Managing Challenging Behaviours in Dementia Care: The Rational use of Antipsychotics, Benzodiazepines, and More

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Objectives

Learning objectives:

1. Review common challenging behaviours in dementia care and an approach to medication management when necessary

2. Describe the rational use of antipsychotics and benzodiazepines, and practical strategies for antipsychotic and benzodiazepine withdrawals.
BPSD = “symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia”

International Psychogeriatric Association Consensus Conference Statement, 1996

Prevalence of neuropsychiatric symptoms:

- 43% of patients with MCI
  - depression (20%)
  - apathy (15%)
  - irritability (15%)

- 75% of patients with dementia (2+ symptoms in 55%)
  - apathy (36%)
  - depression (32%)
  - agitation/aggression (30%)

Lyketsos CG et al. JAMA 2002

BPSD

- reported in 63% of dementia patients living in the community
- “...afflict almost all patients with dementia over the course of their illness”
- “...may have a greater impact on health care resources and caregiver distress than cognitive abnormalities”
- those with behavioral disturbances will enter LTC 2 years earlier

Lyketsos CG et al. JAMA 2002
Mega MS et al. Arch Neurol 1999
P.I.E.C.E.S. framework

Look at the reasons behind the behavior (what's changed?), impact, and risk to individual and others:

- Consider role of Physical factors – e.g., co-morbidities, meds, pain
- Assess “intrinsic factors” (Intellectual, Emotional, Capacities)
- Seek collateral info sources re situational precipitants (Environmental)
- Consider in relation to premorbid personality / Social circumstances

Always consider behavioral interventions first

Ontario’s Strategy for Alzheimer Disease and Related Dementia: Initiative #2

Agitation, Aggression, and Psychosis
Agitation, Aggression, Psychosis
- Nonpharmacologic Strategies

- Assess for physical discomfort
- Avoid confrontation
- Plan structured daily activities (exercise, arts and crafts, gardening, simple housework)
- Assign household chores that can be easily accomplished
- Provide clocks and calendars in clear view
- Avoid interactions with strangers and unfamiliar environments
- Ignore behavior that is only annoying and not a threat
- Reward positive experiences
- [Play soft music; introduce aromatherapy]

Blaszczyk AT, Mathys M. Journal of Pharmacy Practice 2007
Agitation, Aggression, Psychosis
- Nonpharmacologic Strategies

- “Get into their world”, age 3-30, and identify potential triggers
  - PIECES of My Personhood
    - Artful distraction
      - “Mountain top experiences” – proud, positive moments
      - Recognize traumatic experiences – abuse, stressful times
      - Suggest a physical task/activity to help the person feel useful
    - Communicate feeling – smile, sorry, calm
    - Don’t confront the false belief; validate the feeling

Sources: Dr. Ken LeClair, NE LHIN Behavioural Supports Ontario

Agitation, Aggression, Psychosis
- Pharmacologic treatment

- AchEIs
- Memantine
- Antidepressants
  - Citalopram (10-20mg/d)
  - Trazadone (50-250mg/day; limited evidence; watch for sedation, orthostatic hypotension)

Ponteisson AP, et al. JAMA 2014
Blaszczyk AT, Mathys M. Journal of Pharmacy Practice 2007
Okereke DJ, Harvard Dementia Review 2010
Lonergan E, Luxenberg J. Cochrane Database Syst Rev 2009
Tariot PN, et al. Arch Gen Psychiatry 2011
Canadian Coalition for Senior’s Mental Health

www.ccsmh.ca/en/projects/ltc.cfm

### Table 1: Medications for Agitation or Psychosis

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose</th>
<th>Dose &amp; Maximum Dose</th>
<th>Formulations</th>
<th>Adverse Events</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atypical Antipsychotics</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Risperidone</td>
<td>0.25 mg BID or 0.5 mg OD</td>
<td>0.25 mg every 1-6 weeks, max. 3 mg OD</td>
<td>Tablet (25, 50, 100 mg)</td>
<td>Tardive dyskinesia, akathisia, extrapyramidal reactions</td>
<td>Most likely to cause EPS</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5-20 mg QHS</td>
<td>5-20 mg every 6-7 days, max. 35 mg BID or OD</td>
<td>Tablet (5, 10, 15, 20, 30 mg)</td>
<td>Somnolence, weight gain, constipation</td>
<td>Most likely to cause metabolic side effects</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25 mg PO OD</td>
<td>12.5 mg every 2-7 days, up to 50 mg daily dose</td>
<td>Tablet (25, 50, 100, 150 mg)</td>
<td>Hypotension, blurred vision, orthostatic hypotension</td>
<td>Most likely to cause orthostasis</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
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<tr>
<td>Citalopram</td>
<td>10 mg PO OD</td>
<td>10 mg every 1-2 weeks, max. 20 mg</td>
<td>Tablet, liquid forms</td>
<td>Dizziness, sleep disturbance, blurred vision</td>
<td>Most likely to cause EPS</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>20 mg PO OD</td>
<td>20 mg every 1-2 weeks, max. 40 mg</td>
<td>Tablet, liquid forms</td>
<td>Dizziness, sleep disturbance, blurred vision</td>
<td>Most likely to cause EPS</td>
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<tr>
<td><strong>Antihypertensives</strong></td>
<td></td>
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</tr>
<tr>
<td>Carperidine</td>
<td>10 mg PO OD</td>
<td>10 mg every 1-2 weeks, max. 30 mg</td>
<td>Tablet, liquid forms</td>
<td>Sedation, dizziness, orthostatic hypotension, dry mouth</td>
<td>High potential to cause EPS</td>
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<tr>
<td><strong>Typical Antipsychotics</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Haloperidol</td>
<td>0.5 mg PO BID</td>
<td>0.5 mg every 2-3 days, max. 2 mg</td>
<td>Oral, short-acting injectable depot formulations</td>
<td>Tardive dyskinesia, akathisia, extrapyramidal reactions</td>
<td>Most likely to cause EPS</td>
</tr>
</tbody>
</table>

Seitz DP. Canadian Coalition for Senior’s Mental Health. 2012
Risk of Death With Atypical Antipsychotic Drug Treatment for Dementia
Meta-analysis of Randomized Placebo-Controlled Trials

Lon S. Schneider, MD, MS
Karen S. Dagerman, MS
Philip Insel, MS

A majority of elderly patients with dementia develop aggression, delusions, and other neuropsychiatric symptoms during their illness course. Antipsychotic medications are commonly used to treat these behaviors.

Context: Atypical antipsychotic medications are widely used to treat delusions, aggression, and agitation in people with Alzheimer disease and other dementias; however, concerns have arisen about the increased risk for cerebrovascular adverse events, rapid cognitive decline, and mortality with their use.

Objective: To assess the evidence for increased mortality from atypical antipsychotic drug treatment for people with dementia.

Data Sources: MEDLINE (1966 to April 2008), the Cochrane Controlled Trials Register (2005, Issue 1), and meetings presentations (1997-2004), and information from the sponsors were searched using the terms for atypical antipsychotic drugs (aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone), dementia, Alzheimer disease, and clinical trial.

- JAMA 2005 meta-analysis of 15 trials
- Odds Ratio of death = 1.54
- Over 10-12 weeks, “for every 9 to 25 persons helped in these trials there possibly will be 1 death”

Schneider LS, et al. JAMA 2005

The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial

- 164 patients randomized to continue antipsychotic or switch to placebo at 12 months
- 24 m survival 46% vs 71%
- 36 m survival 30% vs 59%
- “avoid protracted periods of treatment with antipsychotic drugs in people with dementia”

Antipsychotic Adverse Events in Persons with Dementia

**Serious Adverse Events**
- 1-2% increased risk of death associated with use of atypical antipsychotics over 6-12 months (odd ratio=1.6, number needed to harm = 50-100)
- Approximately 1% risk of stroke with short-term treatment (relative risk = 2.7)

**Other Adverse Effects**
- Sedation
- Worsening of cognitive impairment and functional decline
- Affect gait, increased risk of falls and fractures
- Extrapyramidal symptoms (risperidone > quetiapine)
- Metabolic changes – blood glucose, dyslipidemia, weight gain

Seitz DP. Canadian Coalition for Senior's Mental Health. 2012

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**Agitation, Aggression, psychosis**
- Pharmacologic treatment - Antipsychotics

- 4th Canadian Consensus Conference on Dementia, 2012:
  Risperidone, olanzapine and aripiprazole can be used for severe agitation, aggression and psychosis where there is a risk of harm to the patient and/or others. The potential benefit of all antipsychotics must be weighed against the significant risks such as cerebrovascular adverse events and mortality (Grade 2A).

- Discontinue antipsychotics drugs
  - after 1 week for delirium
  - after 6 months for psychotic major depression
  - taper within 3 – 6 months for agitated dementia to determine lowest effective maintenance dose

Agitation, Aggression, psychosis
- Pharmacologic treatment - Antipsychotics

- Use atypical antipsychotics short term (6-12 weeks) in cases of “severe physical aggression and severe psychosis causing tangible risk or extreme distress”

- Document use of behavioral/environmental interventions, and education of caregiver/family about benefits and risks

- Use lowest doses necessary for the shortest time period, and monitor for side effects

- “longer-term use of antipsychotics in people with AD is probably inadvisable, other than in exceptional clinical circumstances”

Withdrawal strategies for Antipsychotics in the Cognitively Impaired Elderly
Use of Benzodiazepines and Antipsychotics in Elderly in Canada

Rate of Use (Change from 2001/02 to 2009/10)
- BDZ: 22.6% to 21.1%
- AP: 4.5% to 5.1%

New Starts (Change from 2002/03 to 2009/10)
- BDZ: 4.8% to 4.2%
- AP: 1.7% to 1.6%

% Chronic Users (Change from 2001/02 to 2009/10)
- BDZ: ~50% to ~53%
- AP: ~59% to ~63%

Withdrawal Strategies: Antipsychotics

Abrupt Discontinuation
- Immediate cessation

Gradual Discontinuation
- Dose tapering schedules
  - 25 - 50% dose reduction every 1 – 2 weeks
Antipsychotic Withdrawal in BPSD: Cochrane Review

<table>
<thead>
<tr>
<th>Study</th>
<th>Antipsychotic</th>
<th>Withdrawal Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ballard 2004</td>
<td>Neuroleptic use</td>
<td>Abrupt D/C</td>
</tr>
<tr>
<td>Ballard The DART – AD Trial</td>
<td>Thioridazine, chlorpromazine, haloperidol, trifluoperazine, risperidone</td>
<td>Abrupt D/C</td>
</tr>
<tr>
<td>Bridges-Parlet 1997</td>
<td>NA</td>
<td>Abrupt D/C, equivalent doses of neuroleptics for chlorpromazine doses &lt; 50mg: Dose Taper, equivalent doses of neuroleptics &gt; 50mg chlorpromazine: reduce 50% in week 1, then d/c week 2</td>
</tr>
<tr>
<td>Cohen-Mansfield 1999</td>
<td>Haloperidol, thioridazine or lorazepam</td>
<td>3 week taper</td>
</tr>
<tr>
<td>Devanand 2012</td>
<td>Haloperidol</td>
<td>Abrupt D/C, doses of 0.5 – 1mg daily: Dose Taper, doses of 2 – 3mg daily: reduce to 1mg x 2 weeks, then d/c, doses &gt;4 mg daily: reduce to 2mg x 2 weeks, then d/c</td>
</tr>
<tr>
<td>Devanand 2012</td>
<td>Risperidone</td>
<td>Abrupt D/C</td>
</tr>
<tr>
<td>Findlay 1989</td>
<td>Thioridazine</td>
<td>Dose Taper, reduce 50% in 1st week, then d/c the 2nd week</td>
</tr>
<tr>
<td>Ruths The BENDNURS</td>
<td>Haloperidol, risperidone or olanzapine</td>
<td>Abrupt D/C</td>
</tr>
<tr>
<td>Van Reekum 2002</td>
<td>NA</td>
<td>Dose Taper, reduce 50% in 1st week, 50% reduction in the 2nd week, then d/c</td>
</tr>
</tbody>
</table>

Results of Antipsychotic Withdrawal

- Ballard 2004 (continuation vs. abrupt withdrawal)
  - No significant difference in change in NPI score or key psychiatric behaviours (agitation, psychosis or mood)
  - NPI ≤ 14: abrupt d/c particularly good outcome; NPI > 14: abrupt d/c led to marked behavioural problems
- Pooled: Ballard 2004 + Ballard DART-AD (continuation vs. abrupt withdrawal)
  - No significant difference in NPI scores at 3 months
- Bridges-Parlet (continuation vs. withdrawal)
  - No significant difference in PAB
- Cohen-Mansfield (continuation vs. withdrawal)
  - No difference in CMAI or BPRS scores; Verbal fluency better in withdrawal group
- Devanand 2012
  - 60% relapse rate in d/c vs. 33% relapse rate in continuation group
- Ruths BENDNURS (continuation vs. withdrawal)
  - No significant changes in NPI – Q scores between groups; Patients with behavioural deterioration had higher baseline doses
- Van Reekum (continuation vs. withdrawal)
  - No significant difference in BEHAVE-AD
Results of Antipsychotic Withdrawal: Adverse Effects

- Ballard DART-AD
  - Slight, non-significant advantage in withdrawal group in change parkinsonism severity
- Cohen-Mansfield 1999
  - No significant difference in adverse effects
- Devanand 2012
  - No significant differences in adverse effects
- Findlay 1989
  - No significant differences but trend for greater reduction of adverse effects in withdrawal group
- Van Reekum 2002
  - No difference in EPS between two groups

Factors Associated with Severity of Withdrawal Symptoms

- Abrupt discontinuation
  - Discontinuation syndromes
    - Nausea, vomiting, diarrhea, diaphoresis, cold sweats, muscle aches and pains, insomnia, anxiety and confusion
  - Psychosis
    - Exacerbation or precipitation of severe, rapid onset or supersensitivity psychosis
  - Movement disorders
    - Withdrawal dyskinesias, rebound dystonia, parkinsonism, akathisia
- Receptor affinity
  - Dopaminergic rebound (e.g. risperidone)
  - Cholinergic rebound (e.g. olanzapine)
  - Histaminergic rebound (e.g. clozapine)
  - Serotomergic rebound (e.g. olanzapine)
- Prolonged use
- Half-life of antipsychotic
- Baseline dose
Strategies for successful withdrawal*

- Trial after 3 months on treatment
- No recent change in dose or frequency
- Ensure problematic BPSD symptoms not demonstrated
- Abrupt d/c – reserve for significant drug interaction or severe adverse effect
- Go Slow (esp short half-life, long duration of use, higher dose)
  - 25 – 50% dose reduction every 1 – 2 weeks
- Monitor for relapse, withdrawal effects

* Expert opinion and personal experience

Osser D, et al. NaRCAD 2013

Sleep Disorders
Sleep Disorders

- 14-59% prevalence of sleep disorders in MCI
- 40% of AD patients suffer from sleep disturbances, spending 40% of their time in bed awake
- A major source of stress for caregivers, increasing likelihood of institutionalization
  - Restless leg syndrome
  - REM sleep behavior disorders
  - Obstructive sleep apnea
  - Circadian rhythm sleep disorders

McCurry SM, et al. Sleep Medicine Reviews 2000

Sleep Disorders

- Restless legs syndrome
  - Unpleasant leg sensations that disturb sleep
  - Prevalence 10% in population, increasing with age to 19% in persons >80
    - Eliminate aggravating medications (TCA, SSRI, antipsychotics)
    - Dopamine agonists (ropinirole or pramipexole) – watch for orthostasis

Bloom HG, et al. JAGS 2009
Sleep Disorders

- REM sleep behavior disorders
  - a parasomnia involving vigorous dream-enacting behavior and nightmares
  - typically onsets age 60-70
  - may be due to brainstem disorders or medications
  - affects 50-83% of DLB patients
    - eliminate aggravating medications (TCA, SSRI, MAOI) and caffeine
    - Clonazepam 0.5 -1mg qhs

Sleep Disorders

- Obstructive sleep apnea (OSA)
  - Partial or complete cessations in respirations during sleep due to pharyngeal collapse
  - at risk if neck collar size >17” in men and > 16” in woman
  - prevalence in elderly 24-73%, increases with age even with normal BMI (decline in muscular strength, edentate patients)
  - 50-80% prevalence in persons with dementia
  - OSA → impairments in executive function, working memory, episodic memory, attention, early morning confusion
Sleep Disorders

- **Obstructive sleep apnea**
  - CPAP
  - weight loss, avoid alcohol and sedatives
  - treatment in early dementia may slow disease progression

Bloom HG, et al. JAGS 2009

Sleep Disorders

- **Circadian rhythm sleep disorders**
  - relatively normal sleep that occurs at abnormal times
  - circadian timing is sensitive to environmental light and melatonin, controlled by SCN of hypothalamus
    - **Advanced Sleep Phase Disorder**
      - earlier bedtimes and early morning wakenings, frequent daytime sleepiness
      - prevalence of 1-7% in older adults
    - **Irregular Sleep-Wake Disorder**
      - time asleep broken into at least 3 different periods  erratic day time napping, fragmented shortened night time sleeping
      - common in dementia

Bloom HG, et al. JAGS 2009
Sleep Disorders

- **Circadian rhythm sleep disorders**
  - Advanced Sleep Phase Disorder
    - behavioral management
  - Irregular Sleep-Wake Disorder
    - 30+ minutes sunlight exposure/day, increased social and physical activity during daytime, less night time light and noise
    - bright light therapy + melatonin < 2.5mg

Riemersma-van der Lek RF, et al. JAMA 2008
Bloom HG, et al. JAGS 2009

Sleep Disorders

- Avoid benzodiazepines - use associated with worsened cognition, disinhibited behavior, falls
- Consider - **Trazadone 25-50mg q evening**
  - **Mirtazapine 15-30mg**
Withdrawal strategies for Benzodiazepines in the Cognitively Impaired Elderly

**Benzodiazepine Withdrawal Strategies**

- **Abrupt Discontinuation**
  - Immediate cessation

- **Minimal Intervention**
  - Letter; Self-help booklet
  - Brief consultation; One-time counseling

- **Gradual Discontinuation**
  - Dose-tapering schedules
    - 10–25% every 1–2 weeks

- **Psychotherapy**
  - Cognitive behavioural therapy

- **Gradual Discontinuation + Psychotherapy**
  - Dose tapering + CBT

- **Gradual Discontinuation + Pharmacotherapy**
  - Dose tapering + Adjuvants (paroxetine, melatonin, SSRI, buspirone, trazodone, valproate, carbamazepine, propranolol, imipramine)
BDZ Withdrawal: SR of Non-pharmacological Interventions in Elderly

<table>
<thead>
<tr>
<th>Study</th>
<th>Author</th>
<th>Mean age</th>
<th>Women (%)</th>
<th>Minimum BDZ Use</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Bashir 1994</td>
<td>62</td>
<td>61</td>
<td>3x/wk x 1 yr</td>
<td>MI</td>
</tr>
<tr>
<td>B</td>
<td>Cormack 1994</td>
<td>69</td>
<td>79</td>
<td>1 Rx Q2M x 6M</td>
<td>MI</td>
</tr>
<tr>
<td>C</td>
<td>Gorgels 2005; de Gler 2010</td>
<td>63</td>
<td>72</td>
<td>Rxn x 3M + 60D use</td>
<td>MI</td>
</tr>
<tr>
<td>D</td>
<td>Heather 2004</td>
<td>69</td>
<td>77</td>
<td>1 Rx Q2M x 6M</td>
<td>MI</td>
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<tr>
<td>E</td>
<td>Salorja 2010</td>
<td>73</td>
<td>84</td>
<td>NA</td>
<td>MI</td>
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<tr>
<td>F</td>
<td>Vicens 2006</td>
<td>59</td>
<td>82</td>
<td>5x/wk x 1 y</td>
<td>MI + DT</td>
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<tr>
<td>G</td>
<td>Baillargeon 2003</td>
<td>67</td>
<td>58</td>
<td>OD x 3M</td>
<td>CBT + DT</td>
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<td>H</td>
<td>Morin 2004; Morin 2005</td>
<td>63</td>
<td>50</td>
<td>50% QHS x 3M</td>
<td>CBT + DT</td>
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<tr>
<td>I</td>
<td>Oude Voshar 2003; Oude Voshar 2006</td>
<td>63</td>
<td>70</td>
<td>Rxn x 3M + 60D use</td>
<td>CBT + DT</td>
</tr>
<tr>
<td>J</td>
<td>Tannenbaum 2014</td>
<td>75</td>
<td>69</td>
<td>Mean 1.3mg LZP E/day</td>
<td>MI + DT</td>
</tr>
</tbody>
</table>

Benzodiazepine Cessation Rates

Benzodiazepines: Factors Associated with Severity of Withdrawal

- **Pharmacologic Variables**
  - Higher daily dose of benzodiazepines
  - Potency of benzodiazepine dose
  - Longer duration of benzodiazepine therapy
  - More rapid rate of taper

- **Patient Variables**
  - Diagnosis of panic
  - Higher pre-taper levels of anxiety/depression
  - Higher levels of personality psychopathology
  - Concomitant alcohol and/or substance dependence/abuse

Strategies for Benzodiazepine Withdrawal

- Treat underlying disorder (anxiety, insomnia, seizures) adequately
- Go slow (especially if elderly, long-term use)
- If required, switch to diazepam (equivalent dose)
- Decrease daily dose by 25 – 50% per week initially (may decrease by 10 – 25% for elderly, chronic use and prolonged time frame i.e. every 2 – 4 weeks)
- Slow down taper further once titrated to 50% (taper by 10%, over q 2 – 4 weeks based on patient preference)
- To improve rates of cessation, incorporate CBT
Benzodiazepines: Discontinuation Syndromes

+ Withdrawal
  + Short/intermediate-acting benzodiazepines (occurs within 1 – 2 days)
    + Examples: triazolam, alprazolam, lorazepam, temazepam, oxazepam
  + Long-acting benzodiazepines (occurs within 5 – 10 days)
    + Examples: clobazam, clonazepam, diazepam, flurazepam
  + Insomnia, agitation, anxiety, dysphoria, headache, muscle aches, tremors, twitches, loss of appetite, seizures (acute withdrawal)

+ Pseudo withdrawal
  + Psychological withdrawal which results from patient’s apprehension about discontinuing the drug

Inappropriate Sexual Behavior
Inappropriate Sexual Behavior

- 7-25% of demented patient exhibit inappropriate sexual behaviors
- involvement of frontal lobes, temporo-limbic system, striatum (basal ganglia), or hypothalamus


Inappropriate Sexual Behavior
- Behavioral treatment

- Education for spouse/family and patient
  - reframe sexual expression (desire for closeness, comfort)

- Behavioral modification for inappropriate behavior in public
  - do not ignore, but avoid confrontation
  - simple, repeated explanation of inappropriateness
  - distraction and redirection
  - single room
  - avoid overstimulating TV or radio programs
  - modified clothing (trousers that open at back or no zippers)
  - adequate social and physical activity

Inappropriate Sexual Behavior - Pharmacologic treatment

- eliminate disinhibiting drugs (benzodiazapines), alcohol
- L-dopa can increase sexual behaviors in persons with Parkinson's disease
- no studies on women
- mainly case reports

Inappropriate Sexual Behavior - Pharmacologic treatment

- Paroxetine or Citalopram 20mg/d
- Clomipramine 150-200mg/d
- Quetiapine 25mg/d
- Trazadone 100-500mg/d (→ priapism in 1/6000)
- Gabapentin 300mg TID
- Pindolol 40mg /d divided BID-TID
- Estrogen 0.625mg/d
- Leuprolide acetate 7.5mg IM/month