



Psychosis in Parkinson's disease

Alice Flaherty MD, PhD
Associate professor of neurology and psychiatry
Mass. General Hospital, Harvard Medical School

Parkinson's Preceptorship Program
April 16, 2021

Disclosures

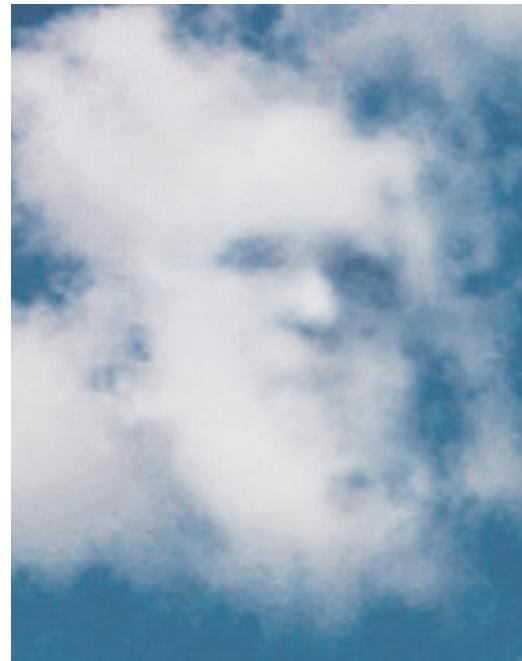
“Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.”

PD non-motor symptoms

- Autonomic: low BP, nausea constipation, incontinence, sweating
- Sleep: restless leg synd., REM behavior disorder, [vivid dreams]
- Cognitive: Distractible, bad multitasking (different from Alz.)
 - Perceptual: Dopamine's effect on perception:
 - Too little dopamine: dulled, disorganized
 - Too much: over-detailed, over-vivid
 - Can cause hallucinations and delusions

What is Parkinson's Disease psychosis?

- Psychosis requires abnormal perception + bad reality testing
- PD psychosis, NINDS-FDA definition, focuses on symptoms
 - Hallucinations: fixed false perceptions
 - Delusions: fixed false beliefs
- Psychosis is a spectrum



PD hallucinations are mostly visual

- Early: webbing over things; felt presence, dream intrusions
- Middle: +insight, small safe animals or kids, often multiple
- Late (with dementia): dead relatives you can talk to



How is PD psychosis different from others?

- **Alzheimer's:** visions of intruders, dead relatives
 - Some PD patients also have Alzheimer's
- **Depression:** delusions of bodily decay
- **Schizophrenia:** auditory command hallucinations
- **PTSD flashbacks:** repetitive reliving of trauma
- **Bonnet syndrome**



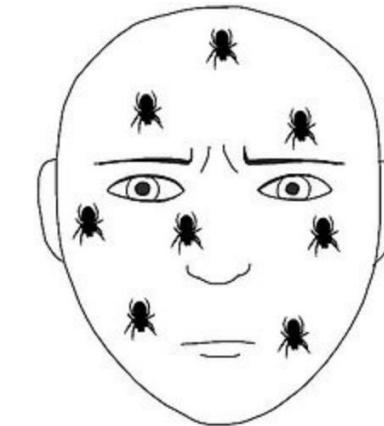
PD psychosis vs. Bonnet syndrome

- Similar: repetitive beings, often small and not frightening, usually normal insight
- Bonnet's is from poor vision-- sensory deprivation
- PD problems with object recognition may also cause deprivation hallucinations



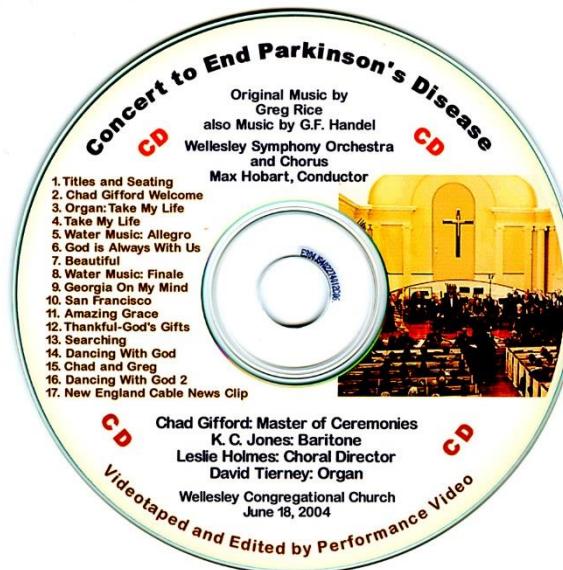
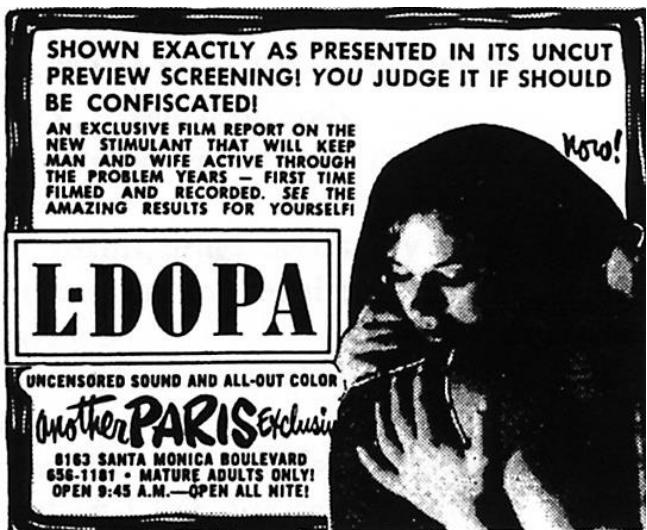
Delusions are more disabling than hallucinations

- Often paranoid
 - Othello syndrome: delusional jealousy
 - Delusional parasitosis
 - Healthcare workers trying to hurt patient
 - FBI surveillance, stealing
- Delusions may combine with med-induced manic features
 - Hypersexuality
 - Obsessive attempts to repair or build machines (“punding”)
 - Gambling, day trading.



Dopamine causes manic “compulsions”

- Gambling, shopping, hypersexuality
- ...also gardening, making art, work obsession, xeroxing....



- Do the same treatments help PD psychosis and manic drives?

PD psychosis requires advanced PD + PD meds

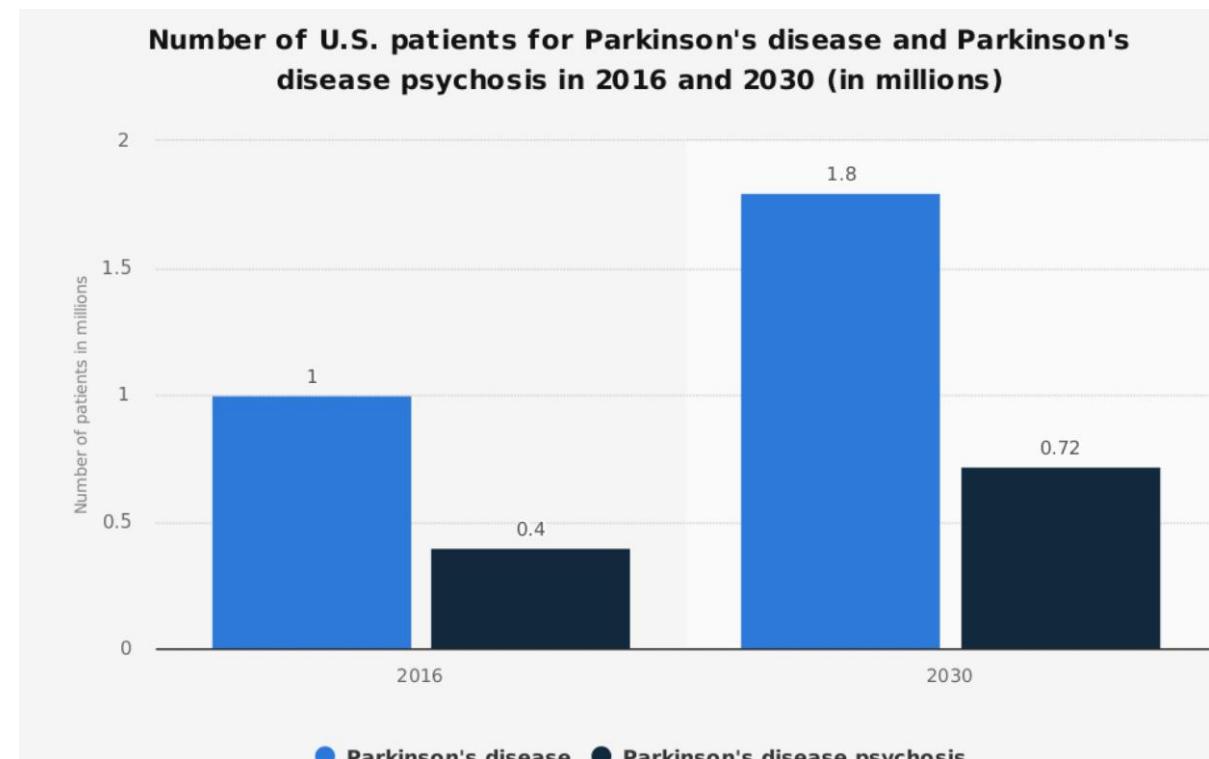
- PD meds + no PD => ~no psychosis
- PD meds + early PD => ~no psychosis
- No PD meds + bad PD => ~no psychosis
- PD meds + bad PD => psychosis common

} Psychosis would suggest atypical parkinsonism

~ = medical equivocation

Incidence of Parkinson's disease psychosis

- ~30% of PD pts eventually get Parkinson's psychosis
- ~50% if minor illusions count
- Patients rarely report it; family often reluctant too.
- # of affected pts will nearly double by 2030



Sources
The Motley Fool; Parkinson's Foundation;
Acadia Pharmaceuticals
© Statista 2018

Additional Information:
United States; Parkinson's Foundation; Acadia Pharmaceuticals

Risk factors for PD psychosis

- High PD med doses, especially dopamine receptor agonists.
- Pre-existing neuropsychiatric conditions
- Using other psychoactive drugs eg sleeping pills, cannabis
- Infectious/metabolic illness
- Unfamiliar surroundings e.g. travel, hospitalization
- Sleep deprivation

Brain receptors important for psychosis

- **~All dopamine receptors: D2, D1, D3, D4, D5**
- Some serotonin receptors: 5-HT2A, 5HT2C, 5-HT3, 5-HT1A, 5HT2C
- Some glutamate receptors: NMDA

How does dopamine cause psychosis?

- It underlies goal-directed motivation, “incentive salience”, wanting
 - Wanting is not the same as liking
 - Increases goal-oriented drives (extreme: delusions)
- It increases vividness of mental images (extreme: hallucinations)
- It helps signal-to-noise discrimination, “obsessional” focus
 - (the opposite of ADHD)
- How can a patient have symptoms of low and high dopamine at the same time?

Initial management of PD psychosis

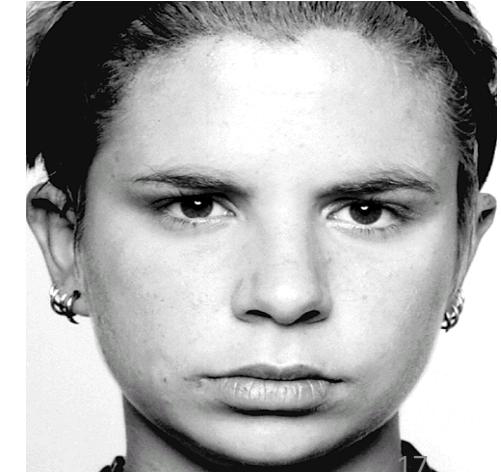
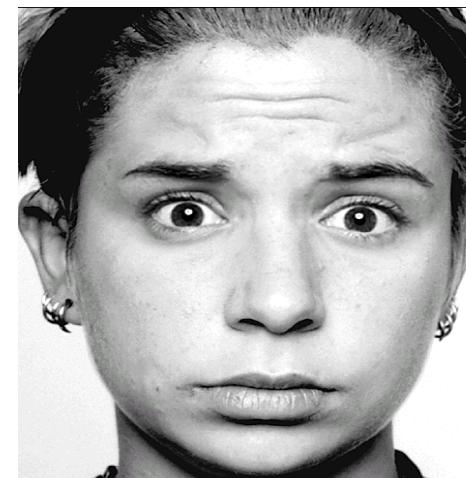
- Lower PD meds in order of nastiness: dopamine receptor agonists > anticholinergics > breakdown inhibitors > levodopa
- Lower L-dopa peaks: small frequent doses, XL meds, Duopa pump
- Deep brain stimulator can lower med needs
- Behavioral interventions: bright light therapy; distractions.

How to communicate with psychotic people

- Attend to nonverbal communication: mirror their emotions
- Reassure them they're safe, and that you want to help
- Speak simply—but don't assume they can't understand
- Give patient time to respond
- Don't argue with delusions:
 - Provide reality checks—but only once.
- Change the subject

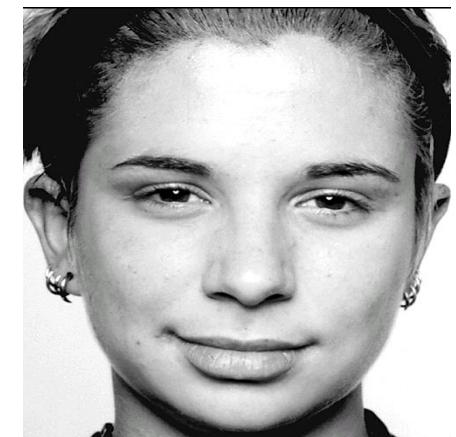
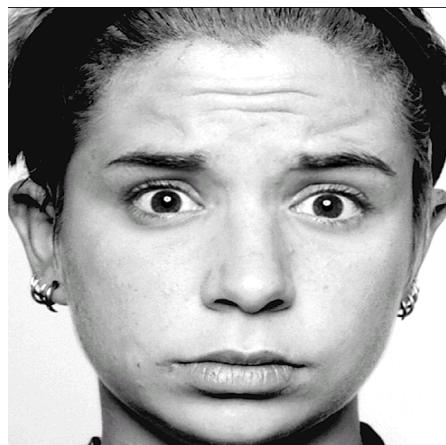
We should mirror negative emotions

- Mirroring their anxiety or anger is not the same as showing yours
 - “I can see how worrisome this must be” – NOT “I’m worried.”
- Mirroring is nonverbal proof that you understand they’re upset.
 - Vs. a soothing tone, which can sound patronizing
 - Reassurance works better when said in a worried tone (D. Roter)
- Mirroring is less work than feigning dispassion



Mirroring is just the start

- Mirroring dimly helps avoid reverberating mirrors.
- Once you're resonating at their frequency, you can start to change it.
- Also works with non-psychotic people: children, bosses....

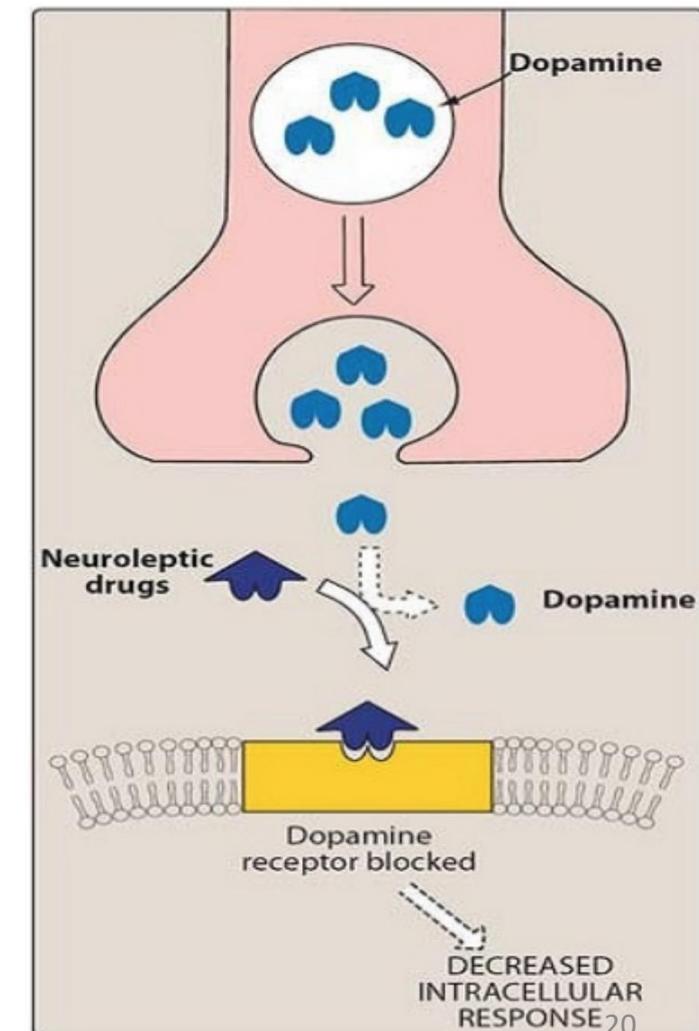


Antipsychotics for PD psychosis

- Standard antipsychotics: worsen PD motor symptoms *more on 5ht/DA, olanz?
- Quetiapine
 - Pros: Easily available, inexpensive, quick acting
 - Cons: Weak, worsens PD motor sx, sedating, orthostatic hypotension
- Clozapine
 - Pros: Powerful, mood-elevating, suppresses dyskinesia and tremor
 - Cons: Sedating, orthostatic hypotension, blood tests, MD paperwork
- Pimavanserin
 - Pros: Doesn't worsen PD, helps daytime alertness *and* sleep at night
 - Cons: Weak, kicks in slowly, expensive, MD paperwork

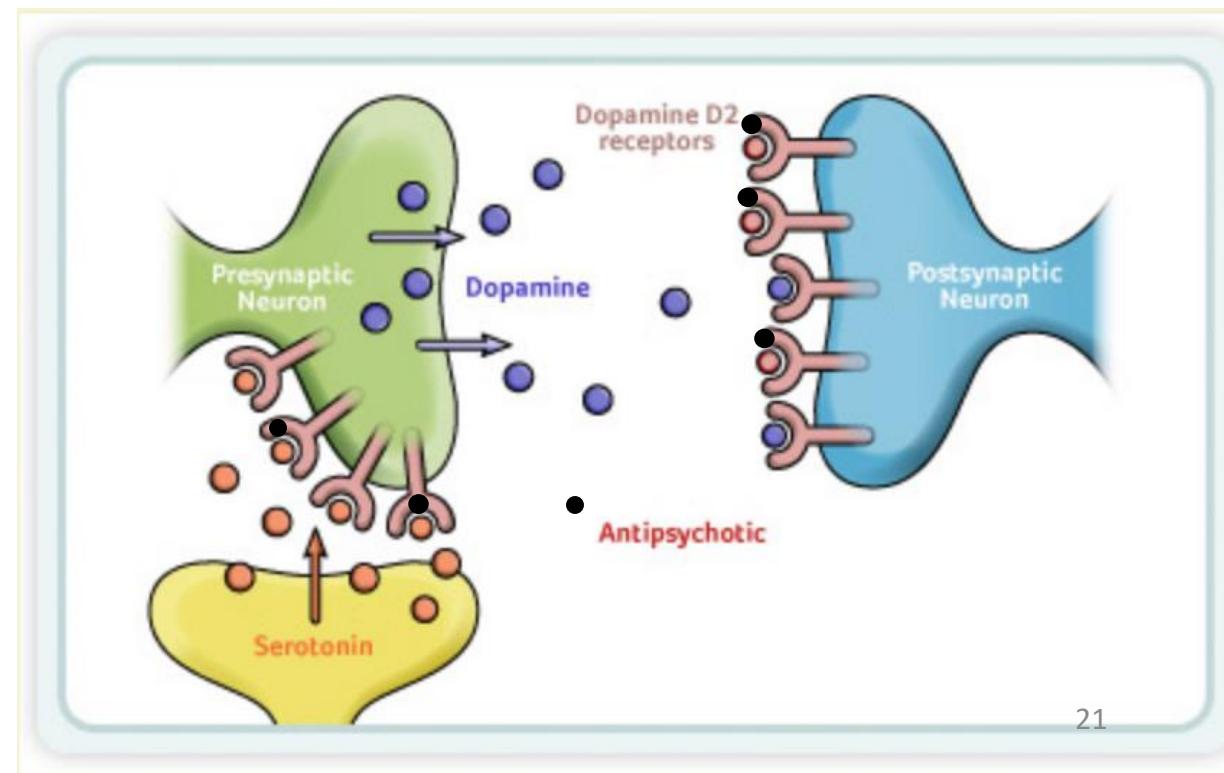
Most antipsychotics block DA receptor activation

- Benefits:
 - Decreased psychotic ideas and motivation
 - Decreased impulsive movements
- Problems:
 - Decreased ideas/motivation overall
 - Constipation
 - Orthostatic hypotension
 - Weight gain—sometimes ok in PD
 - Sedation—sometimes ok in PD
 - Clozapine: aplastic anemia (white blood cells)
 - Since blood tests required, this is rare.



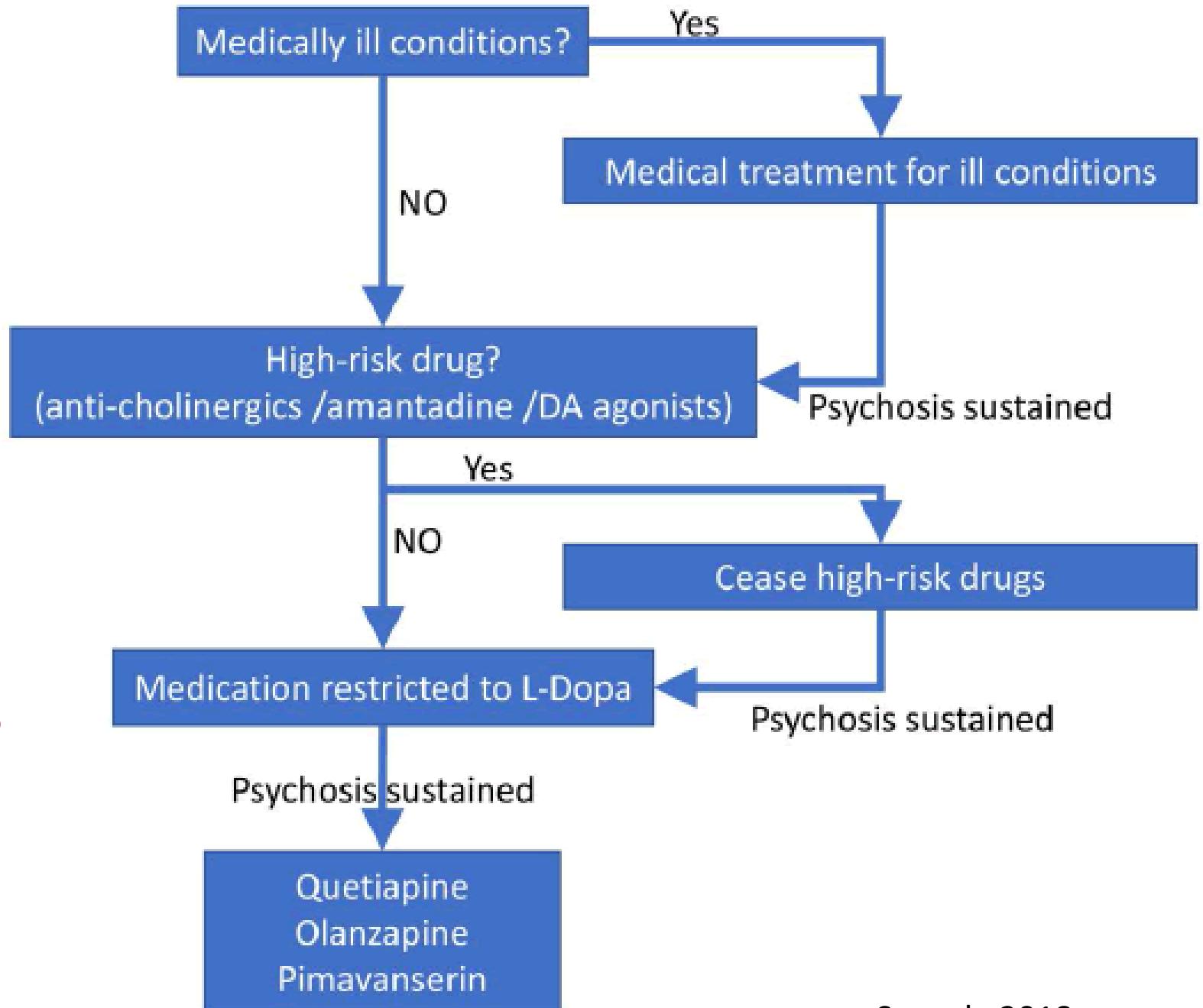
Serotonin receptors can affect psychotic symptoms

- Quetiapine & clozapine bind both serotonin & dopamine receptors
- Pimavanserin binds only serotonin receptors, so no movement side effects, but weak benefit.
 - *Why do I prescribe it anyway to people with bad psychosis?



PD psychosis treatment strategy

And apomorphine?



Family caregiver burden

- Terrifying for patient and caregiver.
- More caregiver burden from psychosis than motor symptoms
 - Financial
 - Time constraints
 - Emotional drain
 - Physical effects
 - Sleep deprivation
 - Injury from lifting pts, being hit
 - Caregivers put off their own MD visits
 - Stress hormones affect immune system, heart, gut



Wounds heal 20% slower in
caregivers of demented pts.
Kiecolt, 1995

PD psychosis burden on healthcare system

- Office phone calls and emergency visits
- Greatly raises risk of nursing home placement
- Patients need 1:1 supervision even when hospitalized.
- High risk of hospital-induced delirium
 - Catch-22: patients will stay delirious until they're home, but can't go home because they're delirious
 - Treatment: lower or stop PD meds

PD psychosis -- summary

- PDP is a growing problem: ~400K pts now, ~700K by 2030.
- PD pts have tradeoff between motor and psychiatric disability
- Current treatments have problems:
 - Most antipsychotics worsen PD motor symptoms
 - Most are sedating, constipating, and cause orthostatic hypotension.
 - Clozapine requires blood tests
 - Pimavanserin is weak, and slow to kick in.
- PDP is PD's most disabling symptom