Dementia update

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Director, Northwest VA PADRECC
Director, OHSU Parkinson Center & Movement Disorder Program
agenda

• Update on diagnosis
  – Amyloid PET scans
  – Blood test for Alzheimer’s

• Update on treatment
  – Cholinesterase inhibitors – higher doses
  – Memantine – changes in manufacture
  – Vitamin E for preservation of ADLs
  – Depakote for symptom management
  – Prazosin for symptom management

Diagnosis of dementia

History, including collateral historian
Examination, including mental status
(Neuropsych if MMSE/MOCA/SLUMS is high)

Rule out treatable causes of cognitive decline:
CBC, chem, B12, TSH
structural brain imaging (CT or MRI)

Alzheimer’s  Vascular dementia  Lewy body  Frontotemporal
Imaging AD pathology in living patients

Use of Florbetapir-PET for Imaging β-Amyloid Pathology

Context: The ability to identify and quantify brain β-amyloid could increase the accuracy of a clinical diagnosis of Alzheimer disease.

JAMA. 2011;305(3):275-283

Congo red

Thioflavin S

Imaging AD pathology in living patients
Imaging AD pathology in living patients

- Florbetapir for PET scans was approved by the FDA April 2012
- Flutemetamol also recently approved (October 2013)
- CMS will not cover them, so no other insurance will cover them, including the VA

FDA statement on amyloid imaging:

- A negative Florbetapir scan:
  - indicates sparse to no neuritic plaques.
  - is inconsistent with a neuropathological diagnosis of Alzheimer's disease at the time of image acquisition.
  - reduces the likelihood that a patient's cognitive impairment is due to Alzheimer's disease.

SOURCE INFORMATION
From the Division of Medical Imaging Products (L.Y., D.R.), Office of New Drugs and the Office of Drug Evaluation IV (C.G.), Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD.
FDA statement on amyloid imaging:

- A positive florbetapir scan:
  - indicates moderate to frequent amyloid neuritic plaques.
  - may be observed in older people with normal cognition and in patients with various neurologic conditions, including Alzheimer's disease.

SOURCE INFORMATION
From the Division of Medical Imaging Products (L.Y., D.R.), Office of New Drugs and the Office of Drug Evaluation IV (C.G.), Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD.

FDA statement on amyloid imaging:

- Important florbetapir scan limitations:
  - A positive scan does not establish a diagnosis of Alzheimer's disease or other cognitive disorder.
  - The scan has not been shown to be useful in predicting the development of dementia or any other neurologic condition, nor has usefulness been shown for monitoring responses to therapies.

SOURCE INFORMATION
From the Division of Medical Imaging Products (L.Y., D.R.), Office of New Drugs and the Office of Drug Evaluation IV (C.G.), Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD.
Blood test for Alzheimer’s disease

Plasma phospholipids identify antecedent memory impairment in older adults

Mark Mapstone1, Anmita K Cheema2, Massimo S Fiandaca4-5, Xiaogang Zhong6, Timothy R Mhyre5, Linda H MacArthur5, William J Half7, Susan G Fisher4,14, Derick R Peterson8, James M Haley10, Michael D Nazar11, Steven A Rich12, Dan J Berlau13,14, Carrie B Peltz13, Ming T Tan6, Claudia H Kawas13 & Howard J Federoff8,5

Received 27 August 2013; accepted 9 January 2014; published online 9 March 2014; doi:10.1038/nm.3466

methods

• Enrolled 525 individuals in a 5 year study
• Divided into AD/MCI, Converters, Normal Controls
• 74 were AD/MCI

• in year 3, compared plasma metabolites in 53 AD/MCI and 53 matched control subjects to identify differences
• Then tested the hypothesis with 21 AD/MCI and 21 matched controls
Untargeted “LASSO” analysis:

Table 1 Putative metabolite markers resulting from binary comparison of the study groups

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>LASSO coefficient</th>
<th>Comparison groups</th>
<th>Mode</th>
<th>Mass/charge ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphatidylinositol (18:0/0:0)</td>
<td>↓ (−0.674)</td>
<td>NC versus Converter_pre</td>
<td>NEG</td>
<td>599.3226</td>
</tr>
<tr>
<td>Proline-asparagine dipeptide</td>
<td>↑ (0.192)</td>
<td>NC versus aMCI/AD</td>
<td>POS</td>
<td>230.1146</td>
</tr>
<tr>
<td>Glycoursodeoxycholic acid</td>
<td>↑ (0.107)</td>
<td>NC versus aMCI/AD</td>
<td>POS</td>
<td>450.3196</td>
</tr>
<tr>
<td>Malic acid</td>
<td>↓ (−0.024)</td>
<td>NC versus aMCI/AD</td>
<td>POS</td>
<td>134.0207</td>
</tr>
</tbody>
</table>

The markers were chosen on the basis of significant predictive value as determined by LASSO coefficient analysis. The positive estimated LASSO coefficient suggests elevation in corresponding comparison group (aMCI/AD and Converter_pre) compared to NC participants. Arrows indicate upregulation or downregulation in the comparison group as compared to the NC participants. NEG, negative; POS, positive.

Targeted analysis:

Table 2 Difference detection of putative metabolites using SID-MRM-MS

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Fold change</th>
<th>Comparison groups</th>
<th>Mode</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC C38:4</td>
<td>↓</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.00417</td>
</tr>
<tr>
<td>Proline</td>
<td>↓</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.00003</td>
</tr>
<tr>
<td>Lysine</td>
<td>↓</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.0020</td>
</tr>
<tr>
<td>Serotonin</td>
<td>↓</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.0160</td>
</tr>
<tr>
<td>Taurine</td>
<td>↓</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.0030</td>
</tr>
<tr>
<td>DOPA</td>
<td>↑</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.0001</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>↓</td>
<td>NC versus Converter_pre</td>
<td>POS</td>
<td>0.00001</td>
</tr>
<tr>
<td>Acylcarnitine C7-DC</td>
<td>↓</td>
<td>NC versus aMCI/AD</td>
<td>POS</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

The arrows indicate upregulation or downregulation in the comparison group as compared to the NC participants. DOPA, dihydroxyphenylalanine; C7-DC, pimelyl-carnitine.
Validation phase:

Supplementary Figure 4. Trend plots for the ten metabolite panel—Validation phase. This figure shows the results of the internal controls (NC) and the disease groups (MCI and AD).

Blood test for AD: conclusions

- Promising initial results from unbiased metabolomics study.
- Still a long way to a validated blood test for AD.
Update on dementia diagnosis:

• New PET studies FDA-approved but not covered by insurance
• Blood test results encouraging but very preliminary.
• Dementia diagnosis continues to be highly dependent on history and exam.

Review of dementia treatment: “cognitive enhancers”

– Cholinesterase inhibitors:
  • Donepezil
  • Galantamine
  • Rivastigmine
– NMDA antagonist
  • Memantine
Review of cognitive enhancers

<table>
<thead>
<tr>
<th></th>
<th>MCI</th>
<th>Mild-moderate AD</th>
<th>Moderate-severe AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Optional</td>
<td>FDA approved</td>
<td>FDA approved</td>
</tr>
<tr>
<td>memantine</td>
<td>Not approved</td>
<td>Not approved</td>
<td>FDA approved</td>
</tr>
</tbody>
</table>

Update on treatment

- *Cholinesterase inhibitors*- 23 mg *donepezil*
- Memantine
- Vitamin E
- Symptomatic treatments
Effectiveness and Tolerability of High-Dose (23 mg/d) Versus Standard-Dose (10 mg/d) Donepezil in Moderate to Severe Alzheimer’s Disease: A 24-Week, Randomized, Double-Blind Study

Martin R. Farlow, MD; Stephen Salloway, MD, MS; Pierre N. Tariot, MD; Jane Yardley, PhD; Margaret L. Moline, PhD; Qin Wang, PhD; Elimor Brand-Schieber, PhD; Heng Zou, MS; Timothy Hsu, MD; and Andrew Satlin, MD
18.6% on 23 mg discontinued due to adverse events compared to 7.9% on 10 mg
How does Aricept 23 compare to 10?

- Marginally greater efficacy on cognition
- No demonstration of benefit on global measures
- More side effects
- Higher cost
- Not available in VA
Namenda/Memantine

- Forest recently announced that they will no longer make the immediate-release tablets that have been the most commonly used form.
- They will continue to make the oral solution and sustained release formulation.

Treatment of dementia: beyond cognitive enhancers:

- Vitamin E
- Symptomatic therapies
  - Valproic acid
  - Prazosin
VA patients with mild to moderate AD on stable dose of CEI randomized to one of four groups:
- placebo
- memantine 10 bid
- vitamin E 2000 IU per day
- memantine plus vitamin E

Duration of intervention = 48 weeks
Groups were well matched on:

- Age (about 78 years old)
- Gender (96-98% male)
- MMSE (about 20)
- Cholinesterase inhibitors (all were on CEI, 65% donepezil, 30% galantamine, 5% rivastigmine)
VA Vitamin E study conclusions:

- Vitamin E associated with slowing of functional decline
- No effect on cognitive measures
- How does this compare with previous literature?
A CONTROLLED TRIAL OF SELEGILINE, ALPHA-TOCOPHEROL, OR BOTH AS TREATMENT FOR ALZHEIMER’S DISEASE

MARY SANO, Ph.D., CHRISTOPHER ERNESTO, M.S., RONALD G. THOMAS, Ph.D., MELVILLE R. KLAUBER, Ph.D., KIMBERLY SCHAER, M.S., MICHAEL GRUNDMAN, M.D., M.P.H., PETER WOODBURY, JOHN GROWDON, M.D., CARL W. COTMAN, Ph.D., ERIC PFEIFFER, M.D., LON S. SCHNEIDER, M.D., AND LEON J. THAL, M.D., FOR THE MEMBERS OF THE ALZHEIMER’S DISEASE COOPERATIVE STUDY

TABLE 1. BASE-LINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF 341 PATIENTS WITH ALZHEIMER’S DISEASE RANDOMLY ASSIGNED TO RECEIVE PLACEBO, SELEGILINE, ALPHA-TOCOPHEROL, OR BOTH AGENTS.*

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>PLACEBO (N = 84)</th>
<th>SELEGILINE (N = 87)</th>
<th>ALPHA-TOCOPHEROL (N = 85)</th>
<th>SELEGILINE AND ALPHA-TOCOPHEROL (N = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>73.5±8.3</td>
<td>72.7±8.9</td>
<td>73.4±7.8</td>
<td>73.9±7.1</td>
</tr>
<tr>
<td>Education (yr)</td>
<td>12.2±3.1</td>
<td>12.4±3.7</td>
<td>12.6±3.3</td>
<td>12.7±3.3</td>
</tr>
<tr>
<td>Duration of Illness (yr)</td>
<td>5.5±2.9</td>
<td>4.8±2.4</td>
<td>5.3±2.7</td>
<td>4.7±2.5</td>
</tr>
<tr>
<td>Female sex (% of patients)</td>
<td>65.5</td>
<td>67.8</td>
<td>65.9</td>
<td>60.0</td>
</tr>
<tr>
<td>Score on Mini–Mental State Examination†</td>
<td>13.3±4.9‡</td>
<td>12.7±5.0</td>
<td>11.3±5.7</td>
<td>12.9±5.7</td>
</tr>
<tr>
<td>Score on Blessed Dementia Scale§</td>
<td>6.1±2.1</td>
<td>6.3±1.9</td>
<td>6.6±2.3</td>
<td>6.4±2.3</td>
</tr>
<tr>
<td>Extrapyramidal signs (% of patients)</td>
<td>19.0</td>
<td>26.4</td>
<td>18.8</td>
<td>24.7</td>
</tr>
<tr>
<td>Clinical Dementia Rating‡</td>
<td>10.9±1.2</td>
<td>11.0±1.2</td>
<td>11.3±1.3</td>
<td>10.9±1.2</td>
</tr>
</tbody>
</table>
A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer’s disease

MARY SAND, Ph.D., CHRISTOPHER ERNESTO, M.S., RONALD G. THOMAS, Ph.D., MELVILLE R. KLUGER, Ph.D., KIMBERLY SCHOLER, M.S., MICHAEL DURLAKIN, M.D., M.P.H., PETER WOODS, JOHN GERSOND, M.D., CARL W. COTMAN, Ph.D., ERIC PREFFER, M.D., LON S. SCHIEFER, M.D., AND LEON J. THAL, M.D., FOR THE MEMBERS OF THE ALZHEIMER’S DISEASE COOPERATIVE STUDY

Results Despite random assignment, the baseline score on the Mini-Mental State Examination was higher in the placebo group than in the other three groups, and this variable was highly predictive of the primary outcome (P<0.001). In the unadjusted analyses, there was no statistically significant difference in the outcomes among the four groups. In analyses that included the baseline score on the Mini-Mental State Examination as a covariate, there were significant delays in the time to the primary outcome for the patients treated with selegiline (median time, 655 days; P=0.012), alpha-tocopherol (670 days, P=0.001), or combination therapy (585 days, P=0.049), as compared with the placebo group (440 days).

Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment

Table 1. Baseline Characteristics of the Subjects.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo Group (N=259)</th>
<th>Donepezil Group (N=253)</th>
<th>Vitamin E Group (N=257)</th>
<th>All Subjects (N=769)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>72.9±7.6</td>
<td>73.1±7.1</td>
<td>72.8±7.3</td>
<td>72.9±7.3</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>121 (47)</td>
<td>112 (44)</td>
<td>119 (46)</td>
<td>352 (46)</td>
</tr>
<tr>
<td>APOE ε4 carrier — no. (%)</td>
<td>136 (53)</td>
<td>147 (58)</td>
<td>141 (55)</td>
<td>424 (55)</td>
</tr>
<tr>
<td>ADAS-Cog score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Original</td>
<td>11.0±4.2</td>
<td>11.2±4.3</td>
<td>11.4±4.4</td>
<td>11.2±4.4</td>
</tr>
<tr>
<td>Modified</td>
<td>17.4+6.0</td>
<td>17.7±6.2</td>
<td>18.0±6.0</td>
<td>17.7±6.1</td>
</tr>
<tr>
<td>MMSE score</td>
<td>27.3±1.8</td>
<td>27.5±1.8</td>
<td>27.2±1.9</td>
<td>27.3±1.8</td>
</tr>
<tr>
<td>CDR sum-of-boxes score</td>
<td>1.87±0.8</td>
<td>1.80±0.8</td>
<td>1.78±0.8</td>
<td>1.82±0.8</td>
</tr>
<tr>
<td>Score on Global Deterioration Scale</td>
<td>2.72±0.6</td>
<td>2.66±0.6</td>
<td>2.64±0.6</td>
<td>2.67±0.6</td>
</tr>
<tr>
<td>Score on Activities of Daily Living Scale</td>
<td>45.87±5.2</td>
<td>46.49±4.3</td>
<td>45.82±4.6</td>
<td>46.06±4.7</td>
</tr>
</tbody>
</table>
Vitamin E

- No benefit in MCI
- Questionable benefit in moderate AD
- Modest effect on ADLs in veterans with mild-moderate AD at 2000 IU per day
- IOM recommends a maximum dose of 1000 IU per day.
Symptomatic therapy for AD

• Depression
• Sleep disturbance
• Psychosis
• Anxiety
• Agitation
Symptomatic therapy for agitation

• Antipsychotic agents
  – associated with increased risk of mortality in dementia, “black box” warning in PDR, must be used with caution

• Valproic acid
  – is frequently used for agitation in dementia

• Prazosin
  – is being developed as an alternative

Table 1. Baseline Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n=160)</th>
<th>Valproate (n=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>76.6 (7.4)</td>
<td>74.9 (8.2)</td>
</tr>
<tr>
<td>Years of education, mean (SD)</td>
<td>13.6 (3.5)</td>
<td>14.0 (3.0)</td>
</tr>
<tr>
<td>Years since AD onset, mean (SD)</td>
<td>5.0 (2.5)</td>
<td>4.6 (2.4)</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>101 (63.1)</td>
<td>83 (54.2)</td>
</tr>
<tr>
<td>Race, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (1.9)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Black</td>
<td>8 (5.0)</td>
<td>8 (5.2)</td>
</tr>
<tr>
<td>White</td>
<td>148 (92.5)</td>
<td>141 (92.2)</td>
</tr>
<tr>
<td>&gt;1 Race</td>
<td>0</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Apolipoprotein E4, No. (%)</td>
<td>39/136 (28.7)</td>
<td>40/132 (30.3)</td>
</tr>
<tr>
<td>Yes</td>
<td>97/136 (71.3)</td>
<td>90/132 (69.7)</td>
</tr>
</tbody>
</table>

MMSE=12-20
Valproic acid and dementia: summary

- Cochrane review (2009) finds no evidence of efficacy of valproate for agitation in dementia.
- Randomized clinical trial (2011) shows no evidence that valproic acid can prevent emergence of behavioral problems.
- Randomized clinical trial (2011) suggests valproic acid may accelerate rate of brain atrophy in AD.
Prazosin for agitation in AD

- Developed by Drs Murray Raskind and Elaine Peskind at Puget Sound VA
- Based on evidence that the ascending noradrenergic system is over-active in AD
- Prazosin is an alpha-1 antagonist

• Possible or probable AD
• Score of 4 or more on the Brief Psychiatric Rating Scale in anxiety, tension, hostility, uncooperativeness, or excitement.
• Randomized to placebo vs prazosin, titrated to 6 mg per day
• (with each dose increase requiring pre-dose systolic BP of ≥ 110)
## Pilot trial of prazosin pilot study population:

<table>
<thead>
<tr>
<th>characteristic</th>
<th>Prazosin N=11</th>
<th>Placebo N=11</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>83.2±11.5</td>
<td>78.1±10.8</td>
</tr>
<tr>
<td>MMSE</td>
<td>9.3±6.6</td>
<td>14±12</td>
</tr>
<tr>
<td>Female/male</td>
<td>4/7</td>
<td>5/6</td>
</tr>
<tr>
<td>Nursing home/community dwelling</td>
<td>6/5</td>
<td>6/5</td>
</tr>
</tbody>
</table>

## Pilot trial of prazosin-outcomes

<table>
<thead>
<tr>
<th>scale</th>
<th>treatment</th>
<th>Group mean change</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPI</td>
<td>prazosin</td>
<td>-19 ± 21</td>
<td>0.012</td>
</tr>
<tr>
<td>&quot;</td>
<td>placebo</td>
<td>-2 ± 15</td>
<td></td>
</tr>
<tr>
<td>BPRS</td>
<td>prazosin</td>
<td>-9 ± 9</td>
<td>0.036</td>
</tr>
<tr>
<td>&quot;</td>
<td>placebo</td>
<td>-3 ± 5</td>
<td></td>
</tr>
<tr>
<td>CGIC</td>
<td>prazosin</td>
<td>2.6 ± 1</td>
<td>0.011</td>
</tr>
<tr>
<td>&quot;</td>
<td>placebo</td>
<td>4.5 ± 1.6</td>
<td></td>
</tr>
</tbody>
</table>
Prazosin for dementia

- Larger clinical trial under way in Seattle
- Prazosin is available for open label use
- The primary morbidity is hypotension

Prazosin for dementia

- Medication initiation and each dose increase requires systolic BP of ≥ 110:
  - 1 mg qhs x 3 days
  - 1 mg bid x 3 days
  - 1 mg qam, 2 mg qpm x 3 days
  - 2 mg bid x 3 days
  - 2 mg qam and 3 mg qpm x 3days
  - 3 mg bid
Treatment of dementia: summary

- Cholinesterase inhibitor: 23 mg donepezil does not have a significant role
- Memantine: expect a change in formulation
- Valproic acid: use with caution, if at all
- Prazosin: consider for off-label use in agitated patients with sufficient blood pressure

Any questions before moving on to the case discussion?
Case study

• 70 year old man is brought in by his family with concerns about cognitive decline.
• No functional decline reported by spouse, but he is repetitive even during the visit, reinforcing impression of memory decline.
• MMSE=28/30
• No significant medical hx, meds, or fam hx
• Balance of general and neuro exams are unremarkable.

Diagnosis update

• Which test is most useful at this point?
• A) amyloid PET scan
• B) FDG PET scan
• C) blood test for Alzheimer’s
• D) neuropsychological assessment
Preferred answer:

- D) neuropsychological assessment

- This is the only option that will help clarify whether this patient’s memory complaint is in the range of normal aging or Mild Cognitive Impairment (MCI)

- Neuropsychological assessment confirms the presence of memory disorder outside the range expected for age, with relative preservation of other cognitive functions.

- In other words, the neuropsych results are consistent with a diagnosis of Mild Cognitive Impairment.
• You proceed to rule out treatable causes of cognitive decline with brain MRI, CBC, chem panel, vitamin B12 level, and TSH. The MRI shows “age-related changes” and the bloodwork is all negative. Your diagnosis at this point is Mild cognitive impairment.

What medications might be considered at this point?

• A) donepezil
• B) memantine
• C) valproic acid
• D) prazosin
Preferred answer

- A) donepezil

- Donepezil has shown modest (and somewhat transient) efficacy in amnestic MCI so is a viable option. Memantine is approved only for moderate to severe AD, and the other options are treatments for agitation, typically in moderate to severe dementia.

- Two years pass and the patient slowly declines on MMSE and in daily function. His MMSE is now 22/30 and he is dependent in managing finances, remembering medications, remembering appointments, and driving, but his basic ADLs (dressing, eating, toileting) are well preserved. He is also frustrated and irritable, snapping at his wife over little things.
What treatment options would you consider at this point:

- A) discontinue donepezil since it is not slowing the progression of disease.
- B) add memantine to donepezil.
- C) add prazosin for agitation
- D) trial of an SSRI

Preferred answer

- D) trial of an SSRI

- There is no absolute right or wrong answer here, but frustration and irritability in early dementia will often respond to an SSRI with relatively few risks.
• Three more years pass with continued gradual decline. The MMSE is now 14/30, and the patient now needs assistance with dressing and grooming, needs food cut up, is occasionally incontinent. He resists efforts to help with his care and he is frequently restless and pacing. He does not have any evidence of hallucinations or delusions.

What treatment options might be considered at this point?

• A) valproic acid
• B) thorazine
• C) quetiapine
• D) prazosin
Preferred answer

• Again, no clear standard of care here, but:
• Little data to support valproic acid use. No psychotic symptoms to justify antipsychotic use. Prazosin is an option, but it is clearly off label use and the published data to date is limited.

• Prazosin fails. The patient now begins to elaborate more clear-cut hallucinations, seeing people and animals which are quite distressing to him.
What treatment options might be considered at this point?

• A) haldol
• B) thorazine
• C) quetiapine
• D) risperdal
• E) avoid antipsychotics at all cost due to PDR black box warning regarding mortality in dementia.

Preferred answer:

• Quetiapine or risperdal.
• Since the patient is having distressing psychotic symptoms, antipsychotic use is justified. Older antipsychotic agents like haldol and thorazine produce significant extrapyramidal (parkinsonian) symptoms in elderly patients. Some older agents also have anticholinergic side effects which aggravate cognitive impairment.
Preferred answer:

- Quetiapine or risperdal.
- Quetiapine has the lowest incidence of extrapyramidal side effects of all the available antipsychotic agents, with the exception of clozaril, which is difficult to prescribe. Risperdal is also a reasonable option as long as the dose remains low; as extrapyramidal side effects begin to emerge at higher doses.

Any questions?