirapex (Pramipexole), Requip (Ropinirole); consider Vistaril (Hydroxazine) as a PRN. Neuroleptics will make it worse.


Differences from my approach:

A. More emphasis on behavioral therapies
B. More favorable views of using neuroleptics and benzodiazepines
C. Less favorable view of anticonvulsants
D. The guidelines point out the less robust data on cognitive enhancers in vascular dementia
E. They are much more comprehensive, especially in areas of treatment plan, working with families, and data behind recommendations
I do not know everything. I know less every day. I tell families that I read the literature and go to meetings, and I hope I do as good, or as poor, of a job of treating this terrible condition as anyone else does. We all need feedback. I appreciate suggestions (or gasp) corrections.