

MANAGEMENT OF DIFFICULT BEHAVIORS IN DEMENTIA



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Objectives

- Understand the prevalence of Behavioral and Psychological Symptoms of Dementia (BPSD) among individuals with dementia and the impact of BPSD on patients, caregivers, and health care providers
- Formulate an approach to the assessment of BPSD
- Implement appropriate management techniques for difficult behaviors in dementia utilizing current evidence base



Definition of Behavioral and Psychological Symptoms in Dementia

- Heterogeneous range of psychological reactions, psychiatric symptoms, and behaviors occurring in people with dementia of any etiology
- Any verbal, vocal, or motor activities not judged to be clearly related to the needs of the individual or the requirements of the situation
- Observable phenomena (not just internal)

Behavioral and Psychological Symptoms in Dementia

Behavioral

- Agitation
- Aggression
- Screaming
- Cursing
- Repetition
- Restlessness
- Wandering
- Sexual disinhibition
- Hoarding
- Urination/defecation
- Questioning

Psychological

- Personality change
- Anxiety
- Depression
- Crying
- Hallucinations
- Delusions
- Apathy
- Elevated mood
- Irritability

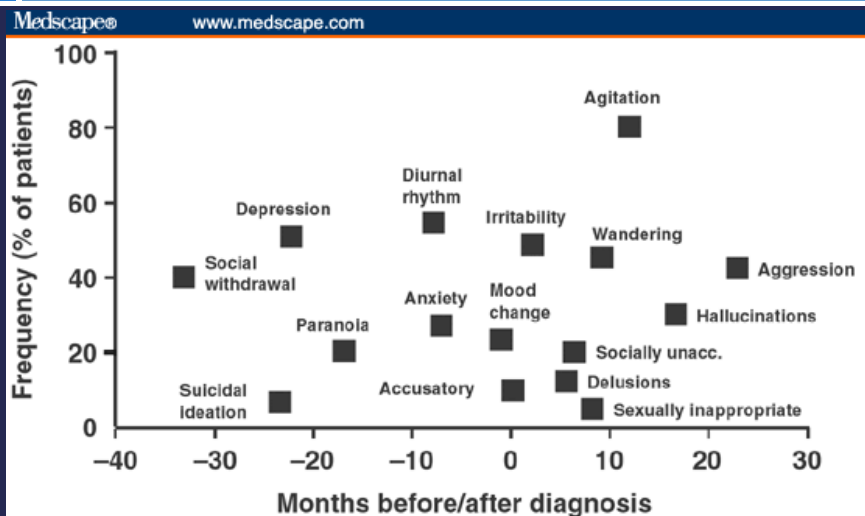
Epidemiology of BPSD

- Dementia prevalence:
 - 60% of community-dwelling elders
 - >80% of nursing home residents

- BPSD prevalence:
 - 90% of people with dementia develop a neuropsychiatric or behavioral symptom during the course of the disease
 - Prevalence increases with disease severity



Peak Frequency of Behaviors in AD as Disease Progresses



Impact of BPSD

- Decreased quality of life for patient
- Increased burden and depression for caregiver
- Primary predictor of nursing home placement
- Higher costs of care
- More rapid disease progression
- Risk to self and others:
 - Falls, assaults on co-patients and staff

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Assessment

- What type of dementia does the patient have?
- What is the stage of dementia?
 - Function
 - Degree of cognitive impairment
 - Ability to express needs
- What psychological symptoms are present?
 - Depression – 50% of nursing home patients
 - Anxiety – 25-40% of patients with dementia
 - Psychosis – 25-45% of patients with dementia

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Assessment

- What behaviors are worrisome?
 - ▣ Risks to patient, caregiver, others
- Context:
 - Antecedent to behavior → Behavior → Consequences
 - ▣ Does wandering place the resident at risk of greater danger or intrude on the privacy of others?
 - ▣ Frail resident means little threat of injury to others if aggressive
 - ▣ Non-compliance with multivitamin vs. insulin
 - ▣ Continued soft spoken talking vs. yelling

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Assessment

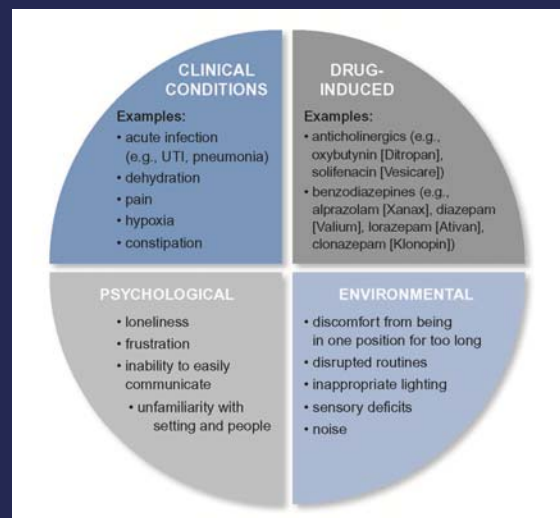
- Assess if this is a symptom of an unmet need, a medical problem, or a psychiatric problem
 - ▣ Acute onset makes one more concerned about a medical etiology
 - Pain, infection, medication, dehydration, hypoxia, delirium
 - ▣ Unmet need: Hunger, thirst, mobility, relief of pain, boredom, loneliness
 - ▣ Environmental trigger: light levels, roommate, overstimulation/understimulation, particular people, moved rooms

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General Principles to Managing BPSD

- Requires biopsychosocial, multidisciplinary approach
- Begin with identification of target symptoms
- Consider safety and quality of life of patient and others
- Correct contributing factors:
 - Medical condition
 - Psychiatric condition
 - Environmental factor
 - Psychosocial problem

Factors Affecting BPSD



Non-Pharmacological Interventions

- Implementation of activities
- Music therapy
- Sensory interventions such as massage
- Minimize environmental change
 - Addition of medications within the first 4 weeks after a change in environment not likely to be helpful
- Control the amount of stimulation
- Enhance communication with slow, clear, one-step instructions and visual cues or gestures
 - Hearing loss
 - Visual impairment
- Sleep and eating patterns

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Pharmacological Interventions

- Initiate non-pharmacological interventions first
- Pharmacological intervention should be initiated concurrently with non-pharmacological interventions in the presence of severe depression, psychosis, or aggression with risk of harm
- Identify target symptoms amenable to pharmacotherapy
- Pharmacological interventions should be initiated at lowest doses, titrated slowly and monitored for effectiveness and safety

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Depression in Dementia

- 25% of patients with dementia have co-morbid depression
 - Vascular and diffuse lewy body > Alzheimer's
- Signs and Symptoms:
 - Low mood and loss of pleasure
 - Self-deprecating remarks or expressions of wish to die
 - Personal or family history of depression
- **First Line Treatment:** escitalopram, citalopram, sertraline, venlafaxine, bupropion, mirtazapine
 - Treat for minimum of 1 year

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Pain in Dementia

- Up to 84% of older people experience some type of chronic pain
- Difficult to assess in moderate to advanced dementia
 - Observe physiological, behavioral, and body language changes as patients may not be able to communicate pain
- May present as agitation or aggression, screaming, wandering
- **Treatment:**
 - Scheduled analgesics
 - May need narcotics – follow stepwise protocol of the American Geriatrics Society

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Anxiety in Dementia

- Common, especially in early stages
 - Fear of being left alone
 - Fear of institutionalization
 - Environment and people are unfamiliar
- Potential Interventions
 - Non-pharmacological:
 - Find reason for worry and reduce/eliminate
 - Find out what patient finds relaxing
 - Surround patient with familiar items and people
 - Pharmacotherapy: caution with adverse effects
 - Antidepressant
 - Anxiolytic

Psychosis in Dementia

- Incidence of psychosis by type of dementia:
 - >50% in Alzheimer's dementia
 - Most common in moderate stage
 - 40% in Vascular dementia
 - 80% in Lewy body dementia (VH is diagnostic criteria)
 - 20% have AH
- Delusions: theft, infidelity of spouse, abandonment
- Hallucinations: visual > auditory
- Treatment: antipsychotics

Treatment of Psychosis: Antipsychotics

- Only treat if distressing to patient or caregiver

Alzheimer's	Lewy Body	Parkinson's
Risperidone 0.25-2mg	Cholinesterase inhibitors	Adjust dopaminergic agent
Olanzapine 2.5-10mg	Quetiapine 12.5-150mg	Quetiapine 12.5-150mg
Quetiapine 25-200mg		

Agitation/Aggression in Dementia

- Physically non-aggressive behaviors
 - Restlessness, repetitive mannerisms, pacing, inappropriate dressing, hiding things
- Physically aggressive behaviors
 - Hitting, pushing, scratching, grabbing, kicking, biting
- Verbally non-aggressive behaviors
 - Negativism, complaining, whining, requests for attention
- Verbally aggressive behaviors
 - Screaming, cursing, strange noises, temper outbursts

Aggression/Agitation: Pharmacological Management with Atypical Antipsychotics

- CATIE-AD: RCT of outpatients with AD comparing olanzapine, risperidone, quetiapine, and placebo for psychosis, agitation or aggression
- Aripiprazole: RCT (10mg) was efficacious in improving psychotic symptoms, agitation, and GAF
- Quetiapine trials have largely been negative
 - 100mg no difference vs placebo; 200mg showed reduction in agitation

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CATIE-AD Trial

- First cost-benefit analysis of second generation antipsychotics in treating non-cognitive symptoms in AD patients
- 421 AD patients with psychosis and aggression randomly assigned to olanzapine, quetiapine, risperidone, or placebo of over 9 months
- No statistical differences between groups, although placebo most often superior in net health benefit analysis
 - Olanzapine group – more impaired on ADL testing- sedation, gait disturbance
 - Placebo group – best ADL score, lower dependence score, lower total health care costs - \$50-100
- Several methodological drawbacks:
 - Subjects were outpatients, less impaired than some BPSD trials
 - High dropout rate compared to other RCTs
 - No washout period
 - Dosage likely too low for quetiapine (mean 56.5mg/day)
- *Authors concluded adverse events offset advantages in efficacy*

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Antipsychotics in LTC

- Only 2 RCTs have examined antipsychotics in AD over 6 months
- Ballard et al (2005) found no difference between quetiapine, rivastigmine, or placebo in agitation over 6 months

Antipsychotics in LTC

- Study – 2008
- Older adults with dementia: 20,682 in community, 20,559 in LTC
- Control: No antipsychotics
- Outcomes: serious events in first 30 days
 - Community dwellers:
 - Atypicals: 13.9% had a serious event (3.2 times higher than control)
 - Typical: 3.8 times higher serious event
 - LTC:
 - Atypicals: 1.9 times higher serious events than control
 - Typical: 2.4 times higher serious event

Atypical Antipsychotic Dosing

Medication	Initial Dose	Titration Schedule	Maximum Daily Dose	Selection Considerations
Risperidone	0.25-0.5mg daily or BID	0.25-0.5mg q 3-7 days	1mg	Drug-induced parkinsonism
Olanzapine	2.5-5mg daily	2.5-5mg q 3-7 days	10mg	↑↑Metabolic side effects
Quetiapine	25-50mg daily or BID	50mg in divided doses q 3-7 days	150mg	
Aripiprazole	2-5mg	2-5mg q 3-7 days	5-10mg	

Switch antipsychotics if no benefit or limited benefit after 2-4 weeks

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Risks of Atypical Antipsychotics

WARNING: INCREASED MORTALITY FOR ELDERLY PATIENTS WITH DEMENTIA RELATED PSYCHOSES. Elderly patients with dementia related psychoses are at increased risk for death compared to placebo. This drug is not approved for the treatment of dementia related psychoses.

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Risks of Atypical Antipsychotics in Dementia

- Meta-analysis of 17 double blind RCT's in elderly dementia patients, April 2005
 - Most of the deaths were either due to heart related events (e.g., heart failure, sudden death) or infections (mostly pneumonia)
 - Mortality: OR=1.6, absolute risk ~1-2%
 - Atypicals 4.5% vs 2.6% placebo
 - Stroke: RR=2.7, absolute risk ~1-2%
 - Risperidone 3.3% vs 1.1% placebo (RR=3.30)
- Risk is double while appreciating that the overall increased risk is small**
- Risk increases with dose and duration
 - Weigh risks vs. benefits
- Warning extended to all antipsychotics in June 2008

Common Adverse Events with Atypical Antipsychotics

- Sedation
- Extrapyramidal Symptoms
- Gait disturbance and falls
- Weight gain, dyslipidemia
 - Greatest risk with olanzapine and quetiapine
 - Women at higher risk

Discontinuation of Antipsychotics

- Treatment should be maintained only if benefits are apparent and discontinuation should be attempted at regular intervals
- RCT of 180 patients with AD and psychosis or agitation who had initially responded to treatment with risperidone
 - Discontinuation of risperidone was associated with an increased risk of relapse over 16 weeks of followup
 - 60 versus 33% in those assigned to early discontinuation
 - 48 versus 15% in those assigned to delayed discontinuation
- DART-AD - RCT of antipsychotic continuation or placebo in LTC residents with dementia who had been stable on antipsychotics for ≥ 3 months for BPSD
 - 2 arms: stop AP & switch to placebo vs. AP use x12 months
 - Stopping long-term antipsychotics reduced mortality by $\sim 25\%$ at 2 years in long-term follow-up
 - Survival at 2yrs: 71% vs. 46%
- 3 placebo controlled withdrawal studies indicated no worsening of behavior when long-term administration of neuroleptics were stopped

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Aggression/Agitation: Pharmacological Management with Typical Antipsychotics

- Some evidence for reduction of behavioral symptoms
- Significant reduction in aggression
- Adverse events higher with typicals when compared to atypicals (EPSE, TD)

Recommendation: Not supported for routine use as therapy for agitation in Alzheimer's Disease

- Risks outweigh the benefits

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Alternatives to Antipsychotics: Antidepressants

- SSRIs have some benefit in treating agitation, paranoia, and psychosis
- 2011 systematic review analyzed 9 randomized controlled trials studying the effects of antidepressant for BPSD
 - ▣ 5 studies compared SSRIs (citalopram, sertraline, fluoxetine, fluvoxamine) to placebo
 - 1 trial found a significant benefit for citalopram in the reduction of neuropsychiatric symptoms
 - No difference in the rates of trial withdrawals due to adverse events
 - ▣ 4 studies compared SSRIs (citalopram, sertraline, fluoxetine) were compared to antipsychotic agents (haloperidol, risperidone, perphenazine)
 - No difference between treatment groups in regard to benefit on BPSD nor on adverse events
- Subsequent RTC of 186 patients with AD and frequent or severe agitation found citalopram (target dose 30 mg daily) significantly reduced agitation and caregiver distress compared with placebo
 - ▣ Caution with dose-dependent QT interval prolongation (FDA max daily dose of 20 mg for patients older than 60 years of age)
- Adverse events include: Headache, GI upset, sweating, hyponatremia, falls, decreased bone mineral density

Recommendation: Despite mixed results in clinical trials, SSRIs are useful in the management of agitation and paranoia in patients with AD, as the symptoms are often driven by a mood disorder that is poorly verbalized

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Alternatives to Antipsychotics: Trazadone

- Cochrane Review
- Rationale: BPSD may be due to serotonergic dysfunction
- A sedating atypical serotonergic antidepressant with a lower rate of adverse effects may help
- Limited data from two small studies

Recommendation: Insufficient evidence to recommend the use of trazodone

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Alternatives to Antipsychotics: Cholinesterase Inhibitors

- ❑ Initial studies focused on cognition, yet there is increasing evidence of a possible behavioral benefit as well
- ❑ Meta-analysis of ChEI studies - Modest but significant behavioral benefit compared with placebo
- ❑ Several post-hoc analyses of studies with galantamine and donepezil suggest beneficial effects on psychosis, agitation, mood, apathy, and aberrant motor behaviors
- ❑ Data review suggest a statistically significant difference
- ❑ But magnitude of effect is small, and of questionable clinical significance

Recommendation: Start a cholinesterase inhibitor for patients with neuropsychiatric symptoms and mild to moderate dementia

Alternatives to Antipsychotics: Memantine

- ❑ 3 studies have examined the effect of memantine on BPSD in moderate-severe AD
- ❑ Post-hoc analysis suggests benefits, particularly for aggressive, agitated behaviors
- ❑ Memantine also appears to delay *emergence of agitation and reduce caregiver distress*
- ❑ Other reviewers question the clinical significance of the benefit

Recommendation: Requires further study

Alternatives to Antipsychotics: Valproate preparations

- Low dose with valproate preparations is ineffective in treating BPSD
- High dose therapy is associated with an unacceptable rate of adverse effects
 - Sedation occurred more frequently than in controls
 - Urinary tract infection was more than in controls

Recommendation: No evidence of efficacy of valproate preparations for treatment of BPSD

Alternatives to Antipsychotics: Carbamazepine

- The Good News:
 - 4 RCTs demonstrate benefit for aggression and agitation
 - Nursing home study where 72% of patients improved versus only 21% placebo
- The Bad News:
 - Subsequent trial found no benefit
 - Concerns about tolerability in elderly, drug-drug interactions, and adverse events unfortunately limit its use

Recommendation: Currently not enough evidence of benefit for carbamazepine to recommend its use for neuropsychiatric symptoms

Alternatives to Antipsychotics: Lamotrigine

- Benefit advocated based on case reports
- No randomized, placebo-controlled studies have been published to date

Recommendation: Requires further study

Alternatives to Antipsychotics: Gabapentin

- One open-label prospective study showing little benefit
- Relatively mild side effect profile

Recommendation: Efficacy is unproven, requires further study

Alternatives to Antipsychotics: Melatonin

- Premise: Circadian rhythm disturbances appear to be associated with depressed mood, impaired cognition, and behavioral and sleep disturbances
 - Suggests a potential benefit for melatonin in patients with dementia
- Studies have had somewhat mixed results, but in the aggregate do not suggest convincing benefit for agitation

Recommendation: Requires further study

Alternatives to Antipsychotics: Benzodiazepines

- Limited evidence supporting use for agitation
- May worsen disinhibition
- Main concern is high rate of adverse events in the elderly - oversedation, ataxia, falls, respiratory suppression, confusion, and even delirium
- Evidence supports only short-term as-needed use for behavioral emergencies

Recommendation: Not recommended for the management of neuropsychiatric symptoms of dementia

Disinhibition

- Disinhibition is a lack of restraint in several ways, including disregard for social conventions, impulsivity, and poor risk assessment
 - discussing personal issues with strangers
 - making inappropriate comments (sometimes sexual)
 - standing uncomfortably close to others
 - taking food from other people's plates
 - taking clothes from other residents' rooms
- Educate families and caregivers
- Redirection, distraction and other creative strategies may decrease the symptoms of disinhibition
- Sometimes SSRIs may decrease disinhibition, and benzodiazepines often increase disinhibition

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Sleep

- Sleep disturbances are common in patients with dementia
- Consider underlying medical illness like sleep apnea
- Minimize medications which have stimulating properties (including cholinesterase inhibitors)
- Maintain daytime activities and enhance sleep hygiene
- Pharmacological intervention could be considered when other approaches have failed, but should be minimized because of side effects
 - Benzodiazepines-Use discouraged due to side effects
 - Trazodone- Limited evidence
 - Mirtazapine- Useful when antidepressant effect desired
 - Antipsychotic medications should not be used routinely for treating sleep disturbances
 - Melatonin-Limited evidence

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Disruptive Vocalizations

- Treat medical and psychiatric syndromes first
 - ▣ Low threshold for suspecting depression
- Address environmental issues and use non-pharmacological interventions
- Underlying pathophysiology is thought to be related to serotonergic deficit
 - ▣ SSRIs
 - ▣ Less evidence for antipsychotics
- Acceptance of residual level of disruptive vocalizations as a reasonable outcome

Inappropriate Sexual Behavior

- Possible causes:
 - ▣ Damage to the frontal lobes
 - ▣ Misinterpreting caregiver's interaction/Misidentifying caregiver
 - ▣ Discomfort or irritation-clothing too warm or tight, genital irritation, urinary retention, UTIs
 - ▣ Need for attention, gratification or intimacy
- Interventions:
 - ▣ Distract and redirect or remove from inappropriate place if necessary
 - ▣ Respond calmly and firmly
 - ▣ Modify clothing
 - ▣ Treat urinary discomfort
- Pharmacological treatment may be necessary, but outcomes are mixed and adverse effects are frequent
 - ▣ **SSRIS (First Line)** may reduce libido
 - ▣ Atypical antipsychotics
 - ▣ Hormone therapy - case series evidence
 - Progesterone 5 mg po daily (10 mg IM weekly)
 - Leuprolide 5-10 mg IM monthly

Wandering

- ❑ Pharmacotherapy is **rarely effective** in the treatment of wandering unless the wandering is due to an associated condition such as mania
- ❑ Interventions of visual and other selective barriers such as mirrors, camouflage, and grids/stripes of tape **MAY** be helpful
- ❑ In institutional settings, safe wandering spaces with electronic locks or alarms may be used
- ❑ Provision should be made for patients to help locate them should wandering occur (bracelets, etc)

Summary

- ❑ Appropriate assessment and diagnosis
- ❑ Assess for underlying medical cause, medication toxicity, delirium, depression, and sensory impairment
- ❑ Identification of target symptoms
- ❑ Consideration of the safety of the patient, their caregiver and others in their environment
- ❑ Non-pharmacological approaches first
 - ❑ Caregiver education
 - ❑ Environmental manipulation
 - ❑ Behavioral approaches
- ❑ If behaviors persist and are sufficiently disturbing to patient or caregiver, or endanger safety, pharmacological interventions can be instituted with appropriate monitoring of effectiveness and safety
- ❑ Attempt to taper and withdraw medications for BPSD after a period of 3 months of behavioral stability