

PSYCHOSIS IN NEURODEGENERATIVE DISORDERS

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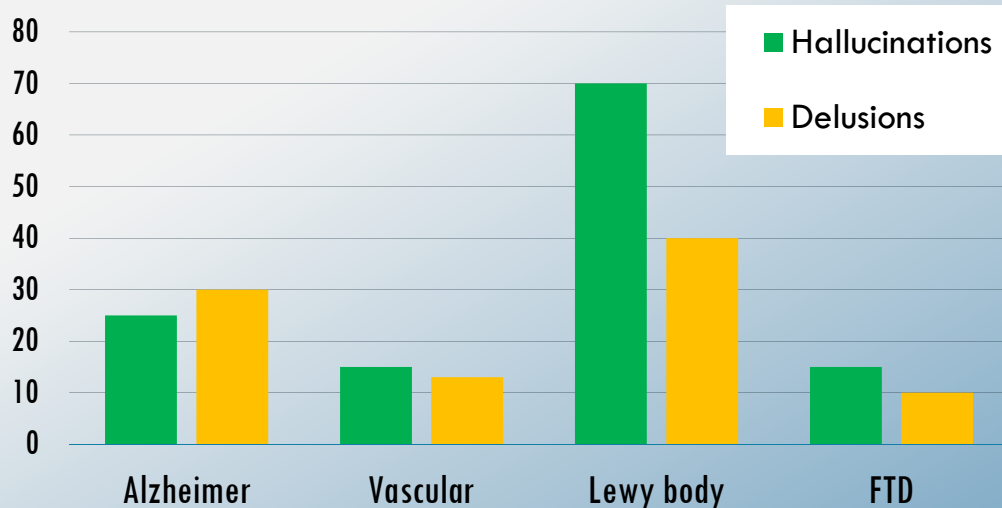
OUTLINE

- Psychosis in dementias
 - Alzheimer disease
 - Lewy body diseases
 - Dementia with Lewy bodies
 - Parkinson disease
- Psychosis in other neurodegenerative processes
- Secondary psychosis
- Treatment options

PSYCHOSIS IN DEMENTIA

- Common—at least 30% of dementia patients
- Occurs across dementia types
- Higher prevalence with disease progression
- Tends to persist, although it may wax and wane
- Sometimes has diagnostic value

PSYCHOSIS IN DEMENTIA



Yudofsky and Hales 2008

EFFECTS OF PSYCHOSIS

Psychosis associated with:

- Cognitive decline in community-dwelling elders
- Rapid progression to severe dementia
- Faster progression to death in newly diagnosed patients

Savva. *Br J Psychiatry* 2009

Peters. *Am J Psychiatry* 2015

TYPES OF DELUSIONS

Common delusions in dementia

- Theft
- Jealousy
- Phantom boarder
- Misidentification (Capgras, Fregoli)
- Reduplicative paramnesia
- Persecution

TYPES OF DELUSIONS

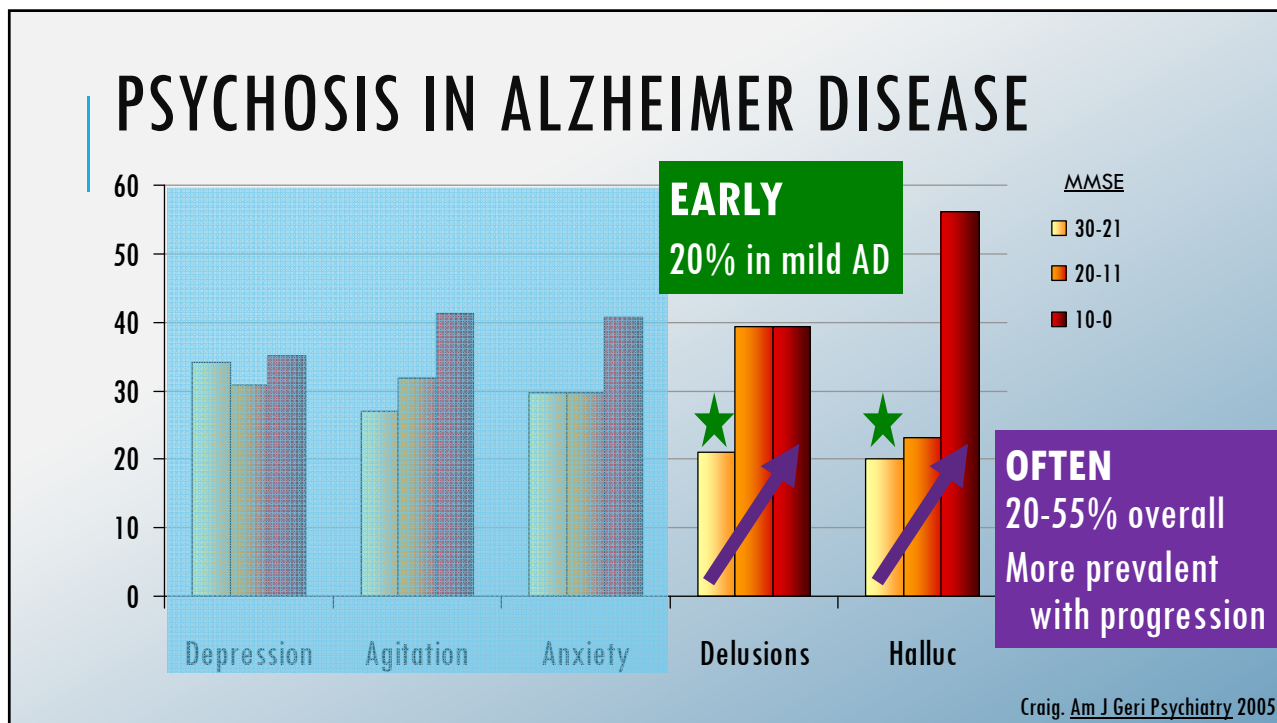
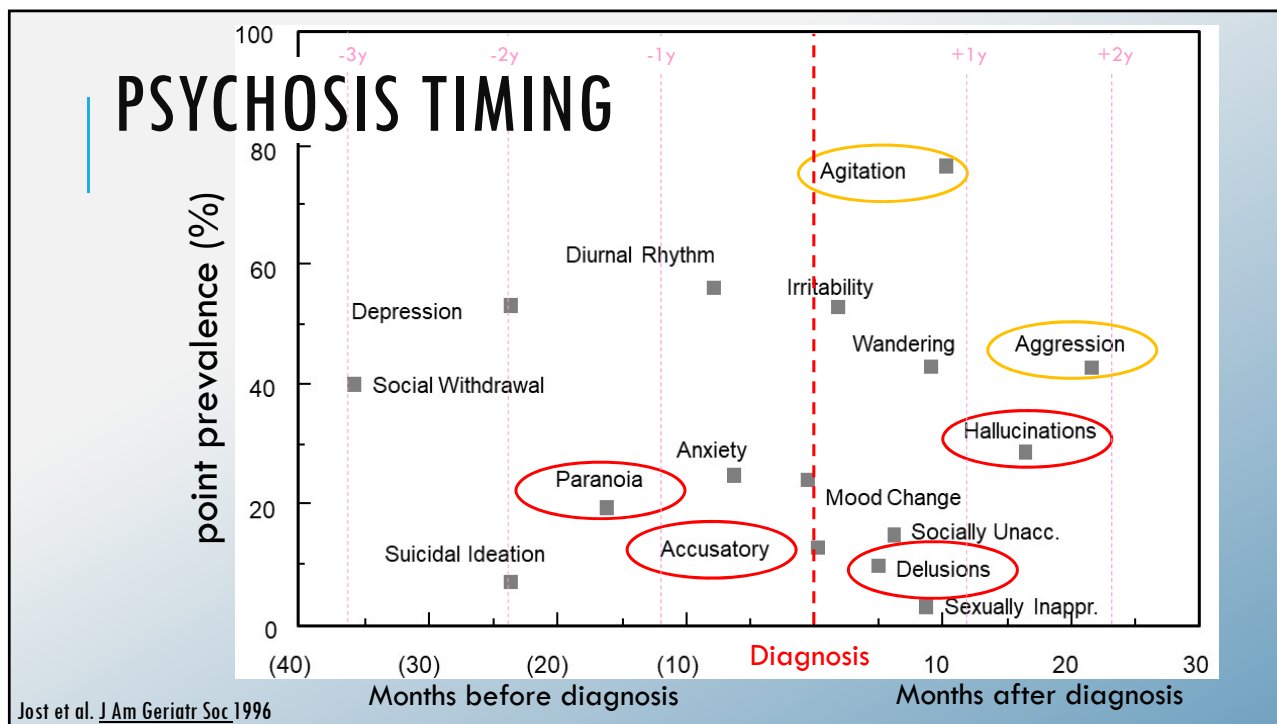
Uncommon delusions in dementia

- Grandiose
- Erotomantic
- Thought broadcasting/insertion/reading/removal
- Cotard
- Delusions of reference

NATURE OF HALLUCINATIONS

Hallucinations in dementia

- Visual most common in dementias
- All modalities can occur
- Qualitatively different from mood and primary psychotic disorders
 - More detailed
 - Typically less systematized



PSYCHOSIS IN LEWY BODY DISEASES

- Core diagnostic features
 - Recurrent well formed visual hallucinations (80%)
 - REM behavior disorder
- Supportive clinical features
 - Hallucinations in other modalities
 - Systematized delusions

McKeith. Neurology 2017

LEWY BODY PSYCHOSIS PHENOMENOLOGY

- “Psychotic prodrome”
 - Presence sensations
 - Passage sensations
 - Hypnagogic and hypnopompic phenomena
- Early psychosis symptoms
 - Visual illusions, scintillations, unexpected movement
 - Domestic and other common animals
 - Children

McKeith. Neurology 2017

LEWY BODY PSYCHOSIS PHENOMENOLOGY

Severe psychosis

- More complex
 - Multiple simultaneous figures
 - Figures become more active and interactive
- Loss of insight
 - More emotional upset (or pleasure)
 - More behavioral responses
 - More disputes with caregivers

PSYCHOSIS IN OTHER DISORDERS

Not uncommon in:

- Huntington disease
- Metachromatic leukodystrophy
- B12 deficiency
- Limbic encephalitis
- Multiple sclerosis
- Neurosyphilis

PSYCHOSIS IN OTHER DISORDERS

Relatively *uncommon* in:

- Cerebrovascular dementia
- Frontotemporal dementia (except C9ORF72 and MND)
- Progressive supranuclear palsy (delusions reported)
- Corticobasal degeneration

CHECK FOR OTHER CAUSES

Delirium due to medical/metabolic problem

- Infection
- Sleep deprivation
- Dehydration
- Hypo/hyperglycemia
- Toxic—EtOH, drugs of abuse, THC, CBD?
- Withdrawal from EtOH, sedative, or antidepressant
- Psychiatric disturbance

IATROGENIC PSYCHOSIS

- Dopaminergics
- Anticholinergics
- Sedatives
- Opioids
- Muscle relaxants

IATROGENIC PSYCHOSIS

- **Dopaminergics**
- Anticholinergics
- Sedatives
- Opioids
- Muscle relaxants

Used for

- Parkinson disease
- Lewy body disease
- Restless legs syndrome
- Progressive supranuclear palsy

Examples

- | | |
|---------------|--------------|
| • Pramipexole | • Selegiline |
| • Ropinirole | • Safinamide |
| • Levodopa | • Levodopa |
| • Rasagiline | • Amantadine |

IATROGENIC PSYCHOSIS

- Dopaminergics
- **Anticholinergics**
- Sedatives
- Opioids
- Muscle relaxants

Used for

- Parkinson disease
- Insomnia
- Anxiety
- EPS
- Depression
- Bladder
- GI

Examples

- Diphenhydramine
- Hydroxyzine
- Benztropine
- Trihexyphenidyl
- TCAs
- Antipsychotics
- Oxybutynin
- Promethazine

IATROGENIC PSYCHOSIS

- Dopaminergics
- Anticholinergics
- **Sedatives**
- **Opioids**
- Muscle relaxants

Used for

- Pain
- Anxiety
- Insomnia
- depression

Examples

- -codone
- -epam

TREATMENT

Choose goals wisely and explain carefully

- Improve quality of life
 - Maximize function
 - Minimize discomfort
 - Suit patient/caregiver lifestyle and wishes
- Eliminating psychotic symptoms is difficult

NONPHARMACOLOGIC TREATMENT

- Minimize physiologic factors
- Treat comorbidities (mood, anxiety, cognition)
- Improve environment
 - Increase and regulate lighting
 - Increase live ambient input (not television)
 - Regular, active schedules
 - Minimize ambiguities

FOR LEWY BODY DISEASES

MINIMIZE DOPAMINE BLOCKADE

- Olanzapine—promising open-label trial, failure since
- Risperidone—no controlled trials, motor decline
- Aripiprazole—disastrous controlled trial
- Anticholinesterases—low risk, low reward
- Ziprasidone—open study n=43 showed no motor decline
- Quetiapine—low risk, low reward in controlled studies

Friedman. *Parkinson Rel Disord* 2010

PD DEMENTIA

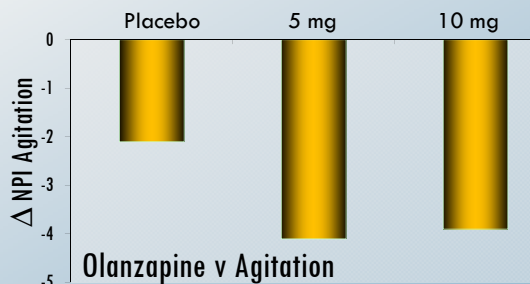
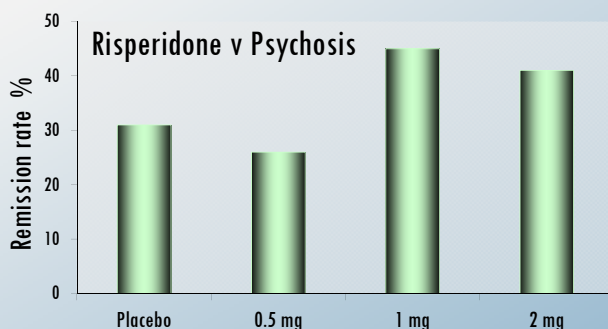
- Pimavanserin
 - FDA approved
 - No dopamine blockade
 - Minimal side effects
- Clozapine
 - Effective at low doses (10% of schizophrenia doses)
 - Possibly improves motor symptoms
 - Black box: agranulocytosis, seizures, myocarditis
 - Extra “bonuses”: drowsiness, sialorrhea, weight gain

	Placebo (n=94)	Pimavanserin 40 mg (n=104)
Nausea	6 (6%)	6 (6%)
Peripheral oedema	3 (3%)	7 (7%)
Urinary tract infection	11 (12%)	14 (13%)
Fall	8 (9%)	11 (11%)
Confusional state	3 (3%)	6 (6%)
Headache	5 (5%)	1 (1%)
Hallucination (including visual)	4 (4%)	7 (7%)

Friedman. *Parkinson Rel Disord* 2010

HELPFUL FOR OTHER SYMPTOMS

- OLANZAPINE—agitation/aggression
- RISPERIDONE—agitation; psychosis
- QUETIAPINE—agitation (200 mg)
- ARIPIPRAZOLE—agitation; psychosis



Tan et al. *Alzheimer's Res & Ther* 2015

Wang et al. *Current Neuropharmacology* 2016

Schneider et al. *Am J Geriatr Psychiatry* 2006

Ballard et al. *Nat Rev Neurosci* 2006

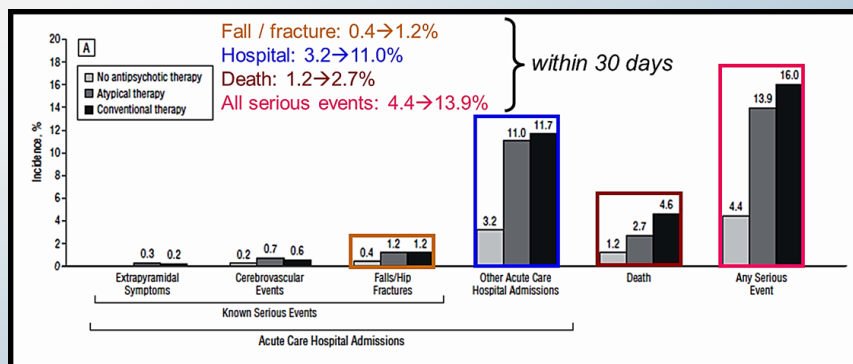
Street et al. *Arch Gen Psychiatry* 2000

Katz et al. *J Clin Psychiatry* 1999

WARNINGS

Minimize duration of treatment

- But, 60% relapse rate if withdrawn (vs 33%) after 4-8 months
- One meta-analysis showed no difference from placebo



Declercq. *Cochrane Collab* 2013

Devanand. *NEJM* 2012

WARNINGS

- Watch carefully for EPS
 - Higher risk of all EPS in individuals with dementia
 - Likely harder to recover in individuals with dementia
- Physiologic monitoring
 - Vitals: orthostatic heart rate & BP, weight
 - Labs: blood glucose, A1C, cholesterol
- Objective behavioral measures when possible

THE UPSHOT

- Common problem in dementia
 - 50% in AD (5.5 million)
 - 80% in LBD (1 million)
 - 30% in PD (1 million)
- Scant data and one (?!) drug
- Evaluate internal and external environments
- Antipsychotics can be effective, but risky

**3.85 million with
dementia-related
psychosis**

