Differentiating Dementia Diagnoses

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<table>
<thead>
<tr>
<th></th>
<th>Delirium</th>
<th>Dementia</th>
<th>Depression</th>
<th>Psychosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Acute</td>
<td>Insidious</td>
<td>Variable</td>
<td>Slow</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Short</td>
<td>Lengthy</td>
<td>Variable recurrent</td>
<td>Variable recurrent</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Fluctuating</td>
<td>Progressive</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Consciousness</strong></td>
<td>Clouded</td>
<td>Clear (until later)</td>
<td>Mostly unimpaired</td>
<td>Unimpaired</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>Poor</td>
<td>Preserved (early)</td>
<td>Poor</td>
<td>Poor</td>
</tr>
<tr>
<td><strong>Cognition</strong></td>
<td>Impaired</td>
<td>Impaired</td>
<td>Variable</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Delirium</td>
<td>Dementia</td>
<td>Depression</td>
<td>Psychosis</td>
</tr>
<tr>
<td>----------------------</td>
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</tr>
<tr>
<td>Hallucinations</td>
<td>Common visual</td>
<td>Infrequent</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Delusions</td>
<td>Unstructured</td>
<td>Uncommon</td>
<td>Paranoid (occasionally)</td>
<td>Maintained</td>
</tr>
<tr>
<td>Orientation</td>
<td>Poor</td>
<td>Poor</td>
<td>Usually good</td>
<td>Good</td>
</tr>
<tr>
<td>Short term memory</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Speech</td>
<td>Incoherent</td>
<td>Dysphasia</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Psychomotor behavior</td>
<td>Lethargic/agitated</td>
<td>Normal</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Physical illness</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
<td>Usually absent</td>
</tr>
</tbody>
</table>
The Middle Aged Brain – The Bad News!

BMJ 2012 – for those age 45-49 ability to reason declined 3.6% by the time they were 55-59 years old

– Keeping overall health is the key
  – exercise in particular

Singh-Manoux A et al. BMJ 2012;344:bmj.d7622
Cognitive Impairment
Main Causes

Degenerative
- Alzheimer’s
- Fronto-temporal lobe/Pick’s
- Lewy Body Dementia
- Parkinson’s Dementia
- ALS/MND
- MS
- Huntington’s

Vascular
- Multi-Infarct Dementia
- Pellagra
- Vasculitis
- Lupus

Infectious
- HIV
- CJD
- Syphilis
- Herpes Simplex
- Fungal
- Bacterial

Structural
- Normal Pressure Hydrocephalus
- Neoplasm
- Alcohol / Drugs
- Trauma
- Subdural Hematoma

Metabolic
- Electrolyte Imbalance
- Medications
- Wilson’s
- Whipple’s
- Thyroid
- B12/Folate
- Hepatic
History - Onset and Duration

Gradual & chronic
- Alzheimer’s Disease (AD)

Rapidly progressive
- Vascular Disease
- Hashimoto’s hypothyroid
  • Myxoedematous psychosis
- Creutzfeldt–Jakob disease (CJD)
- Vasculitis
- Cancer
- ↓ Thiamine
- Cerebral infection

Acute
- Delirium
- Vascular Dementia
- Transient Global Amnesia
  - Acute onset of anterograde amnesia
  - No alteration in consciousness
  - No cognitive impairment other than amnesia
  - No loss of personal identity
  - No focal neurology or epileptic features
  - No recent history of head trauma or seizures
  - Attack must resolve within 24 hr

Step-wise
- Vascular Dementia
History

• Past Medical History
  – Head Injury
    • Normal Pressure Hydrocephalus
    • Sub-dural hematoma
    • Sub-arachnoid haemorrhage
  – Epilepsy
    • Creutzfeldt–Jakob disease (CJD)
    • Vascular
    • Cancer

• Past employment history
  – Exposure to
    • Lead
    • CO
    • Mercury
  – Education level
  – Sleep Apnea Sx
  – Syphilis
  – Test or not to test??
History

• Behaviour > Cognitive
  – Executive Function
    • Lewy Body, Parkinson’s Disease Dementia (PDD)
    • Vascular
    • Fronto-Temporal Lobe dementia (FTD)
  – Personality Changes
    • FTD
    • Vascular

• Cognitive > Behaviour
  – Short Term memory loss
    • Alzheimer's Disease (AD)
History

• Family History of Dementia
  – Early Onset Alzheimer’s
  – Some types of Fronto-Temporal Lobe dementia

• Medications
  – Benzodiazepines
  – Anti-cholinergics
  – Many others

• Lifestyle Questions
  – Smoking
    • Buerger’s Disease
    • blockages in the blood vessels of extremities
    • Inflamed blood vessels and Blood clots
  – IV Drug Use, Gay male
    • HIV related dementia
  – ETOH – how much, how often?
Physical Exam

Neurologic Exam
- Cognitive Test
- Cranial Nerves
- PEARL, Hearing
- Visual Fields, EOMs
- Romberg, pronator drift
- Gait
- RAM, heel to shin, finger to nose
- DTR
- UE and LE strength

Routine
- Cardiovascular
- Carotid Bruit
- Respiratory
- Abdomen
- Thyroid
“Reversible” Dementia

• Rates unclear, given that studies use different interpretations of word “reversible”

  – Srikanth & Nagaraja (2005) 18% cases potentially treatable, 15% improved with treatment

  – Freter et al (1998) 23% cases potentially treatable, 3% improved with treatment

• Commonest causes of treatable dementia were in descending order (Clarfield 1988):

  • Depression
  • Medications
  • Normal Pressure Hydrocephalus
  • Thyroid disorders
  • Subdural Hematoma
  • Neoplasms
  • ETOH
  • Calcium disorders
  • Hepatic disorders
  • B12
Investigations

• **BLOODS**
  – LFTs
  – Electrolytes (include Ca++)
  – Renal Function
  – FBC
  – B12 and Folate
  – CRP
  – Thyroid
    - Serum Medication levels
  - Glucose

• **URINE**

• **HEAD SCANNING**
  – CT
  – MRI
Mild Cognitive Impairment (MCI)

- Memory impaired but are otherwise functioning well and do not meet clinical criteria for dementia

- Symptoms include
  - Memory complaint, preferably with corroboration
  - Intact activities of daily living
  - Progression MCI → dementia ~ 10-15% per year in clinic-based studies (Mariani et al, 2007)

- There are currently no recommended treatments for MCI
  - Medication review
  - Exercise and social engagement

Cognitive Impairment
Degenerative Sub-types

Cortical

- Frontal Temporal Lobe
- Alzheimer’s Disease
  - Early Onset
  - Late Onset
- Lewy Body Dementia
- CJD

Sub-Cortical – basal ganglia, Motor

- Cortico-basilar
  - Semantic aphasia
  - Progressive Nonfluent Aphasia
  - Progressive Supranuclear Palsy
- Parkinson’s Dementia
- Huntington’s
Imaging for Alzheimer’s Disease

MRI preferred to allow for 3D measurement. Only obvious in end stages.

- Extreme hippocampal and medial temporal lobe atrophy
- Severe global atrophy
PET Scan beta amyloid deposits

Rowe, et al., J Nucl Med November 1, 2011 vol. 52 no. 11 1733-1740
### Table 1. FDA-Approved Drugs for Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulations</th>
<th>Usual Daily Dosage</th>
<th>Starting Dose/Titration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholinesterase Inhibitors</td>
<td></td>
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</tr>
<tr>
<td>Donepezil – Aricept (Eisai/PD-RX)</td>
<td>5 or 10 mg tabs; 5 or 10 mg orally disintegrating tabs</td>
<td>5-10 mg once</td>
<td>5 mg once/d; after 4-6 wks increase to 10 mg once/d</td>
</tr>
<tr>
<td>Aricept ODT (Eisai/PD-RX)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Galantamine – immediate-release generic</td>
<td>4, 8 or 12 mg tabs; 4 mg/mL soln</td>
<td>16-24 mg divided bid</td>
<td>8 mg/d divided bid; after 4 wks increase to 16 mg/d, then after 4 wks to 24 mg/d</td>
</tr>
<tr>
<td>Razadyne 1 (Ortho-McNeil)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>extended-release generic</td>
<td>8, 16 or 24 mg caps</td>
<td>16-24 mg once</td>
<td>8 mg once/d; after 4 wks increase to 16 mg/d, then after 4 wks to 24 mg/d</td>
</tr>
<tr>
<td>Razadyne ER (Ortho-McNeil)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivastigmine – Exelon (Novartis)</td>
<td>1.5, 3, 4.5 or 6 mg caps; 2 mg/mL soln</td>
<td>6-12 mg divided bid</td>
<td>3 mg/d divided bid; increased in increments of 3 mg/d q 2wks to 12 mg/d</td>
</tr>
<tr>
<td>transdermal Exelon Patch (Novartis)</td>
<td>4.6 mg/24 hours or 9.5 mg/24 hours</td>
<td>9.5 mg/24 hours</td>
<td>4.6 mg/24 hours; after 4 weeks if tolerated, increase to 9.5 mg/24 hours</td>
</tr>
<tr>
<td>Tacrine – Cognex (Shionogi)</td>
<td>10, 20, 30, 40 mg caps</td>
<td>120-160 mg/day divided qid</td>
<td>10 mg 4x/day; after 4 weeks increase to 20 mg qid</td>
</tr>
<tr>
<td>NMDA-Receptor Antagonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memantine – Namenda (Forest/PD-RX)</td>
<td>5 or 10 mg tabs; 2 mg/mL soln</td>
<td>20 mg, once or divided bid</td>
<td>5 mg once/d; increase to 20 mg/d in increments of 5 mg q wk</td>
</tr>
</tbody>
</table>

1. Formerly Reminyl.
2. Every 4 weeks for dementia associated with Parkinson's disease.

**Treatment Guidelines from The Medical Letter**, January 1, 2010 (Issue 89)
Vascular Dementia

- Previously thought to be about 20% of all dementias

- Now thought that there is very little ‘pure vascular dementia’

- Does the ischaemic changes from cardiovascular disease promote plaques and tangles?

- The Nun Study: lacunar strokes increase dementia risk 20 fold with fewer plaques and neurofibrillary tangles before showing signs of dementia.

TREATMENT:

Cardiovascular Health

Exercise

Active Mind
CLOX: an executive clock drawing task

Royall, Cordes, Polka
*J Neurol Neurosurg Psychiatry*
1998;64:588-594
# Vascular Dementia Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vascular Dementia</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Sudden or gradual</td>
<td>Gradual</td>
</tr>
<tr>
<td>Progression</td>
<td>Slow, stepwise fluctuation</td>
<td>Constant insidious decline</td>
</tr>
<tr>
<td>Neurological findings</td>
<td>Evidence of focal deficits</td>
<td>Subtle or absent</td>
</tr>
<tr>
<td>Memory</td>
<td>Mildly affected</td>
<td>Early and severe deficit</td>
</tr>
<tr>
<td>Executive function</td>
<td>Early and severe</td>
<td>Late</td>
</tr>
<tr>
<td>Dementia type</td>
<td>Subcortical</td>
<td>Cortical</td>
</tr>
<tr>
<td>Neuroimaging</td>
<td>Infarcts or white matter lesions</td>
<td>Normal; hippocampal atrophy</td>
</tr>
<tr>
<td>Gait</td>
<td>Often disturbed early</td>
<td>Usually normal</td>
</tr>
<tr>
<td>Cardiovascular history</td>
<td>Transient ischemic accidents, strokes, vascular risk factors</td>
<td>Less common</td>
</tr>
</tbody>
</table>
Lewy Body and Parkinson’s Disease Dementia

**LBD**
- Cognitive Impairment
- Parkinson’s Dx occurs around the same time or after dementia dx
- Fluctuating Cognition
- Visual Hallucinations
- Varying alertness and attention
- Delusions
- Unexplained syncope
- Rapid eye movement sleep disorder
- Neuroleptic sensitivity
- Depression

**PDD**
- Cognitive Impairment
- Parkinson’s Dx for at least 1 year
Lewy Body Dementia Treatment

- Cholinesterase inhibitor first choice
  - Rivastigmine may decrease psychiatric symptoms particularly apathy, anxiety, hallucinations, and delusions
  - Donepezil and Galantamine have shown improvement in neuropsychological testing
  - Memantine improved cognition

- Typical anti-psychotics are contraindicated due to hypersensitivity

- Levodopa/carbidopa can help motor symptoms but make the neuropsychologic sx worse

- SSRI for depression

- Clonazepam treatment of choice for rapid eye movement sleep behaviour disorder
Frontotemporal Lobe Dementia

- Described by Pick in 1892
- Disinhibition
- Impulsivity
- Impersistence
- Inertia
- Loss of social awareness
- Neglect of personal hygiene
- Mental rigidity, stereotyped behavior

- Utilization behavior - i.e., a tendency to pick up and manipulate any object in the environment
- Echolalia, perseveration
<table>
<thead>
<tr>
<th>Fronto-temporal Lobe Dementia</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Specific atrophy</td>
<td>✓ Diffuse atrophy</td>
</tr>
<tr>
<td>✓ Apraxia – late</td>
<td>✓ Apraxia – early</td>
</tr>
<tr>
<td>✓ Marked personality change – early in the disease</td>
<td>✓ Subtle personality changes</td>
</tr>
<tr>
<td>✓ Memory impairment – late in the disease</td>
<td>✓ Memory Impairment – early in the disease</td>
</tr>
<tr>
<td>✓ Little response to ACHase Inhibitors</td>
<td>✓ Good response to ACHase inhibitors</td>
</tr>
<tr>
<td>✓ Pick inclusion bodies on pathology</td>
<td>✓ Neurofibrillary plaques and tangles</td>
</tr>
</tbody>
</table>