Better Management of Psychoses in the Elderly

Suzanne Clifford

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Better Management of Psychoses in the Elderly

4 Hours Category 1

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Psychiatrist in Charge of Dementia Services, McLean Hospital

OBJECTIVE

By actively participating in this meeting, attendees will consider advances in the diagnosis and treatment of geriatric psychoses leading to enhanced patient outcomes.

AGENDA

7:30 a.m.-8:30 a.m. Registration/Continental Breakfast
8:30 a.m.-10:00 a.m. Enhancing Diagnosis of Psychoses in the Elderly
10:15 a.m.-11:45 a.m. Improving Patient Outcomes in Geriatric Psychoses
11:45 a.m.-12:30 p.m. Faculty Panel/Question-and-Answer Period

Supported by an unrestricted educational grant from Eli Lilly and Company.

*Not all speakers will appear at each meeting. Faculty subject to change without notice.
Key Slides

Enhancing Diagnosis of Psychoses in the Elderly

Objectives of Discussion

- What are the causes of late-life psychosis?
- How does late-life psychosis present?
- Assessment of behavioral disturbance in older patients
- Managing behavioral disturbances
  - Nonpharmacological approaches
  - Pharmacological approaches
    - Non-neuroleptic
    - Antipsychotics
- What is the data supporting pharmacological approach?

Presentation of Late-Life Psychosis

- Behavioral disturbance
  - Verbal
  - Vocal
  - Motor
- Psychiatric disturbance
  - Thought disorder
  - Delusions
  - Hallucinations
  - Affective disturbance

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Key Slides

Behavioral Disturbance Results in:

- Social isolation
- Caregiver burnout
- Institutional placement
- Increased use of medication
- Polypharmacy
- Increased risk of falls and injury
- Inappropriate use of restraints

Causes of Late-Life Psychosis

Psychotic Symptoms Can Occur in:

- Dementia
- Delirium
- Affective illness
- Late-onset schizophrenia
- Recurrence of early-onset schizophrenia

Definition

- Alzheimer's disease (AD) is a progressive dementia characterized by a slow decline in memory, language, visuospatial skills, personality and cognition

Cummings & Benson, 1992

Better Management of Psychoses in the Elderly
Key Slides

Differential Diagnosis of Dementia

• Causes of dementia can include:
  - Alzheimer’s dementia
  - Lewy body dementia
  - Vascular disease (including multi-infarct dementia)
  - Parkinson’s disease
  - Pick’s disease
  - Huntington’s disease
  - Normal pressure hydrocephalus

Differential Diagnosis of Dementia (Cont.)

• Causes of dementia can include:
  - Metabolic disorders, including vitamin B_{12} deficiency, chronic drug intoxication, hypothyroidism and alcoholism
  - Infectious causes including HIV, neurosyphilis and bacterial meningitis
  - Major depression
  - The clinical diagnosis of Alzheimer’s disease can be made with 85% to 90% accuracy

Epidemiology

• 4 million Americans with AD
• 14 million by year 2050
• 1% of those of age 60-65
• Doubles every 5 years
• 1 in 3 over age 85 with AD
• Death between 3-20 years after onset

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Key Slides

Epidemiology (Cont.)

- 4th leading cause of death after heart disease, cancer and stroke
- 50% of nursing home residents suffer from AD and related conditions
- Cost $100 billion annually
- $174,000 per lifetime
- Majority of the costs borne by caregivers

Imaging Presentations in AD

Reproduced from Doraiswamy PM, 1998

Clinical Presentation

- Memory impairment
- Word-finding difficulties
- Difficulty performing complex tasks (e.g., keeping checkbook, cooking)
- Geographic or temporal disorientation
- Day-night disorientation
- Language deterioration (e.g., empty speech)
- Difficulties with simple chores

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Key Slides

Clinical Presentation (Cont.)
- Troublesome behavior including:
  - Wandering
  - Irritability
  - Depression
  - Hallucinations, delusions
  - Agitation
  - Incontinence
  - Total dependence on caregivers

Diagnosis of AD is One of Inclusion
- Diagnosis of AD can be made on basis of typical presentation in majority of cases
- Insidious onset of progressive memory and functional decline in a clear state of consciousness in later life is usually AD

Dementia, Depression, Delirium

<table>
<thead>
<tr>
<th></th>
<th>Dementia</th>
<th>Depression</th>
<th>Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of consciousness</td>
<td>Alert</td>
<td>Alert</td>
<td>Waxes/wanes</td>
</tr>
<tr>
<td>Course</td>
<td>Chronic</td>
<td>Chronic or acute</td>
<td>Acute</td>
</tr>
<tr>
<td>Other features</td>
<td>—</td>
<td>Neuro-vegetative signs</td>
<td>Medical causes</td>
</tr>
</tbody>
</table>
**Key Slides**

### Late-Life Psychotic Symptoms: Psychiatric Causes—Depression

#### Characteristics of Early-Onset vs. Late-Onset Depression

<table>
<thead>
<tr>
<th>Feature</th>
<th>Early-Onset</th>
<th>Late-Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of depression</td>
<td>Common</td>
<td>Less common</td>
</tr>
<tr>
<td>Coexisting medical/neurologic problems</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>

Adapted from: Addonizio, Alexopoulos. Int J Geriatr Psychiatry, 1993;8:41-47

### Synonyms of Delirium

- Organic brain syndrome
- Cerebral insufficiency
- Metabolic encephalopathy
- Acute confusional state
- Toxic psychosis
- Organic psychosis
- Reactive psychosis

### Medical Causes of Delirium/Agitation

- UTIs
- Bowel impaction
- Recent onset of illness/surgery
- Recent change in medication/polypharmacy
- Sleep disturbances: primary, secondary
- Chronic/acute pain
- Cardiovascular disease
- Visual impairment
- Poor nutrition
- Respiratory infection

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Key Slides

Medical Disorders Associated with Delirium
- Hypo/hyperglycemia
- Hypo/hyperthyroidism
- Cushing's disease
- Parkinson's disease
- Sodium/potassium imbalance
- B₁₂ and folate deficiency
- Sleep deprivation
- HIV
- Alcohol withdrawal

Medications Associated with Delirium
- Anticholinergics (diphenhydramine, TCAs, conventional antipsychotics)
- Steroids
- Sedatives/hypnotics (toxicity/withdrawal)
- Narcotics

Laboratory and Other Exams
- Chem 20, complete blood count (CBC), syphilis, B₁₂, folate, thyroid function tests (TFTs), urinalysis (UA), urine drug screen
- Magnetic resonance imaging (MRI) or computed tomography (CT) at time of diagnosis
- The following are rarely indicated—not as routine:
  - Electroencephalogram (EEG) (sleep-deprived with temporal lobe leads will increase yield)
  - Single-photon emission computed tomography (SPECT)/positron emission tomography (PET)
Key Slides

Mini-Mental State Exam (MMSE)
- Not a diagnostic test; use as screening tool
- Scores are influenced by multiple noncognitive factors (age, education, language, culture)
- General rate of decline in AD is 2-4 points/year; rate of decline is dependent on level of severity
- Useful for establishing baseline, assessing treatment response and following patient over time

Progression of Constructional Disturbances in Alzheimer's Disease (AD)

(A) 1 year after onset (B) 3 years after onset (C) 8 years after onset

Neurochemistry
- Decrease in acetylcholine synthesis
- Decrease in the enzyme choline acetyltransferase
- Other neurotransmitter systems likely involved

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**Key Slides**

**AD: The Cholinergic Hypothesis**

- Acetylcholinesterase degrades acetylcholine

- Alzheimer's disease

- Frontal cortex

- Parietal cortex

- Basal forebrain

- Hippocampus

- Occipital

**Anticholinergic Antidepressant Medications**

- Amitriptyline
- Clomipramine
- Doxepin
- Imipramine
- Nortriptyline
- Paroxetine

**Anticholinergic Antipsychotic Medications**

- Thioridazine
- Mesoridazine
- Chlorpromazine
- Clozapine

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Key Slides

AD Treatment Strategies

Cholinergic Agents

- Initiating treatment
  - Diagnosis: mild-to-moderate AD
  - May improve behavioral disturbances in severe AD
  - Few contraindications
  - Counsel regarding appropriate expectations

- Monitoring response
  - Caregiver report of behavior and function
  - Cognitive test scores
  - Medication side effects

Cholinesterase Inhibitors for AD

- Tacrine (Cognex)*
- Donepezil (Aricept)*
- Rivastigmine (Exelon)
- Metrifonate
- Galantamine (Reminyl)

*FDA approved

Other Possible Interventions for Cognition

- Estrogen
- NSAIDs
- Ginkgo biloba
- Vitamin E

Better Management of Psychoses in the Elderly
Agitation and Caregiver Burnout Behaviors

Behaviors

- Physical violence
- Catastrophic reactions
- Hitting
- Making accusations
- Suspiciousness
- Incontinence
- Memory disturbance

Rabin P. Int Psychogeriatr. 1991;3(3):319-324

Delusions in Alzheimer's Disease

- 30-85% of patients have delusions
- Common beliefs/behaviors
  - Marital infidelity
  - Patients, staff are trying to hurt me
  - Staff, family members are impersonators
  - Personal harm
  - People stealing things
  - My house is not my home
  - Strangers living in my home
  - Misidentification of people
  - People on TV are real


What is "Agitation"?

- Any inappropriate verbal, vocal or motor activity that is not an obvious expression of need
- It is not a diagnostic term but a group of symptoms that can result from a variety of medical or psychiatric conditions

Adapted from: Mansfield C et al. (Various references)
Key Slides

Ideal Outcomes of Intervention

- Removal of all signs and symptoms of disturbance
- Minimization of side effects
- Compliance with treatment goals
- No recurrences
- Functional reintegration—not behavioral containment

Psychosis and Agitation

Nonpharmacologic Management

- Reassure, distract
- Set-up routines
- Remove offending pharmacologic agents
- Assess and adjust environmental triggers and other potential sources of agitation
- Ensure support for the caregiver and/or staff

- No medication is approved by the U.S. Food and Drug Administration for the treatment of behavioral disturbance in dementia

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Key Slides

Choice of Pharmacotherapy Is Based on:
- Diagnosis
- Target symptoms
- Medication effects
- Medication side effects
- Costs
- Comorbidity

General Principles of Geriatric Pharmacotherapy
- Combine with behavioral intervention
- Treat underlying medical problem
- Start low, go slow—increase only if necessary
- Give medication an adequate trial
- Choose medication based on S/E profile
- Dosing decisions based on patient subtype

Pharmacotherapy
- Anticonvulsants
- Antidepressants
- Trazodone
- Benzodiazepines
- Buspirone
- Acetylcholinesterase inhibitors
- Antipsychotics

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Key Slides

Benzodiazepines

- Minimal efficacy data
- Sedating
- Further inhibit learning and memory
- Cause falls
- Paradoxical disinhibition

Conventional Antipsychotics

Meta-Analysis of Controlled Trials
- 33 studies: comparison of conventional antipsychotics to placebo or to each other in elderly patients with dementia
- In no study was antipsychotic treatment statistically better than placebo
- Combined analysis showed modest efficacy; 18% of patients did better on antipsychotics than on placebo
- Considerable toxicity was evidenced


Tardive Dyskinesia in Middle-Aged and Elderly Outpatients (N=439)


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Key Slides

Development of TD
Olanzapine- and Haloperidol-Treated Pts*

*1-Yr Incidence*: Olanz = 0.52% (N=513); Hal = 7.45% (N=114)

\[ \text{Days of Therapy} \]
\[ \% \text{ of Pts with TD} \]

\[ \text{Olanzapine} \]
\[ \text{Haloperidol} \]

*Double-blind treatment; \(^*\)Excluding probable withdrawal dyskinesias prior to wk 6;

Clinical Consequences of Hyperprolactinemia

- Sexual dysfunction
  - Diminished libido
  - Decreased arousal
  - Orgasmic dysfunction
  - Impotence
- Reproductive dysfunction
  - Anovulation
  - Chaotic menses
  - Subfertility
  - Decreased estrogen
  - Decreased testosterone
- Breast pathology
  - Galactorrhea
  - Breast enlargement
  - PRL-sensitive dysplasia (?)
- Hypogonadism
  - Bone demineralization
  - Damage to cardiovascular endothelium
  - Behavioral dysfunction
  - Depression
  - Memory deficits
  - Psychopathology

Olanzapine vs. Risperidone in Schizophrenia: Effects on Prolactin

\[ \text{Mean Prolactin Change from Baseline, ng/ml} \]

\[ \text{Olanzapine} \]
\[ \text{Risperidone} \]

\[ \text{Week 8} \]
\[ 2.30^{*} \]
\[ 0.07 \]

\[ \text{Week 28} \]
\[ 1.97^{*} \]
\[ 0.02 \]

*Risperidone significantly greater than olanzapine; p<.001; Tran et al. J Clin Psychopharmacol. 1997;17:407-418

Better Management of Psychoses in the Elderly
**Key Slides**

**Criteria for a Novel Antipsychotic Drug**

- Lower incidence of EPS and TD
- Broader efficacy profile
- Minimal effect on prolactin levels

**Dopamine Pathways**

- Mesocorticolimbic = Antipsychotic Effect
- Nigrostriatal = Movement Disorders
- Tuberoinfundibular = Prolactin

**Risperidone: Psychosis and Aggressive Behavior in Dementia**

- 12-week, randomized, multicenter, placebo-controlled, fixed risperidone dose (0.5, 1, 2 mg/day) study
- 625 patients (hospital or nursing home)
  - 43% female
  - Mean age: 83 ± 8 years

Katz et al. J Clin Psychiatry. 1999(Feb);60(2):107-115

Better Management of Psychoses in the Elderly
Risperidone: Psychosis and Aggressive Behavior in Dementia (Cont.)

- Diagnoses
  - Alzheimer's dementia: 73%
  - Vascular dementia: 16%
  - Mixed dementia: 11%


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Risperidone: Psychosis and Aggressive Behavior in Dementia

Behave-AD Aggressiveness Score

<table>
<thead>
<tr>
<th>Change from Baseline to Endpoint</th>
<th>Placebo (N=161)</th>
<th>Risperidone 0.5 mg (N=146)</th>
<th>Risperidone 1 mg (N=148)</th>
<th>Risperidone 2 mg (N=162)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>4.80</td>
<td>4.75</td>
<td>4.65</td>
<td>5.10</td>
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</table>

*p<0.05 vs. placebo; Katz et al. J Clin Psychiatry. 1999(Feb);50(2):107-115

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Risperidone: Psychosis and Aggressive Behavior in Dementia

<table>
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<tr>
<th>Disease</th>
<th>Placebo (N=162)</th>
<th>0.5 mg/Day (N=149)</th>
<th>1 mg/Day (N=148)</th>
<th>2 mg/Day (N=165)</th>
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</thead>
<tbody>
<tr>
<td>Injury</td>
<td>37</td>
<td>33</td>
<td>28</td>
<td>32</td>
</tr>
<tr>
<td>Edema, peripheral</td>
<td>6</td>
<td>16</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Pain</td>
<td>8</td>
<td>8</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Fever</td>
<td>7</td>
<td>10</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Somnolence</td>
<td>7</td>
<td>10</td>
<td>16</td>
<td>28</td>
</tr>
<tr>
<td>Agitation</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Extrapyramidal disorder</td>
<td>7</td>
<td>6</td>
<td>13</td>
<td>21</td>
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</tbody>
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Better Management of Psychoses in the Elderly
Key Slides

Risperidone: Psychosis and Aggressive Behavior in Dementia (Cont.)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=163)</th>
<th>0.5 mg/Day (N=149)</th>
<th>1 mg/Day (N=148)</th>
<th>2 mg/Day (N=165)</th>
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</thead>
<tbody>
<tr>
<td>Rhinitis</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Cough</td>
<td>8</td>
<td>11</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Upper respiratory</td>
<td>4</td>
<td>10</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall</td>
<td>19</td>
<td>16</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>Urinary infection</td>
<td>12</td>
<td>15</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Purpura</td>
<td>12</td>
<td>17</td>
<td>12</td>
<td>10</td>
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</table>

Katz et al. J Clin Psychiatry. 1999(Feb);60(2):107-115

Risperidone in the Elderly

- Effective therapy
- Significant adverse events >1 mg
- Narrow therapeutic window
- Raises prolactin (? significance in elderly)

Quetiapine in the Elderly

- Efficacy trial in dementia ongoing
- Safety in psychotic disorders in the elderly established (mixed diagnoses)
- Median total dose = 100 mg/day
- Dosing in dementia not established


Better Management of Psychoses in the Elderly
**Key Slides**

**Olanzapine: Psychosis and Agitation in Dementia**

**Study Design**
- N=206
- Washout and placebo lead in (3-14 days)
- 6-week, double-blind, acute treatment
  - Placebo
  - Olanzapine 5 mg/day
  - Olanzapine 10 mg/day (titration from 5 mg)
  - Olanzapine 15 mg/day (titration from 5 mg)
- 18-week open label: 5-15 mg/day of olanzapine (ongoing, data not available)

*Street et al, 3rd Congress of European Federation of Neurological Societies, 1998*

**Olanzapine: Psychosis and Agitation in Dementia**

**NPI/NH: Agitation/Aggression Item**

Mean Change from Baseline (LOCF)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Placebo</th>
<th>Olanzapine 5 mg</th>
<th>Olanzapine 10 mg</th>
<th>Olanzapine 15 mg</th>
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</thead>
<tbody>
<tr>
<td>7.40</td>
<td></td>
<td></td>
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<td>8.38</td>
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<tr>
<td>8.35</td>
<td></td>
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<td>7.90</td>
<td></td>
<td></td>
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</tbody>
</table>

* p<.05 vs. placebo; Significantly greater improvement on the agitation/aggression item of the NPI was seen in patients treated with 5 or 10 mg/day of olanzapine compared to placebo; LOCF = last observation carried forward; Street et al, 3rd Congress of European Federation of Neurological Societies, 1998*

**Olanzapine: Psychosis and Agitation in Dementia**

**NPI/NH Core Total: Agitation, Delusions, and Hallucinations**

Mean Change from Baseline (LOCF)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Placebo</th>
<th>Olanzapine 5 mg</th>
<th>Olanzapine 10 mg</th>
<th>Olanzapine 15 mg</th>
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<tr>
<td>14.76</td>
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<td></td>
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<tr>
<td>14.44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.14</td>
<td></td>
<td></td>
<td></td>
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</table>

* p<.001 vs. placebo; Significantly greater improvement in the sum of agitation, delusions and hallucinations score of the NPI was seen in patients treated with 5 or 10 mg/day of olanzapine compared to placebo; LOCF = last observation carried forward; Street et al, 3rd Congress of European Federation of Neurological Societies, 1998*

Better Management of Psychoses in the Elderly
**Key Slides**

**Olanzapine: Psychosis and Agitation in Dementia**

**Acute Extrapyramidal Symptoms**

<table>
<thead>
<tr>
<th>Simpson-Angus</th>
<th>AIMS</th>
<th>Barnes Akathisia</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Olanzapine 5 mg</td>
</tr>
<tr>
<td>Mean Change from Baseline (LOCF)</td>
<td>0.50</td>
<td>-1.00</td>
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</table>

AIMS = abnormal involuntary movement scale; LOCF = last observation carried forward; Street et al. 3rd Congress of European Federation of Neurological Societies, 1998

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**Olanzapine: Psychosis and Agitation in Dementia**

**Treatment-Emergent Potential Peripheral Anticholinergic Adverse Events**

<table>
<thead>
<tr>
<th>Olanzapine (N, %)</th>
<th>Placebo (N=46)</th>
<th>5 mg (N=56)</th>
<th>10 mg (N=50)</th>
<th>15 mg (N=54)</th>
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<tbody>
<tr>
<td>Constipation</td>
<td>2 (4.3)</td>
<td>2 (3.6)</td>
<td>3 (6.0)</td>
<td>4 (7.5)</td>
</tr>
<tr>
<td>Fecal impaction</td>
<td>1 (2.1)</td>
<td>1 (1.8)</td>
<td>1 (2.0)</td>
<td>2 (3.8)</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>0</td>
<td>0</td>
<td>1 (2.0)</td>
<td>0</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>1 (2.1)</td>
<td>3 (5.4)</td>
<td>1 (2.0)</td>
<td>0</td>
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<tr>
<td>Urinary retention</td>
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<td>0</td>
<td>1 (2.0)</td>
<td>1 (1.9)</td>
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<tr>
<td>Amblyopia</td>
<td>0</td>
<td>1 (1.8)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

No significant differences were found among placebo and olanzapine treatment groups.

---

**Olanzapine: Psychosis and Agitation in Dementia**

**Mini-Mental State Exam (MMSE) Total**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>7.25</th>
<th>7.31</th>
<th>6.62</th>
<th>6.44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Change from Baseline (LOCF)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

*Sum of all items; LOCF = last observation carried forward; Street et al. 3rd Congress of European Federation of Neurological Societies, 1998

**Better Management of Psychoses in the Elderly**

ZY · 9371 688

Zyprexa MDL 1596 Confidential-Subject to Protective Order
Zyprexa MDL Plaintiffs' Exhibit No.04090
Key Slides

Evidence for Olanzapine Improving Cognition

- Using *in vivo* microdialysis, olanzapine raises brain acetylcholine levels\(^1\)
- 5-HT\(_3\) receptor antagonists increase acetylcholine release\(^2\)
- Acetylcholine M\(_2\) receptor antagonist increase acetylcholine release\(^3\)


Reduction of Psychotic Symptoms in Patients with Lewy Body Dementia (LBD) Treated with Olanzapine

**Background**

- Approximately 15-25% of elderly demented patients have cortical or subcortical Lewy bodies
- Most cases of DLB (~75%) have clinical and pathological features of Alzheimer's dementia, of which DLB has some overlap

Street et al. European Neuropsychopharmacology. 1999;9(suppl 5)

Reduction of Psychotic Symptoms in Patients with Lewy Body Dementia (LBD) Treated with Olanzapine (Cont.)

**Background**

- Core clinical features usually include:
  - Fluctuating cognition, attention and alertness
  - Recurrent visual hallucinations and other psychotic symptoms
  - Spontaneous motor features of parkinsonism

Street et al. European Neuropsychopharmacology. 1999;9(suppl 5)

Better Management of Psychoses in the Elderly
Reduction of Psychotic Symptoms in Patients with Lewy Body Dementia (LBD) Treated with Olanzapine

Background: DLB Diagnosis and Treatment

- Susceptible to confusional, agitational effects of neuroleptics
- Susceptible to parkinsonian effects of neuroleptics

Street et al. European Neuropsychopharmacology. 1999;9(suppl 8)

Reduction of Psychotic Symptoms in Patients with Lewy Body Dementia (LBD) Treated with Olanzapine (Cont.)

Background: DLB Diagnosis and Treatment (Cont.)

- Important to differentiate DLB from pure AD due to differences in treatment response
  - More impairment on attentional, executive, visuospatial tasks than in AD
  - Fluctuating, rapid progression
  - Extrapyramidal symptoms similar to Parkinson’s but less severe
  - Better response to cholinesterase inhibitors than in AD

Street et al. European Neuropsychopharmacology. 1999;9(suppl 8)

Reduction of Psychotic Symptoms in Patients with Lewy Body Dementia (LBD) Treated with Olanzapine

Primary Objective: DLB Analysis

- To assess the efficacy of 5, 10 and 15 mg/day of olanzapine compared to placebo in the treatment of psychosis among patients in nursing care facilities who have Alzheimer’s disease and possible dementia with Lewy bodies

Street et al. European Neuropsychopharmacology. 1999;9(suppl 8)

Better Management of Psychoses in the Elderly

ZY 9371 690

ZY 00585920
Assessments and Analysis Methods: Efficacy

- Primary measure
  - NPI/NH psychosis total: sum of hallucinations and delusions items

- Secondary measures
  - Other NPI/NH items
  - Brief Psychiatric Rating Scale (BPRS)
  - Mini-Mental State Examination (MMSE)

NPI/NH Psychosis Total

Delusions and Hallucinations

Baseline: 12.10  14.00  11.86  9.29

Mean Change from Baseline (LOCF)

Improvement

-12  -10  -8  -6  -4  -2  0  2  4  6  8  10  12

Placebo
  - Olanzapine 5 mg
  - Olanzapine 10 mg
  - Olanzapine 15 mg

\[ t^{*}=0.056 \text{ vs. placebo}; \quad **=0.003 \text{ vs. placebo}; \text{Significantly greater improvement in sum of delusions and hallucinations items with 5 mg/day of olanzapine; Numerically greater improvement with 10 mg/day of olanzapine} \]

NPI/NH Psychosis Total

Delusions and Hallucinations

Mean Change from Baseline (Mean Change from Baseline)

-15  -10  -5  0  5

Weeks of Double-Blind Therapy

-5  0  5  10  15  20

Placebo
  - 5 mg
  - 10 mg
  - 15 mg

\[ t^{*}=0.05; \quad p=0.10 \text{ vs. placebo}; \quad *p=0.05 \text{ vs. placebo}; \text{Significant improvement on the NPI psychosis total items with 5 mg/day olanzapine; Changes in patients receiving 10 or 15 mg/day were not significantly different from those in patients receiving placebo} \]
Key Slides

### NPI/NH Core Total
Agitation/Aggression, Delusions and Hallucinations

<table>
<thead>
<tr>
<th>Improvement</th>
<th>Baseline:</th>
<th>Mean Change to Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>19.10</td>
<td>-2.90</td>
</tr>
<tr>
<td>Olanzapine, 5 mg</td>
<td>20.00</td>
<td>-7.00</td>
</tr>
<tr>
<td>Olanzapine, 10 mg</td>
<td>20.86</td>
<td>-6.14</td>
</tr>
<tr>
<td>Olanzapine, 15 mg</td>
<td>15.43</td>
<td>-15.05**</td>
</tr>
</tbody>
</table>

*p=0.062 vs. placebo; **p=0.004 vs. placebo; Significantly greater improvement on the NPI core total items with 5 mg/day of olanzapine; Numerically greater Improvement with 10 or 15 mg/day

### MMSE Total
(Sum of All Items)

<table>
<thead>
<tr>
<th>Improvement</th>
<th>Baseline:</th>
<th>Mean Change to Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>6.10</td>
<td>+2.40</td>
</tr>
<tr>
<td>Olanzapine, 5 mg</td>
<td>8.80</td>
<td>+2.67</td>
</tr>
<tr>
<td>Olanzapine, 10 mg</td>
<td>6.67</td>
<td>5.00</td>
</tr>
<tr>
<td>Olanzapine, 15 mg</td>
<td>5.07</td>
<td></td>
</tr>
</tbody>
</table>

*p=0.507 vs. placebo; **p=0.035 vs. placebo; Significantly greater improvement in cognitive functioning with 5 mg/day of olanzapine; Numerically greater improvement with 10 mg/day; Patients receiving 15 mg/day were not significantly different from those receiving placebo

### Antipsychotic Treatment of Maladaptive Behaviors in Dementia

- **N = 2,747**
- Geriatric psychiatric inpatients with a primary DSM-IV discharge diagnosis of dementia disorder
- **Purpose:** compare improvements in maladaptive behaviors associated with 1 of 3 antipsychotic agents: haloperidol, olanzapine or risperidone

Tunis et al. Institute of Psychiatric Sources, New Orleans, 1998

Better Management of Psychoses in the Elderly
Key Slides

Outcome Instrument:
Psychogeriatric Dependency Rating Scale (PDRS)

- Behaviors rated
  - Disruptive
  - Manipulative
  - Wandering
  - Socially objectionable
  - Demanding interaction
  - Communication difficulties
  - Noisy
  - Active aggression
  - Passive aggression
  - Verbal aggression
  - Restless
  - Destructive (self)
  - Destructive (property)
  - Affect-related
  - Delusions/hallucinations
  - Speech content

- Scored as 1 = never, 2 = occasionally, 3 = frequently

Tunis et al. Institute of Psychiatric Sources, New Orleans, 1999

PDRS Behavioral Changes in Occurrence from Admission to Discharge

Olanzapine vs. Risperidone

Change in behavior occurrences (Score)

PDRS Behaviors
Higher scores indicate greater improvement in behaviors
Tunis et al. Institute of Psychiatric Sources, New Orleans, 1999

PDRS Behavioral Changes in Occurrence from Admission to Discharge

Olanzapine vs. Haloperidol

Change in behavior occurrences (Score)

PDRS Behaviors
Higher scores indicate greater improvement in behaviors
Tunis et al. Institute of Psychiatric Sources, New Orleans, 1999

Better Management of Psychoses in the Elderly
Chronic Schizophrenia in the Geriatric Patient

- Early age of onset
- Severe negative symptoms
- Poor adaptive functioning
- Severe cognitive impairment
- Require lengthy institutional care
- Late-onset schizophrenia has a different presentation

Differentiating Late- and Early-Onset Schizophrenia

<table>
<thead>
<tr>
<th></th>
<th>Early Onset</th>
<th>Late Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions of persecution</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Sensory hallucinations</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Formal thought disorder</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Blunted affect</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>


Olanzapine vs. Haloperidol in the Treatment of Elderly Patients with Schizophrenia and Related Psychotic Disorders

Study Design

- Global
- Geriatric patients; age ≥65 years
- N=59
- Schizophrenia/schizophreniform disorder/schizoaffective disorder, in/outpatient, BPRS_{16} ≥18 or intolerant of current therapy


Better Management of Psychoses in the Elderly
Olanzapine vs. Haloperidol in the Treatment of Elderly Patients with Schizophrenia and Related Psychotic Disorders (Cont.)

Study Design

• 6 weeks acute, extension
• 2 treatment groups
  • Olanzapine, 5-10 mg/day
  • Haloperidol, 5-20 mg/day


Conclusions

Efficacy Findings

• Olanzapine was numerically greater than haloperidol in the treatment of overall and negative symptom psychopathology and depressive symptoms
• Lower rate of discontinuation because of lack of efficacy with olanzapine than with haloperidol


Conclusions

Safety Findings

• Lower rate of discontinuation because of adverse events with olanzapine than with haloperidol
• Olanzapine-treated patients had statistically significantly less EPS than haloperidol-treated patients
• Olanzapine had a superior adverse-event profile versus haloperidol


Zy9371 694.001

Better Management of Psychoses in the Elderly
Key Slides

Choice of Medication Is the Behavior

- Withdrawn, irritable, dysphoric?
  - Consider antidepressant
- Hyperactive, pressured, sexual?
  - Consider mood stabilizing agent or novel antipsychotic agent
- Paranoid, hallucinating, psychotic?
  - Consider novel antipsychotic
- Physically aggressive, violent?
  - Consider novel antipsychotic
- Restless, situation specific, anxious?
  - Consider serotonergic agent or buspirone

Conclusion and Summary

- Late-life psychosis usually presents as agitation
- Nonpharmacological interventions should be used in combination with pharmacological
- Drug choice should be based on side effect profile
- The novel antipsychotics, by virtue of their side effect profile, are the preferred agents
- Olanzapine and risperidone are both excellent choices with some definite advantages that would favor olanzapine
- Reintegration, not containment is the goal of treatment

Better Management of Psychoses in the Elderly
Key Slides

Improving Patient Outcomes in Geriatric Psychoses

Challenges in Nursing Home Psychiatry

- State hospitals have been replaced by nursing homes
- Psychiatric care often delivered by nonpsychiatrists
- Crucial role of nonphysician staff
- Staff educational needs, support and turnover
- Excessive reliance on pharmacological interventions

*Ketzel, Hendrie HH. Psychiatr Ann. 1985;25(7):408

OBRA 87

- Purpose was to standardize NH regulations and improve quality of care
- Medication errors and excessive use of psychoactive medication are indicators of poor-quality care

Better Management of Psychoses in the Elderly
OBRA 87
- Resident assessment—MDS
  - Initial goal to improve patient assessment and individual care planning
  - Currently, financial and outcomes tracking instrument
  - Guidelines for all aspects of resident care, including psychoactive medication use
  - Facilities are responsible for physician prescribing practices

OBRA Requirements for Antipsychotic Drug Use in Nursing Facilities
- Appropriate diagnosis/target symptoms
- Monitoring for therapeutic outcomes and adverse effects
- Gradual dose reduction unless "clinically contraindicated"

Antipsychotic Drug Therapy for Behavioral Symptoms Associated with Dementia
- Symptoms are persistent and cause decreased functional capacity or severe distress
- Resident is dangerous to self/others
- "Treatable medical dx or modifiable environmental conditions" addressed

Better Management of Psychoses in the Elderly
Key Slides

Role of Nonpharmacologic Interventions

- Observe patterns of behaviors prior to drug therapy
- Restructure care routine prior to drug therapy
- Use adjunctively when drug therapy is necessary to ameliorate behavioral symptoms

Psychoactive Medication Utilization in Nursing Facilities 1974-1998

- 1974: 7 residents
- 1998: 18.6 residents


Better Management of Psychoses in the Elderly
Key Slides

1999 Federal Survey Procedure Changes

- 24 “Quality Indicators” (QI) in 11 different domains
- Comparison of facility MDS data to state-wide averages
- Increased scrutiny if score above 90th percentile in any area or any score in “sentinel event” categories: fecal impaction, dehydration, pressure ulcers

Quality Indicators: Implications for Psychiatry

- Symptoms of depression without antidepressant therapy
- Anxiolytic and hypnotic use
- Hypnotic use > 2 times in past week
- Use of 9 or more different medications
- Antipsychotic use for behavioral symptoms

1999 Federal Guideline Change: Daily Antipsychotic Dosage for Residents with “Organic Mental Disorders”

- Risperidone 2 mg
- Olanzapine 10 mg
- Quetiapine 200 mg
- Risperidone dose reduced from 4 mg/dl new geriatric EPS data
- “Not maximum doses ... establish a point where higher levels need to be explained”

Better Management of Psychoses in the Elderly
Potentially Inappropriate Medication Use

Beers Criteria

- Divided into high and lower severity criteria
- Subdivided into inappropriate medications and inappropriate diagnosis/medication combination
- Basis—potential risks outweigh benefits or safer alternatives available


Beers Criteria Protocol

- Resident is over 65 years old
- Has been in the facility over 7 days
- Or appears to be experiencing a noticeable ADR within the first 7 days

Diagnosis/Medication Combinations

High Severity
- COPD + sedatives/hypnotics = CO₂ retention and ↓ respiratory drive
- Exception—lorazepam, oxazepam or alprazolam (short t₁/₂)
- Use after "assessment and optimal tx" of COPD symptoms
- PRN use is "prefer"
Key Slides

Diagnosis/Medication Combinations
High Severity

- Arrhythmias + any TCA = "may induce arrhythmias"
  - No distinction between low dose for neurogenic pain vs. therapeutic dose for depression

Diagnosis/Medication Combinations
High Severity

- BPH + any anticholinergic = impairment of micturition and ↑ risk of obstruction
  - Antihistamines (diphenhydramine)
  - GI antispasmodics (propantheline)
  - All TCAs (amitriptyline)
  - Antiparkinsonism (benztropine)
  - Narcotics (considered lower severity)
  - Short-term use o.k. per guidelines

High Severity Criteria

Medications

- Amitriptyline—for neurogenic pain only, document consideration of risk/benefit and alternative therapies
- Doxepin—very anticholinergic and sedating
- Long t₁/₂ BDZ or meprobamate—↑ incidence of falls, cognitive impairment

Better Management of Psychoses in the Elderly
Key Slides

**Diagnosis/Medication Combinations**

- **Lower Severity**
  - Insomnia + CNS stimulants = sleep disorder exacerbation
  - Decongestants
  - Theophylline
  - Methylphenidate
  - SSRIs and desipramine
  - MAO inhibitors
  - Beta-agonists (albuterol)

- **Diagnosis/Medication Combinations**
  - **Lower Severity**
    - Constipation + anticholinergics or narcotics = worsened constipation
    - TCAs
    - GI antispasmodics
    - Codeine et al
    - Antiparkinsonism (benztropine)
    - Sedating antihistamines

- **Lower Severity Criteria**
  - Medications
    - Sedating antihistamines including diphenhydramine et al
    - No hypnotic use
    - Use lowest effective dose for dermatologic indications
    - Peripheral and central anticholinergic effects
    - Short-term use

Better Management of Psychoses in the Elderly
Key Slides

Determination of Compliance with Guidelines

• Facility identified risks, assessed resident and determined potential benefit outweighs risk of ADR
  • Why is the medication a “drug of choice” for the resident??
  • Facility continually assessed the drug and determined that this is a “valid therapeutic intervention for the resident”

Improving Outcomes and Avoiding Medication-Related Survey Citations

• Team with consultant pharmacist and review drug regimens
• If possible, eliminate “inappropriate” drugs
• For patients prescribed “inappropriate” drugs
  • Document diagnosis
  • Clearly document benefit > risk
    • Lack of negative outcomes (example)
    • Maintenance of functional status

Economic Impact of Diseases and Drug-Related Problems

Source: Alzheimer’s Disease Education and Referral Center, National Cancer Institute, American Diabetes Association, Arthritis Association, National Center for Health Statistics

Better Management of Psychoses in the Elderly
"Antipsychotics cause the most adverse effects of any of the psychotropic medications (prescribed for the elderly) and are second only to diuretics with respect to adverse drug reactions in general."


Quality Indicators: Negative Outcomes Potentially Associated with Antipsychotic Use

- Fall Fractures
- Incontinence UTIs
- Pressure Ulcers
- Cognition
- ADL Dependency
- Weight Loss

Potential Causes of Antipsychotic-Related Adverse Events

- Medical and psychiatric polypharmacy
- Drug-drug interactions
- Drug-disease interactions
- Age-related changes in receptor sensitivity and organ function

Better Management of Psychoses in the Elderly
Key Slides

Polypharmacy in the Treatment of Dementia-Related Behavioral Symptoms

- Study of long-term use of risperidone for dementia-related behaviors in 2 NH
- Retrospective review; N=57
- Mean nonpsychotropic drugs/patient = 3.3

Atypical Antipsychotics: Geriatric Dosing Issues

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Maximum Dose (mg/Day) (OBRA)</th>
<th>Adjust Dose for Renal Impairment</th>
<th>Adjust Dose for Hepatic Impairment</th>
<th>Active Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Clearance 1.50% in moderate-severe RI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>10</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>200</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>


Pharmacokinetic Interactions: Risperidone

- Monitoring Somnolence, Orthostatic hypotension, Falls, EPS

Better Management of Psychoses in the Elderly
Suzanne -

Mangji's three slides (page 40-41) on Pharmacokinetic Interactions is very confusing, not to mention not totally accurate.

*All SSRI's - including Zoloft* has PY5206 interaction potential and 3A4.

Not sure of the value of these slides. If we keep them - should include Sertaline in SSRIs class.

ZY 9371 707
Pharmacokinetic Interactions: Olanzapine

\[ \text{Olanzapine} + \text{Fluvoxamine, Fluoroquinolones} \rightarrow \text{Monitoring} \]
\[ \text{Somnolence, Ataxia, Falls} \]

Significant inducers: cigarette smoke, carbamazepine

Pharmacokinetic Interactions: Quetiapine

\[ \text{Quetiapine} + \text{Fluvoxamine, Clarithromycin, Nefazodone, Itraconazole, Diltazem, Grapefruit juice} \rightarrow \text{Monitoring} \]
\[ \text{Somnolence, Orthostatic hypotension, Falls} \]

Significant inducers: phenytoin, thioridazine

Falls and Psychotropic Drugs in the Elderly

- Poor prognosis post-hip fracture
- CHF, pressure ulcers, fear of ambulation
- Annualized mean cost: $754/fall in NH (Cooper, 1997)

Cooper J. Consultant Pharmacist, 1997;12:1306-1309

Better Management of Psychoses in the Elderly
Key Slides

Orthostatic Hypotension and Atypical Antipsychotics

- Risperidone > quetiapine > olanzapine
- Zarate (1997): retrospective review of 122 psychogeriatric inpatients
  - Hypotension: 45.9%
  - Symptomatic: 9.8%
    - Onset 3.2 ± 3.2 days (1-13)
    - 41.7% concurrent antihypertensives
    - 58.3% concurrent SSRI or valproate

Orthostatic Hypotension and Atypical Antipsychotics

- Quetiapine
  - Tarlati: postural hypotension—15%
  - McManus: postural hypotension—13%

- Olanzapine
  - Lane: olanzapine 5-20 mg vs. haloperidol 5-20 mg—NS change in vital signs
  - Street: olanzapine 5-15 mg vs. placebo—NS change in vital signs

Cardiovascular Effects of Atypical Antipsychotics in the Elderly

- Peripheral edema: risperidone; likely dose related
- QT prolongation: most data with risperidone
  - Madhusoodanan: 9/103 QTc > 450 ms
  - Zarate: 2/122 cardiac arrest
  - Katz: risperidone 0.5-2 mg/day—NS change in vital signs vs. placebo


Better Management of Psychoses in the Elderly

ZY 9371 709
Key Slides

Cardiovascular Effects of Atypical Antipsychotics in the Elderly

- Quetiapine
  - McManus\textsuperscript{1}: NS change in ECG or intervals
- Olanzapine
  - Street\textsuperscript{2}: olanzapine 5-15 mg—NS change in ECG vs. placebo


Drug-Related Risk Factors: Torsades de Pointes

- Diuretics
- Antiarrhythmic agents
- Propafenone
- Cisapride
- Cyclic antidepressants
- Antipsychotics
  - Phenothiazines, haloperidol, pimozide, investigational

Viskin S. Lancet. 1999;354(9190):1635-1633

Geriatric Weight Gain and Atypical Antipsychotics

- Diabetes, cardiovascular disease, osteoarthritis
- Geriatric data
  - Madhusoodanan\textsuperscript{1}: olanzapine +1.85 lb; risperidone NS
  - Witterling\textsuperscript{2}, Kinon\textsuperscript{3}: older patients gain less weight
- Treatment plan: dietary counseling and weight monitoring


Better Management of Psychoses in the Elderly
**Key Slides**

**Assessment of Geriatric Weight Loss**
- Comprehensive assessment for potential sources of weight loss/anorexia
  - Medications or medical conditions
  - Need for assistance with meal preparation or eating
  - Dietary preferences
  - Supplements
  - Dentures

**Atypical Antipsychotics and Seizures**
- July 1999 HCFA guidelines discourage use of any antipsychotic in NH patients with hx of seizure
  - Documentation should include risk/benefit assessment and monitoring of seizure frequency

**Decreasing the Risk of Antipsychotic-Induced Seizures**

**Risk Factors**
- Pre-existing seizure disorder
- Abnormal EEG without seizure history
- Pre-existing CNS pathology
- Rapid increases in antipsychotic dose


Better Management of Psychoses in the Elderly
**Comparison of Antipsychotic Associated Seizure Incidence**

- Quetiapine
- Olanzapine
- Risperidone
- Clozapine 300-599 mg/day
- Clozapine <300 mg/day
- Phenothiazines

% Incidence: 0 0.5 1 1.5 2 2.5 3


---

**The EPS Cascade**

- Gait Instability
- Bradykinesia
- Fall → Fracture
- Esophageal Dysmotility
- Weight Loss
- Agitation → Restraint
- Aspiration
- Pressure Ulcer
- Feeding Tube
- Pneumonia

---

**Neuroleptic-Induced Parkinsonism (NIP): Use of Conventional Antipsychotics in Dementia**

- NIP detected within 1 week of beginning perphenazine (mean dose = 8 mg)\(^1\)
- At 9 months of low-dose thioridazine or haloperidol, 66.7% had developed NIP\(^2\)
  - Mean dose = 25.9 ± 18.2 mg/day CPZ equivalents

\(^2\)Caligiuri MP, Rockwell E, Jeste DV. Am J Geriatr Psychiatry. 1998;6:75-82

Better Management of Psychoses in the Elderly

45
Key Slides

Tardive Dyskinesia in Older Patients: Risperidone and Haloperidol

- Heterogeneous sample; N=61
- Both groups had received risperidone or haloperidol <3 months prior to study
  - Median daily dose = 1 mg
  - Baseline modified SAS (p<0.04) and AIMS (p<0.03) scores higher in risperidone group
  - 9-month endpoint, cumulative incidence of TD >> haloperidol group (p<0.05)


EPS and Atypical Antipsychotics in Dementia with Behavioral Symptoms

- Risperidone: EPS in therapeutic dose range
- Quetiapine: small, significant improvement-SAS; NS change—AIMS
- Olanzapine: NS change in SAS or AIMS vs. placebo at 5-15 mg/day


Length of Therapy: Antipsychotics for Behavioral Symptoms in Dementia

- Optimal duration of treatment unknown
- Ongoing assessment of efficacy and ADRs
  - Antipsychotics for severe aggression: consensus guidelines recommend 2-3 months stable behavior before dose reduction
  - HCFA: 2 attempts to reduce dose over 1-year period


Better Management of Psychoses in the Elderly
Key Slides

Antipsychotic Drug Discontinuation

- Gradual taper except in cases of acute toxicity
- Abrupt discontinuation
  - Cholinergic rebound
    - Thioridazine, clozapine
    - N/V, diaphoresis, insomnia
  - Withdrawal dyskinesias
  - Relapse or rebound syndrome


Withdrawal of Haloperidol, Thioridazine and Lorazepam in the Nursing Home

![Graph showing drug and placebo effects on CMAI (Cohen-Mansfield Agitation Inventory) scores for Physical Aggression and Verbal Agitation]

- DB controlled crossover trial: 60% completed
- Mean duration of therapy: 16.6 months
- No behavioral or functional differences detected after placebo crossover


ADR Prevention Strategies

- Choose therapy according to target symptoms
- Consider comorbid conditions and concomitant drugs prior to drug therapy selection
- Careful titration
- Educate caregiver/patient
- Minimum effective dose

Better Management of Psychoses in the Elderly 47
Key Slides

Prospective Identification of High Risk Patients

- Older than 85 years
- >6 active medical dx
- Prior ADR
- Low body weight (BMI<22 kg/m²)
- Decreased renal function (ClCr<50 ml/min)
- Digoxin, warfarin, lithium
- Anticonvulsants, antipsychotics, hypnotics, narcotics, benzodiazepines, anticholinergics
- Polypharmacy


ADR Prevention Strategies

- Routinely review and débride drug regimens, particularly for patients at high risk of negative outcomes
  - Falls
  - Cognitive impairment
  - Pressure ulcers
  - Weight loss
  - Behavioral disorders

Conclusions

- ADRs occurring in older adults are costly, may result in suboptimal efficacy and contribute significantly to morbidity and mortality
- Potential adverse effect burden should be evaluated prior to atypical antipsychotic selection
- Prospective evaluation of medical comorbidity and concurrent drug therapy will likely result in improved therapeutic outcomes and decreased ADRs with the newer atypicals

Better Management of Psychoses in the Elderly
Selected Internet Resources

- www.mayo.edu/geriatrics-rst/Dementia_I_ToC.html
- www.mayo.edu/geriatrics-rst/Dementia_II_ToC.html
- www.mayo.edu/geriatrics-rst/Dementia_III_ToC.html
- www.mayo.edu/geriatrics-rst/Behav_ToC.html
- www.alzheimers.org/
- www.caregiver.org/
- www.brain.nwu.edu/
Appendix

Reisberg et al.

Appendix A: Behavioral Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD)

Part I: Symptomatology
Assessment Interval: Specify: _____ wks.
Total Score: ________

A. Paranoid and Delusional Ideation

1. “People are Stealing Things” Delusion
   (0) Not present
   (1) Delusion
   (2) Delusion that people are coming into the home and hiding objects or stealing objects
   (3) Talking and listening to people coming into the home

2. “One’s House is Not One’s Home” Delusion
   (0) Not present
   (1) Conviction that the place in which one is residing is not one’s home (e.g., packing to go home; complaints while at home, of “take me home”)
   (2) Attempt to leave domiciliary to go home
   (3) Violence in response to attempts to forcibly restrict exit

3. “Spouse (or Other Caregiver) is an Impostor” Delusion
   (0) Not present
   (1) Conviction that spouse (or other caregiver) is an impostor
   (2) Anger toward spouse (or other caregiver) for being an impostor
   (3) Violence toward spouse (or other caregiver) for being an impostor

4. “Delusion of Abandonment” (e.g., to an Institution)
   (0) Not present
   (1) Suspicion of caregiver plotting abandonment or institutionalization (e.g., on telephone)
   (2) Accusation of a conspiracy to abandon or institutionalize
   (3) Accusation of impending or immediate desertion or institutionalization

5. “Delusion of Infidelity”
   (0) Not present
   (1) Conviction that spouse and/or children and/or other caregivers are unfaithful.
   (2) Anger toward spouse, relative, or other caregiver for infidelity
   (3) Violence toward spouse, relative, or other caregiver for supposed infidelity
Appendix

6. “Suspiciousness/Paranoia” (other than above)

(0) Not present
(1) Suspicious (e.g., hiding objects that he/she later may be unable to locate)
(2) Paranoid (i.e., fixed conviction with respect to suspicions and/or anger as a result of suspicions)
(3) Violence as a result of suspicions
Unspecified?

Describe

7. Delusions (other than above)

(0) Not present
(1) Delusional
(2) Verbal or emotional manifestations as a result of delusions
(3) Physical actions or violence as a result of delusions
Unspecified?

Describe

B. Hallucinations

8. Visual Hallucinations

(0) Not present
(1) Vague: not clearly defined
(2) Clearly defined hallucinations of objects or persons (e.g., sees other people at the table)
(3) Verbal or physical actions or emotional responses to the hallucinations

9. Auditory Hallucinations

(0) Not present
(1) Vague: not clearly defined
(2) Clearly defined hallucinations of words or phrases
(3) Verbal or physical actions or emotional response to the hallucinations

10. Olfactory Hallucinations

(0) Not present
(1) Vague: not clearly defined
(2) Clearly defined
(3) Verbal or physical actions or emotional responses to the hallucinations
11. Haptic Hallucinations

(0) Not present
(1) Vague: not clearly defined
(2) Clearly defined
(3) Verbal or physical actions or emotional responses to the hallucinations

12. Other Hallucinations

(0) Not present
(1) Vague: not clearly defined
(2) Clearly defined
(3) Verbal or physical actions or emotional responses to the hallucinations
Unspecified?
Describe ________________________________________________________________
_____________________________________________________________________

C. Activity Disturbances

13. Wandering: Away from Home to Caregiver

(0) Not present
(1) Somewhat, but not sufficient to necessitate restraint
(2) Sufficient to require restraint
(3) Verbal or physical actions or emotional responses to attempts to prevent wandering

14. Purposeless Activity (Cognitive Abulia)

(0) Not present
(1) Repetitive, purposeless activity (e.g., opening and closing pocketbook, packing and unpacking clothing, repeatedly putting on and removing clothing, opening and closing drawers, insistent repeating of demands or questions)
(2) Pacing or other purposeless activity sufficient to require restraint
(3) Abrasions or physical harm resulting from purposeless activity

15. Inappropriate Activity

(0) Not present
(1) Inappropriate activities (e.g., storing and hiding objects in inappropriate places, such as throwing clothing in wastebasket or putting empty plates in the oven; inappropriate sexual behavior, such as inappropriate exposure)
(2) Present and sufficient to require restraint
(3) Present, sufficient to require restraint, and accompanied by anger or violence when restraint is used

D. Aggressiveness
Appendix

16. Verbal Outbursts
   (0) Not present
   (1) Present (including unaccustomed use of foul or abusive language)
   (2) Present and accompanied by anger
   (3) Present, accompanied by anger, and clearly directed at other persons

17. Physical Threats and/or Violence
   (0) Not present
   (1) Threatening behavior
   (2) Physical violence
   (3) Physical violence accompanied by vehemence

18. Agitation (other than above)
   (0) Not present
   (1) Present
   (2) Present with emotional component
   (3) Present with emotional and physical component
   Unspecified?
   Describe________________________________________________________
   ________________________________________________________________

E. Diurnal Rhythm Disturbances

19. Day/Night Disturbance
   (0) Not present
   (1) Repetitive wakenings during night
   (2) 50% to 75% of former sleep cycle at night
   (3) Complete disturbance of diurnal rhythm (i.e., less than 50% of former
       sleep cycle at night)

F. Affective Disturbance

   (0) Not present
   (1) Present
   (2) Present and accompanied by clear affective component
   (3) Present and accompanied by affective and physical component (e.g.,
       "wrings hands" or other gestures)

21. Depressed Mood: Other

   (0) Present
   (1) Present (e.g., occasional statement "I wish I were dead," without clear
       affective concomitants)
   (2) Present with clean concomitants (e.g., thoughts of death)
   (3) Present with emotional and physical concomitants (e.g., suicide gestures)
   Unspecified?
   Describe_______________________________________________________
   ________________________________________________________________

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Appendix

G. Anxieties and Phobias

22. Anxiety Regarding Upcoming Events (Godot Syndrome)

(0) Not present
(1) Present: Repeated queries and/or other activities regarding upcoming appointments and/or events
(2) Present and disturbing to caregivers
(3) Present and intolerable to caregivers

23. Other Anxieties

(0) Not present
(1) Present
(2) Present and disturbing to caregivers
(3) Present and intolerable to caregivers

Unspecified? __________________________
Describe __________________________

24. Fear of Being Left Alone

(0) Not present
(1) Present: Vocalized fear of being alone
(2) Vocalized and sufficient to require specific action on part of caregiver
(3) Vocalized and sufficient to require patient to be accompanied at all times

25. Other Phobias

(0) Not present
(1) Present
(2) Present and of sufficient magnitude to require specific action on part of caregiver
(3) Present and sufficient to prevent patient activities

Unspecified? __________________________
Describe __________________________

Part 2: Global Rating

With respect to the above symptoms, they are of sufficient magnitude as to be:

(0) Not at all troubling to the caregiver or dangerous to the patient
(1) Mildly troubling to the caregiver or dangerous to the patient
(2) Moderately troubling to the caregiver or dangerous to the patient
(3) Severely troubling or intolerable to the caregiver or dangerous to the patient
### SIMPSON-ANGUS SCALE (SAS)

Enter appropriate code in boxes below.

<table>
<thead>
<tr>
<th>1. GAIT</th>
<th>6. LEG PENDULOUSNESS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCORE</strong></td>
<td><strong>SCORE</strong></td>
</tr>
<tr>
<td>0 = Normal</td>
<td>0 = The legs swing freely</td>
</tr>
<tr>
<td>1 = Mild diminution in swing while the patient is walking</td>
<td>1 = Slight diminution in the swing of the legs</td>
</tr>
<tr>
<td>2 = Obvious diminution in swing suggesting shoulder rigidity</td>
<td>2 = Moderate resistance to swing</td>
</tr>
<tr>
<td>3 = Stiff gait with little or no arm swing noticeable</td>
<td>3 = Marked resistance and damping of swing</td>
</tr>
<tr>
<td>4 = Rigid gait with arms slightly pronated; or stooped-shuffling gait with propulsion and retropulsion</td>
<td>4 = Complete absence of swing</td>
</tr>
<tr>
<td>9 = Not rateable</td>
<td>9 = Not rateable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. ARM DROPPING</th>
<th>7. HEAD DROPPING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCORE</strong></td>
<td><strong>SCORE</strong></td>
</tr>
<tr>
<td>0 = Normal, free fall with loud slap and rebound</td>
<td>0 = The head falls completely with a good thump as it hits the table</td>
</tr>
<tr>
<td>1 = Fall slowed slightly with less audible contact and little rebound</td>
<td>1 = Slight slowing in fall, mainly noted by lack of slap as head meets the table</td>
</tr>
<tr>
<td>2 = Fall slowed, no rebound</td>
<td>2 = Moderate slowing in the fall quite noticeable to the eye</td>
</tr>
<tr>
<td>3 = Marked slowing, no slap at all</td>
<td>3 = Head falls stiffly and slowly</td>
</tr>
<tr>
<td>4 = Arms fall as though against resistance: as though through glue</td>
<td>4 = Head does not reach examining table</td>
</tr>
<tr>
<td>9 = Not rateable</td>
<td>9 = Not rateable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. SHOULDER SHAKING</th>
<th>8. GLABELLAR TAP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCORE</strong></td>
<td><strong>SCORE</strong></td>
</tr>
<tr>
<td>0 = Normal</td>
<td>0 = 0-5 blinks</td>
</tr>
<tr>
<td>1 = Slight stiffness and resistance</td>
<td>1 = 6-10 blinks</td>
</tr>
<tr>
<td>2 = Moderate stiffness and resistance</td>
<td>2 = 11-15 blinks</td>
</tr>
<tr>
<td>3 = Marked rigidity with difficulty in passive movement</td>
<td>3 = 16-20 blinks</td>
</tr>
<tr>
<td>4 = Extreme stiffness and rigidity with almost a frozen joint</td>
<td>4 = 21 or more blinks</td>
</tr>
<tr>
<td>9 = Not rateable</td>
<td>9 = Not rateable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. ELBOW RIGIDITY</th>
<th>9. TREMOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCORE</strong></td>
<td><strong>SCORE</strong></td>
</tr>
<tr>
<td>0 = Normal</td>
<td>0 = Normal</td>
</tr>
<tr>
<td>1 = Slight stiffness and resistance</td>
<td>1 = Mild finger tremor, obvious to sight and touch</td>
</tr>
<tr>
<td>2 = Moderate stiffness and resistance</td>
<td>2 = Tremor of hand or arm occurring spasmodically</td>
</tr>
<tr>
<td>3 = Marked rigidity with difficulty in passive movement</td>
<td>3 = Persistent tremor of one or more limbs</td>
</tr>
<tr>
<td>4 = Extreme stiffness and rigidity with almost a frozen joint</td>
<td>4 = Whole body tremor</td>
</tr>
<tr>
<td>9 = Not rateable</td>
<td>9 = Not rateable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. WRIST RIGIDITY</th>
<th>10. SALIVATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCORE</strong></td>
<td><strong>SCORE</strong></td>
</tr>
<tr>
<td>0 = Normal</td>
<td>0 = Normal</td>
</tr>
<tr>
<td>1 = Slight stiffness and resistance</td>
<td>1 = Excess salivation so that pooling takes place if mouth is open and tongue is raised</td>
</tr>
<tr>
<td>2 = Moderate stiffness and resistance</td>
<td>2 = Excess salivation is present and might occasionally result in difficulty speaking</td>
</tr>
<tr>
<td>3 = Marked rigidity with difficulty in passive movement</td>
<td>3 = Speaking with difficulty because of excess salivation</td>
</tr>
<tr>
<td>4 = Extreme stiffness and rigidity with almost a frozen joint</td>
<td>4 = Frank drooling</td>
</tr>
<tr>
<td>9 = Not rateable</td>
<td>9 = Not rateable</td>
</tr>
</tbody>
</table>
Appendix

ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

Instructions: Complete examination procedure before making ratings. When rating movements, rate highest severity observed and rate movements that occur upon activation one less than those observed spontaneously.

(Put appropriate code in boxes below)

FACIAL AND ORAL MOVEMENTS
1. Muscles of facial expression
e.g., movements of forehead, eyebrows, peri orbital area, cheeks: include frowning, blinking, smiling, grimacing.
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

2. Lips and perioral area
e.g., puckering, pouting, smacking.
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

3. Jaw
e.g., biting, clenched, chewing, mouth opening, lateral movements.
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

4. Tongue
   Rate only if increase in movement both in and out of mouth, not inability to sustain movement.
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

EXTREMITY MOVEMENTS
5. Upper (arms, wrists, hands, fingers)
   Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous) and athetoid movements (i.e., slow, irregular, complex, serpentine). Do not include tremor (i.e., repetitive, regular, rhythmic).
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

6. Lower (legs, knees, ankles, toes)
e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot.
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

EXTREMITY MOVEMENTS (cont'd)
7. Neck, shoulders, hip
e.g., rocking, twisting, squirming, pelvic gyrations.
   - 0 = None
   - 1 = Minimal (may be extreme normal)
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

TRUNK MOVEMENTS
8. Severity of abnormal movements.
   - 0 = None/normal
   - 1 = Minimal
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

9. Incapacitation due to abnormal movements.
   - 0 = None/normal
   - 1 = Minimal
   - 2 = Mild
   - 3 = Moderate
   - 4 = Severe

10. Patient's awareness of abnormal movements
    Rate only patient's report.
    - 0 = No awareness
    - 1 = Aware, no distress
    - 2 = Aware, mild distress
    - 3 = Aware, moderate distress
    - 4 = Aware, severe distress

GLOBAL JUDGEMENTS

DENTAL STATUS
Any current problems with teeth: □ YES □ NO
Does patient usually wear dentures?: □ YES □ NO

ZY 9371 724
BARNES AKATHISIA RATING SCALE (BAS)

INSTRUCTIONS

Patient should be observed while seated, and then standing while engaged in neutral conversation (for a minimum of 2 minutes in each position). Symptoms observed in other situations, for example, while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

Put appropriate code in box below.

OBJECTIVE

0 = Normal, occasional fidgety movements of the limbs
1 = Presence of characteristic restless movements: shuffling or tramping movements of the legs and feet or swinging of one leg, while sitting, and/or rocking from foot to foot or “walking on the spot” when standing, but movements present for less than half the time observed
2 = Observed phenomena, as described in (1) above, which are present for at least half the observation period
3 = Patient is constantly engaged in characteristic restless movements, and/or has the inability to remain seated or standing without walking or pacing, during the time observed

SUBJECTIVE

AWARENESS OF RESTLESSNESS

0 = Absence of inner restlessness
1 = Nonspecific sense of inner restlessness
2 = Patient is aware of an inability to keep the legs still, or a desire to move the legs, and/or complains of inner restlessness aggravated specifically by being required to stand still
3 = Awareness of an intense compulsion to move most of the time and/or reports a strong desire to walk or pace most of the time

DISTRESS RELATED TO RESTLESSNESS

0 = No distress
1 = Mild
2 = Moderate
3 = Severe

GLOBAL CLINICAL ASSESSMENT OF AKATHISIA

0 = Absent - no evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia
1 = Questionable - nonspecific inner tension and fidgety movements
2 = Mild Akathisia - awareness of restlessness in the legs and/or inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress
3 = Moderate Akathisia - awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing
4 = Marked Akathisia - subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least 5 minutes. The condition is obviously distressing
5 = Severe Akathisia - The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia
# BRIEF PSYCHIATRIC RATING SCALE (BPRS)

Please enter the score for the term which best describes the patient's condition.

<table>
<thead>
<tr>
<th>Term</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = not assessed, 1 = not present, 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe</td>
<td></td>
</tr>
</tbody>
</table>

1. **SOMATIC CONCERN**
   Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have a realistic basis or not.

2. **ANXIETY**
   Worry, fear, or over-concern for present or future. Rate solely on the basis of verbal report of patient's own subjective experiences. Do not infer anxiety from physical signs or from neurotic defense mechanisms.

3. **EMOTIONAL WITHDRAWAL**
   Deficiency in relating to the interviewer and to the interviewer situation. Rate only the degree to which the patient gives the impression of failing to be in emotional contact with other people in the interview situation.

4. **CONCEPTUAL DISORGANIZATION**
   Degree to which the thought processes are confused, disconnected, or disorganized. Rate on the basis of integration of the verbal products of the patient; do not rate on the basis of patient's subjective impression of his own level of functioning.

5. **GUILT FEELINGS**
   Over-concern or remorse for past behavior. Rate on the basis of the patient's subjective experiences of guilt as evidenced by verbal report with appropriate affect; do not infer guilt feelings from depression, anxiety or neurotic defenses.

6. **TENSION**
   Physical and motor manifestations of tension "nervousness", and heightened activation level. Tension should be rated solely on the basis of physical signs and motor behavior and not on the basis of subjective experiences of tension reported by the patient.

7. **MANNERISMS AND POSTURING**
   Unusual and unnatural motor behavior, the type of motor behavior which causes certain mental patients to stand out in a crowd of normal people. Rate only abnormality of movements; do not rate single heightened motor activity here.

8. **GRANDIOSITY**
   Exaggerated self-opinion, conviction of unusual ability or powers. Rate only on the basis of patient's statements about himself or self-in-relation-to-others, not on the basis of his demeanor in the interview situation.

9. **DEPRESSIVE MOOD**
   Despondency in mood, sadness. Rate only degree of despondency; do not rate on the basis of inferences concerning depression based upon general retardation and somatic complaints.

10. **HOSTILITY**
    Animosity, contempt, belligerence, disdain for other people outside the interview situation. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others; do not infer hostility from neurotic defenses, anxiety, or somatic complaints. (Rate attitude toward interviewer under "uncooperativeness").

11. **SUSPICIOUSNESS**
    Belief (delusional or otherwise) that others have now, or have had in the past, malicious or discriminatory intent toward the patient. On the basis of verbal report, rate only those suspicions which are currently held whether they concern past or present circumstances.

12. **HALLUCINATORY BEHAVIOR**
    Perceptions without normal external stimulus correspondence. Rate only those experiences which are reported to have occurred within the last week and which are described as distinctly different from the thought and imagery processes of normal people.

13. **MOTOR RETARDATION**
    Reduction in energy level evidenced in slowed movements. Rate on the basis of observed behavior of the patient only; do not rate on the basis of patient's subjective impression of own energy level.

14. **UNCOOPERATIVENESS**
    Evidence of resistance, unfriendliness, resentment and lack of readiness to cooperate with the interviewer. Rate only on the basis of the patient's attitude and responses to the interviewer and the interview situation; do not rate on basis of reported resentment or uncooperativeness outside the interview situation.

15. **UNUSUAL THOUGHT CONTENT**
    Unusual, odd, strange or bizarre thought content. Rate here the degree of unusualness, not the degree of disorganization of thought processes.

16. **BLUNTED AFFECT**
    Reduced emotional tone, apparent lack of normal feeling or involvement.

17. **EXCITEMENT**
    Heightened emotional tone, agitation, increased reactivity.

18. **DISORIENTATION**
    Confusion or lack of proper association for person, place or time.
### Drugs Used in the Treatment of Psychiatric and Neurological Disorders

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Drug Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>abecarnil</td>
<td>Tindal</td>
<td>Antianxiety</td>
</tr>
<tr>
<td>acetophenazine</td>
<td></td>
<td>Antipsychotic (phenothiazine)</td>
</tr>
<tr>
<td>adatanserin</td>
<td></td>
<td>Antianxiety</td>
</tr>
<tr>
<td>adinazolam</td>
<td>Deracyn</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>alprazolam</td>
<td>Xanax ER</td>
<td>Antianxiety; benzodiazepine</td>
</tr>
<tr>
<td>amantadine</td>
<td>Symmetrel, Symadine</td>
<td>Antiparkinsonian; antiviral</td>
</tr>
<tr>
<td>amesergide</td>
<td></td>
<td>Antidepressant</td>
</tr>
<tr>
<td>amitriptyline</td>
<td>Elavil, Endep, Enovil</td>
<td>Antidepressant (tricyclic) with sedative effects</td>
</tr>
<tr>
<td>amobarbital</td>
<td>Amytal, Dexamyl</td>
<td>Sedative-hypnotic; barbiturate; anticonvulsant</td>
</tr>
<tr>
<td>amoxapine</td>
<td>Asendin</td>
<td>Antidepressant (tricyclic); mild sedative action; neuroleptic</td>
</tr>
<tr>
<td>antiepilepticirne</td>
<td></td>
<td>Antiepileptic</td>
</tr>
<tr>
<td>aripiprazole</td>
<td></td>
<td>Antipsychotic; antagonist at D₂ receptors; agonist at presynaptic dopamine autoreceptors</td>
</tr>
<tr>
<td>benzotropine</td>
<td>Cogentin</td>
<td>Anticholinergic; antihistamine; antiparkinsonian</td>
</tr>
<tr>
<td>besipirine</td>
<td></td>
<td>Anti-Alzheimer's</td>
</tr>
<tr>
<td>biperiden</td>
<td>Akineton</td>
<td>Anticholinergic; antiparkinsonian</td>
</tr>
<tr>
<td>bromocriptine</td>
<td>Parlodel</td>
<td>Dopamine receptor agonist</td>
</tr>
<tr>
<td>buprenorphine</td>
<td>Buprenex</td>
<td>Antiaddiction</td>
</tr>
<tr>
<td>buspironone</td>
<td>Wellbutrin</td>
<td>Antidepressant (aminoketone)</td>
</tr>
<tr>
<td>butabarbital</td>
<td>BuSpar</td>
<td>Antianxiety (azaspirodiene)</td>
</tr>
<tr>
<td>cabergline</td>
<td>Butisol, Butalan, Buticaps</td>
<td>Sedative; barbiturate</td>
</tr>
<tr>
<td>carbamazepine</td>
<td>Epitol, Tegretol</td>
<td>Dopamine agonist; antiparkinsonian</td>
</tr>
<tr>
<td>carbidopa/levodopa</td>
<td>Sinemet</td>
<td>Anticonvulsant; antimanic</td>
</tr>
<tr>
<td>carphenazine</td>
<td>Proketazone</td>
<td>CNS agent; Geomatrix delivery formulation</td>
</tr>
<tr>
<td>chlor Diazepoxide</td>
<td>Libritabs, Librium</td>
<td>Antipsychotic (phenothiazine)</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>Thorazine, Ormazine</td>
<td>Benzodiazepine; sedative-hypnotic</td>
</tr>
<tr>
<td>chlorprothixene</td>
<td>Taractan</td>
<td>Antipsychotic (phenothiazine); antiemetic</td>
</tr>
<tr>
<td>citalopram</td>
<td>Celaxa</td>
<td>Antipsychotic (thioxanthenes)</td>
</tr>
<tr>
<td>clidinium</td>
<td>Librax, Quarzan</td>
<td>Antidepressant (selective serotonin reuptake inhibitor)</td>
</tr>
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<td>clomipramine</td>
<td>Anafranil</td>
<td>Anticholinergic</td>
</tr>
<tr>
<td>clonazepam</td>
<td>Klonopin</td>
<td>Antidepressant (tricyclic)</td>
</tr>
<tr>
<td>clonidine</td>
<td>Catapres</td>
<td>Anticonvulsant; benzodiazepine</td>
</tr>
<tr>
<td>clorazepate</td>
<td>Tranxene</td>
<td>Antihypertensive; a-adrenergic agonist</td>
</tr>
<tr>
<td>clorgyline</td>
<td></td>
<td>Antianxiety; benzodiazepine; anticonvulsant</td>
</tr>
<tr>
<td>clozapine</td>
<td>Clozaril</td>
<td>Antidepressant (monoamine oxidase inhibitor)</td>
</tr>
<tr>
<td>cyproheptadine</td>
<td>Periactin</td>
<td>Antipsychotic (dibenzazepine)</td>
</tr>
<tr>
<td>dantrolene</td>
<td>Dantrium</td>
<td>Antihistamine; antiserotonergic</td>
</tr>
<tr>
<td>deprenyl</td>
<td></td>
<td>Antispasticity</td>
</tr>
<tr>
<td>desipramine</td>
<td>Norpramin, Perto fane</td>
<td>Anti-Alzheimer's; antiParkinsonian</td>
</tr>
<tr>
<td>dextfenfluramine</td>
<td>Redux</td>
<td>Antidepressant (tricyclic)</td>
</tr>
<tr>
<td>dextroamphetamine</td>
<td>Dexedrine, Adderall</td>
<td>Antiobesity</td>
</tr>
</tbody>
</table>

This list is provided for your convenience in referencing medications that may be discussed at this conference. Inclusion in no way constitutes an endorsement of any drug by faculty and staff of CME, Inc., nor does omission of any psychotherapeutic drug indicate inacceptability as a treatment option. (Copyrights and trademarks are not shown.)

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# Drugs Used in the Treatment of Psychiatric and Neurological Disorders

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Drug Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>diazepam</td>
<td>Valium</td>
<td>Antianxiety; benzodiazepine; anticonvulsant</td>
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<tr>
<td>diazepam (rectal delivery system)</td>
<td>Diastat</td>
<td>Sedative</td>
</tr>
<tr>
<td>dihydroergotamine</td>
<td>Migranal</td>
<td>Nasal spray formulation of DHE 45 for migraine</td>
</tr>
<tr>
<td>diltiazem</td>
<td>Cardizem</td>
<td>Calcium channel blocker</td>
</tr>
<tr>
<td>diphenhydramine</td>
<td>Benadryl</td>
<td>Antianxiety; antihistamine; antiparkinsonian</td>
</tr>
<tr>
<td>disulfiram</td>
<td>Antabuse</td>
<td>Antiaddiction</td>
</tr>
<tr>
<td>divalproex</td>
<td>Depakote</td>
<td>Anticonvulsant; antimanic</td>
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<tr>
<td>donepezil</td>
<td>Aricept</td>
<td>Boosts levels of acetylcholine</td>
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<tr>
<td>doxepin</td>
<td>Adapin, Sinequan</td>
<td>Antidepressant (tricyclic)</td>
</tr>
<tr>
<td>droperidol</td>
<td>Inapsine</td>
<td>Neuroleptic (tranquilizer)</td>
</tr>
<tr>
<td>eletriptan</td>
<td></td>
<td>5-HT, receptor agonist</td>
</tr>
<tr>
<td>ergoloid</td>
<td>Hydergine</td>
<td>Anti-Alzheimer's</td>
</tr>
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<td>ProSom</td>
<td>Hypnotic (triazolobenzodiazepine)</td>
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<td>etorodorb</td>
<td>Antilon</td>
<td>Anticonvulsant; antiepileptic</td>
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<tr>
<td>excitatory amino acid</td>
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<td>Treatment for central nervous system diseases</td>
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<tr>
<td>(EAA) receptor ligands</td>
<td></td>
<td></td>
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<tr>
<td>felbamate</td>
<td>Felbatol</td>
<td>Treatment for therapy-resistant onset seizures</td>
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<td>fenfluramine</td>
<td>Pondimin</td>
<td>Appetite suppressant (nonamphetamine)</td>
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<tr>
<td>flesinoxan</td>
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<td>Antianxiety; antidepressant</td>
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<tr>
<td>flumazenil</td>
<td>Romazicon</td>
<td>Imidazobenzodiazepine; benzodiazepine receptor antagonist</td>
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<tr>
<td>fluphenazine</td>
<td>Prolixin</td>
<td>Antipsychotic (phenothiazine)</td>
</tr>
<tr>
<td>flurazepam</td>
<td>Dalmane</td>
<td>Hypnotic</td>
</tr>
<tr>
<td>fluvoxamine</td>
<td>Luvox</td>
<td>Antidepressant (selective serotonin reuptake inhibitor)</td>
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<tr>
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<td>Cerebyx</td>
<td>Anticonvulsant</td>
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<td>gabapentin</td>
<td>Neurontin</td>
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<td>Reminyl</td>
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<td>Paxipam</td>
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<td>Haldol</td>
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<td>hydroxyzine</td>
<td>Atarax, Marax, Vistaril</td>
<td>Antianxiety; antihistamine; antiemetic; sedative</td>
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<tr>
<td>idebenone</td>
<td>Avan</td>
<td>Cognition enhancer</td>
</tr>
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<td>iloperidone</td>
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<tr>
<td>imipramine</td>
<td>Tofranil</td>
<td>Antidepressant (tricyclic)</td>
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<tr>
<td>isocarboxazid</td>
<td>Marplan</td>
<td>Antidepressant (monoamine oxidase inhibitor)</td>
</tr>
<tr>
<td>L-dopa, levodopa</td>
<td>Atamet, Larodopa, Doper, Sinemet</td>
<td>Antiparkinsonian</td>
</tr>
<tr>
<td>lamotrigine</td>
<td>Lamictal</td>
<td>Anticonvulsant; antiepileptic</td>
</tr>
<tr>
<td>lazarabemide</td>
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<td>Antiparkinsonian</td>
</tr>
<tr>
<td>levacecamine</td>
<td>Alcar</td>
<td>Cognition enhancer; neuroprotective</td>
</tr>
<tr>
<td>(acetyl-L-carnitine)</td>
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<td></td>
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<tr>
<td>levomepromazine</td>
<td>Aviva</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>linopirine</td>
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<td>Cognition enhancer</td>
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<tr>
<td>lithium</td>
<td>Eskalith, Lithobid</td>
<td>Antimanic</td>
</tr>
<tr>
<td>lorazepam</td>
<td>Ativan</td>
<td>Antianxiety; benzodiazepine</td>
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</table>

ZY 9371 728
## Drugs Used in the Treatment of Psychiatric and Neurological Disorders

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Drug Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>loxapine</td>
<td>Loxitane, Loxapine</td>
<td>Antipsychotic (dibenzoazepine)</td>
</tr>
<tr>
<td>maprotiline</td>
<td>Ludiomil</td>
<td>Antidepressant (tetracyclic)</td>
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<td>mephobarbital</td>
<td>Mebaral</td>
<td>Antianxiety; anticonvulsant; barbiturate</td>
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<td>mesoridazine</td>
<td>Serentil</td>
<td>Antipsychotic (phenothiazine)</td>
</tr>
<tr>
<td>methadone</td>
<td>Dolophine</td>
<td>Antiaaddiction</td>
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<td>Ritalin</td>
<td>Stimulant</td>
</tr>
<tr>
<td>metrifonate</td>
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<td>Acetylcholinesterase inhibitor</td>
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<tr>
<td>midazolam</td>
<td>Versed</td>
<td>Sedative; benzodiazepine</td>
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<tr>
<td>mirtazapine</td>
<td>Remeron</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>moclobemide*</td>
<td>Aurorix</td>
<td>Antipanic; antidepressant (reversible inhibitor of monoamine oxidase type A [RIMA])</td>
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<tr>
<td>mofegiline</td>
<td>Moban</td>
<td>Antiparkinsonian</td>
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<tr>
<td>molindone</td>
<td>Relex</td>
<td>Antipsychotic (dihydropindolone)</td>
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<td>naimefene</td>
<td>Narcan</td>
<td>Antagonist to narcotics; antiaddiction</td>
</tr>
<tr>
<td>naltrexone</td>
<td>ReVia, Trexan</td>
<td>Antiaaddiction</td>
</tr>
<tr>
<td>naratriptan</td>
<td>Amerge</td>
<td>Opioid antagonist; antiaddiction (alcohol)</td>
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<tr>
<td>nefazodone</td>
<td>Serzone</td>
<td>5-HT&lt;sub&gt;1D&lt;/sub&gt; receptor agonist for migraine</td>
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<tr>
<td>neurotrophin-3 (NT-3)</td>
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<td>Antidepressant</td>
</tr>
<tr>
<td>nimodipine</td>
<td>Nimotop</td>
<td>Treatment for peripheral neuropathies, nerve injury and neurodegenerative diseases</td>
</tr>
<tr>
<td>olanzapine</td>
<td>Zyprexa</td>
<td>Calcium channel blocker; anti-Alzheimer's</td>
</tr>
<tr>
<td>ondansetron</td>
<td>Zofran</td>
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</tr>
<tr>
<td>paroxetine</td>
<td>Paxil</td>
<td>Antidepressant (selective serotonin reuptake inhibitor)</td>
</tr>
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<td>pemoline</td>
<td>Cylert</td>
<td>Stimulant</td>
</tr>
<tr>
<td>perphenazine</td>
<td>Etrafon, Triavil, Trilafon</td>
<td>Antipsychotic (phenothiazine)</td>
</tr>
<tr>
<td>phenelzine</td>
<td>Nardil</td>
<td>Antidepressant (monoamine oxidase inhibitor)</td>
</tr>
<tr>
<td>phentermine</td>
<td>Adipex-P, Fastin</td>
<td>Antiobesity</td>
</tr>
<tr>
<td>phosphatidylserine</td>
<td>BC-PS</td>
<td>Anti-Alzheimer's; cognition enhancer</td>
</tr>
<tr>
<td>physostigmine</td>
<td>Synapton SR</td>
<td>Cholinergic; cognition enhancer</td>
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<tr>
<td>pindolol</td>
<td>Visken</td>
<td>β-adrenergic receptor blocker (β-blocker or β-adrenergic antagonist)</td>
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<td>pramipexole</td>
<td>Miapex</td>
<td>Antiparkinsonian</td>
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<td>Centrax</td>
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<td>Compazine</td>
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<td>Sparine</td>
<td>Antipsychotic</td>
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<td>Inderal</td>
<td>Antianxiety; antihypertensive</td>
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<tr>
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<td>Vivactil</td>
<td>Antidepressant (tricyclic)</td>
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<tr>
<td>quazepam</td>
<td>Doral</td>
<td>Hypnotic; benzodiazepine</td>
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<tr>
<td>quetiapine</td>
<td>Seroquel</td>
<td>Dopamine and serotonin (5-HT&lt;sub&gt;2&lt;/sub&gt;) antagonist; antipsychotic</td>
</tr>
<tr>
<td>remoxipride</td>
<td>Roxiam</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>risperidone</td>
<td>Risperdal</td>
<td>Antipsychotic</td>
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<tr>
<td>rizatriptan</td>
<td>Maxalt</td>
<td>5-HT&lt;sub&gt;1D/1B&lt;/sub&gt; receptor agonist for migraine</td>
</tr>
</tbody>
</table>

*Not available in the U.S.
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Drug Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>ropinirole</td>
<td>Requip</td>
<td>Antiparkinsonian</td>
</tr>
<tr>
<td>roxindole</td>
<td></td>
<td>Antidepressant</td>
</tr>
<tr>
<td>sabeluzole</td>
<td></td>
<td>Treatment for dementia in Alzheimer's disease</td>
</tr>
<tr>
<td>selegiline, l-deprenyl</td>
<td>Eldepryl, Carbex</td>
<td>Antidepressant (monoamine oxidase inhibitor [MAO-I-type B])</td>
</tr>
<tr>
<td>sertraline</td>
<td>Zoloft</td>
<td>Antidepressant (selective serotonin reuptake inhibitor)</td>
</tr>
<tr>
<td>sibutramine</td>
<td>Meridia</td>
<td>Antiobesity</td>
</tr>
<tr>
<td>stripental</td>
<td></td>
<td>Anticonvulsant</td>
</tr>
<tr>
<td>suaronacrine</td>
<td></td>
<td>Cholinesterase inhibitor; anti-Alzheimer's</td>
</tr>
<tr>
<td>tacrine</td>
<td>Cognex</td>
<td>Anti-Alzheimer's; cognition enhancer</td>
</tr>
<tr>
<td>temazepam</td>
<td>Restoriil</td>
<td>Hypnotic; benzodiazepine</td>
</tr>
<tr>
<td>thioridazine</td>
<td>Mellaril</td>
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</tr>
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<td>Navane</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>tiagabine</td>
<td>Gabitril</td>
<td>Gamma-aminobutyric acid (GABA) reuptake inhibitor; anticonvulsant</td>
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<tr>
<td>SB202026</td>
<td>Memric</td>
<td>Muscarinic M-1 partial agonist; anti-Alzheimer's</td>
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<td>tocapone</td>
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<td>Enzyme inhibitor; adjunctive therapy with levodopa; antiparkinsonian</td>
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<td>Topamax</td>
<td>Anticonvulsant</td>
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<tr>
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<td>Parnate</td>
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<tr>
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<td>Desyrel</td>
<td>Antidepressant (atypical; selective serotonin reuptake inhibitor)</td>
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<td>Halcion</td>
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<tr>
<td>trifluoperazine</td>
<td>Stelazine</td>
<td>Antianxiety; antipsychotic</td>
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<td>Vesprin</td>
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<td>Anticholinergic</td>
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<td>Surmontil</td>
<td>Antidepressant (tricyclic)</td>
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<td>valproate</td>
<td>Depakene, Depakote</td>
<td>Anticonvulsant</td>
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<td>venlacrin</td>
<td>Mentane</td>
<td>Cholinesterase inhibitor</td>
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<td>Calcium channel inhibitors</td>
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<td>Sabril</td>
<td>Treatment for refractory epilepsy</td>
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<td>xanomeline</td>
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<td>M-1 agonist; anti-Alzheimer's</td>
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<td>yohimbine</td>
<td>Yocon, Dayto Himbin, Yohimex</td>
<td>Sympatholytic</td>
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<td>zafrodron</td>
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<tr>
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<td>Ambien</td>
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<tr>
<td>zomatriptan</td>
<td>Zomig</td>
<td>Selective serotonin 5-HT$_{1B}$ receptor agonist</td>
</tr>
</tbody>
</table>
We Want Your Feedback!

Please complete and submit your evaluation from this program so we may learn from your constructive feedback. Thank you!
INSTRUMENTS

MDS -

Pittsberg

Zeldox

- EPS
- QTc
- 1 trial 7/10 pts didn't show efficacy
- Geriatrics

Risperidone - auto inhibition - build up - falls - titration

- EPS & TD
- Orthostatic hypotension - slow titration
- Narrow therapeutic window - safety concerns
- Prolactin elevation
- Adjust dose for renal impairment
- BID
- Active metabolite
- Peripheral edema - likely dose-related
- QT prolongation
- High end dose
- Quetiapine - grapefruit juice - zithromax

- CYP450 3A4 inhibitors + Seroquel = somnolence & orthostatic hypotension & falls
- Complicated dosing
- Postural hypotension 13-15%
- Cataracts