Pharmacological Treatment of Aggression in the Elderly

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Self-Assessment Question 1

Which of the following statements is true?

A. Aggression is a rare among demented patients.

B. Aggression in the elderly has many etiologies, requiring thoughtful differential diagnosis.

C. Aggression in the elderly is rarely serious.

D. Several pharmacologic agents are FDA-Indicated for treatment of aggressive behavior in the elderly.

E. All of the above

Self-Assessment Question 2

Which of the following has been correlated with an increased likelihood of aggressive behavior in demented patients?

A. Physical pain
B. Depression
C. Psychosis
D. Disorientation
E. All of the above

Self-Assessment Question 3

Which of the following complications can complicate pharmacologic treatment of aggression?

A. Sedation
B. Gait disturbance
C. Aspiration
D. Respiratory depression
E. All of the above

Self-Assessment Question 4

Which of the following medication classes has NOT been used successfully in treating aggressive demented patients?

A. Typical and atypical antipsychotic medications
B. Anticonvulsants
C. Antidepressants
D. Stimulants
E. Cholinesterase inhibitors

Self-Assessment Question 5

Which of the following atypical antipsychotics is currently available in depot injection form?

A. Olanzapine
B. Risperidone
C. Quetiapine
D. Aripiprazole
E. None of the above

Major Points

- Aggression in the elderly is a common concomitant of dementia
- Many other causes of aggression in the elderly need be considered
- Behavioral approaches should be considered prior to pharmacotherapy
- Although no pharmacotherapy has been FDA-indicated for treating aggression in the elderly, a variety of options are supported by available data.

Aggression in Dementia Prevalence 23.7%-96%

- Definitions/assessment
- Dementia and aggression

Lyketsos et al. Mental and behavioral disturbances in dementia: findings from the Cache County study on memory in aging. Am J Psychiatry 2000;157:708-714; Keene et al. Natural history of aggressive behavior in dementia. J Geriatr Psychiatry 1999; 14:541-548

Other Causes of Aggression in Elderly

- Delirium and post-CVA
- Bipolar and schizophrenia
- Suicide-homicide, delusional disorder
- Psychopathology and criminality

Homicide-Suicide

- Incidence 0.4-0.9 per 100,000 for those >55
- Years 1988-1994: higher rates annually for older individuals for every year but two.
- Two subtypes: amorous-jealous, and the declining health.

Cohen et al. Homicide-suicide in older persons. Am J Psychiatry 1998; 155:390-396

Aggressive behavior

Verbal or physical behavior intended to harm others.

Not all aggressive behavior is dangerous or injurious.

Assaultive behavior

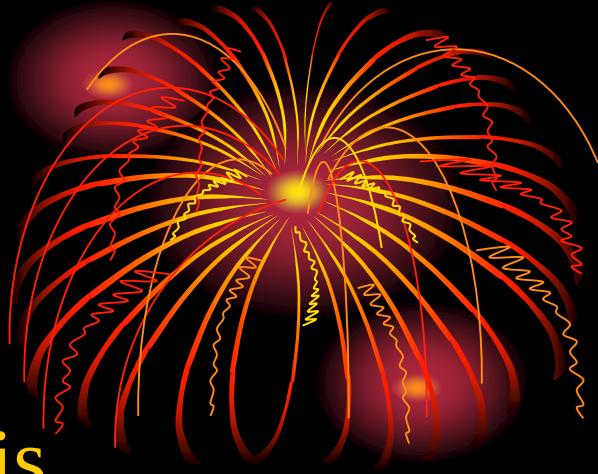
Unwelcome physical contact or the intent to engage in unwelcome physical contact which has the potential to cause physical harm.

Disruptive behavior

Verbal or motor activity which interferes with the functioning of the environment or with the functioning of others.

Disruptive behavior may not necessarily be assaultive or aggressive, but often reflects agitation.

Agitation



- Motor or verbal activity that is purposeless, excessive, unresponsive to suggestion, and does not advance any goal that is in the person's interest.
- A manifestation of an underlying serious mental illness or dementing condition
- Disrupts some aspect of daily functioning
- Not necessarily assaultive, aggressive, or disruptive to others

Components of agitation that lead to aggression

- Restlessness
- Pacing
- Repetition
- Negativism
- Cursing
- Verbal aggression
- Hitting-throwing
- Requests for attention

Behaviors that lead to aggressive incidents

- Wandering
- Sundowning
- Shadowing
- Modeling
- Exit seeking
- Bathing-dressing can lead to incidents.

Resident-to-Resident Violent Incidents

- Cases N=250 (median age 81)
- Controls N=486 (median age 83)

39 Fractures

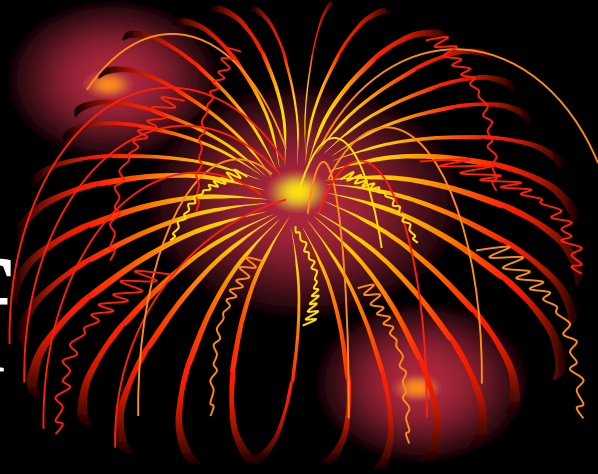
6 Dislocations

105 bruises or hematomas

113 lacerations

Shinoda-Tagawa et al: Resident to Resident violent Incidents in Nursing Homes. JAMA 2004; 291:591-598

Characteristics of Patients at Risk of Injury



	Crude Odds Ratio	Adjusted OR (age, ADLs,cognition)
• Wandering	7.2	2.8
• Verbally abusive	5.7	1.9
• Physically abusive	5.0	1.1
• Socially disruptive	5.0	1.6
• Resists care	3.2	1.0

Shinoda-Tagawa et al. Resident to resident violent Incidents in nursing homes. JAMA 2004; 291:591-598

Biological Correlates of Aggression in Alzheimer's

- 5HTTPR* Allele and L*/*L genotype (1)
- Choline acetyltransferase activity in midfrontal and superior frontal cortex (2)
- Left anterior temporal, bilateral dorsofrontal, right parietal cortex hypoperfusion (3)
- Medial temporal hypoperfusion (4)

1. Minger et al. Cholinergic deficits contribute to behavioral disturbance in patients with dementia. Neurology 2000;55:1460-1467; 2. Hirono et al: Left frontotemporal hypoperfusion is associated with aggression in patients with dementia. Arch Neur 2000;57:861-866; 3. Sukonick et al:The 5-HTTPR*S/*L polymorphism and aggressive behavior in Alzheimer disease. Arch Neurol 2001; 58;1425-1428; 4. Lanctot et al: Medial temporal hypoperfusion and aggression in Alzheimer disease. Arch Neurol 2004;61:1731-1737.

High risk situations

- Bathing, dressing, toileting
- Sudden movements
- Change of location

Psychopathological Correlates in Dementia

- Psychosis explains 22% of variance in aggression scores
- Depression (1)
- Disorientation—verbal aggression
- Pain (2)

1. Lyketsos et al. Physical aggression in dementia patients and its relationship to depression. Am J Psychiatry 1999; 156:66-71;
2. Cohen-Mansfield et al. Predictors of aggressive behaviors: a longitudinal study in senior day care centers. J Gerontol Psychol Sci 1998; 53B:P300-P330

Assessment

- Social Dysfunction and Aggression Scale-9 (SDAS-9)
- Nurses Observation Scale for Inpatient Evaluation (NOSIE)
- Cohen-Mansfield Agitation Inventory (CMAI)
- Brief Psychiatric Rating Scale (BPRS)
- Behavioral Pathology in Alzheimer’s Disease (BEHAVE-AD)

Pharmacological Treatment Principles

- Treat acute medical conditions which contribute
- Rule out medication effects, eg anticholinergics
- Add one new agent at a time
- Increase doses with appropriate caution
- Avoid: gait disturbance, respiratory depression, aspiration, sedation
- Oral haloperidol 2 to 3 mg daily better than 0.5 to 0.75 mg

Devanand DP et al. A randomized, placebo-controlled dose-comparison trial of haloperidol for psychosis and disruptive behaviors in Alzheimer's disease. Am J Psychiatry 1998;155:1512-1520

Plasma Haloperidol Levels

- 1.45 to 1.65 ng/ml: 20% reduction in BPRS
- Oral haloperidol dose did not correlate with reduction in BPRS
- Psychosis, suspiciousness, aggression respond

Pelton et al. Uselfulness of plasma haldoperidol levels for monitoring clinical efficacy and side effects in Alzheimer patients with psychosis and behavioral dyscontrol. Am J Geriatr Psychiatry 2003;11:186-193

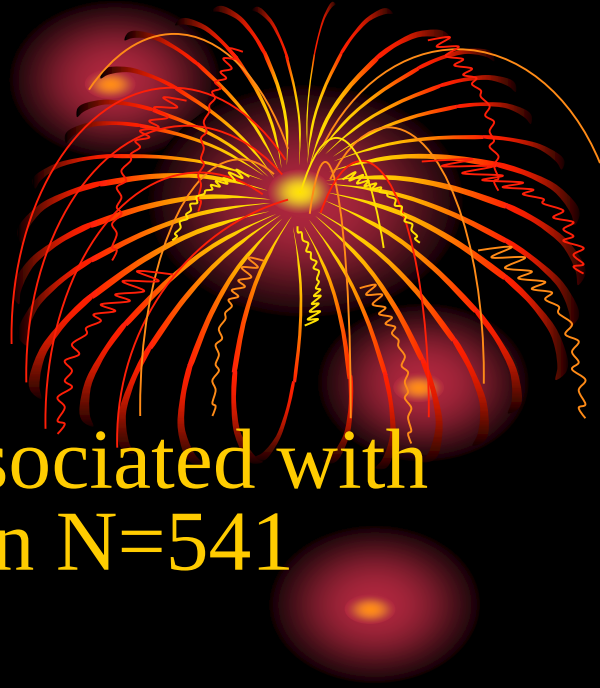
Atypical Antipsychotics

	Advantages	Disadvantages
• Risperidone	depot	hypotension
• Olanzapine	IM	weight gain
• Quetiapine	PD	prolonged QTc
• Aripiprazole	PD	EPS
• Clozapine	Neg Sx	anticholinergic
• Ziprasidone	IM	prolonged QTc

Anticonvulsants

	Advantages	Disadvantages
• Valproate	tolerable	3-5 day onset
• Carbamazepine	tolerable	CYP 2D6-induction
• Gabapentin	pain control	no mood effect
• Topiramate	weight control	no mood effect

Antidepressants



- Aggressive behavior closely associated with moderate to severe depression in N=541 patients with dementia (1)
- Citalopram 10 to 20 mg and perphenazine 6.5mg +/- 1.7 mg--both better than placebo (2)
- Trazodone about equal to haloperidol (3)

1. Lyketsos et al. 1999; 2. Pollock et al. Comparison of citalopram, perphenazine, and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. Am J Psychiatry;159;460-465; 2. Sultzer et al. A double blind comparison of trazodone and haloperidol for treatment of agitation in patients with dementia Am J Geriatr Psychiatry 1997; 5: 60-69; 3. Eeren in Raskin et al. Association of depression with agitation in elderly nursing home residents. J Geriatr Psychiatry Neurol 2003 16 (1): 4-7

Acetylcholinesterase inhibitors/NMDA agents

- Donepezil — No data
- Galantamine — No data
- Rivastigmine — 2 yr trial showed reduced aggression[1]
- Memantine — No data

1. Rosler et al. Effects of two year treatment with the cholinesterase inhibitor rivastigmine on behaviaoral symptoms in Alzheimer's disease. Neuropsychiatry Neruopsycholo Behav Neurol 1998/1999; 11:211-216

Other agents

- Buspirone
- Benzodiazepines
- Beta-blockers
- Lithium
- Anti-androgenic agents

Light Therapy

- Morning bright light delayed the acrophase of agitation rhythm by >1.5 hours
- Bright light was associated with improved caregivers' ratings
- Brightly light had little effect upon observational ratings of agitation

Ancoli-Israel et al. Effect of light on agitation in institutionalized patients with severe Alzheimer's Disease. Am J Geriatr Psychiatry 2003; 11:194-203

Summary: Treatment of Aggressive Behavior

- Identify risk factors and treat proactively
- Identify and address treatable medical conditions
- Choose least harmful interventions
- Consider side effects and medication interactions before beginning treatment

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Self-Assessment Question Answers

1. B
2. E
3. E
4. D
5. B