Depression and Dementia

Dr Michal Boyd, RN, NP, ND, FCNA(NZ), FAANP
Nurse Practitioner – Waitemata District Health Board

Senior Lecturer, The University of Auckland,
School of Nursing & Freemason’s Dept of Geriatric Medicine

Auckland, New Zealand
<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>
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<tr>
<td><strong>Course</strong></td>
<td>Fluctuating</td>
<td>Progressive</td>
<td>Variable</td>
<td>Variable</td>
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<tr>
<td><strong>Consciousness</strong></td>
<td>Clouded</td>
<td>Clear (until later)</td>
<td>Mostly unimpaired</td>
<td>Unimpaired</td>
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<tr>
<td><strong>Attention</strong></td>
<td>Poor</td>
<td>Preserved (early)</td>
<td>Poor</td>
<td>Poor</td>
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<tr>
<td><strong>Cognition</strong></td>
<td>Impaired</td>
<td>Impaired</td>
<td>Variable</td>
<td>Normal</td>
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<tr>
<td></td>
<td>Delirium</td>
<td>Dementia</td>
<td>Depression</td>
<td>Psychosis</td>
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<tr>
<td>Hallucinations</td>
<td>Common visual</td>
<td>Infrequent</td>
<td>Rare</td>
<td>Common</td>
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<tr>
<td>Delusions</td>
<td>Unstructured</td>
<td>Uncommon</td>
<td>Paranoid (occasionally)</td>
<td>Maintained</td>
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<tr>
<td>Orientation</td>
<td>Poor</td>
<td>Poor</td>
<td>Usually good</td>
<td>Good</td>
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<tr>
<td>Short term memory</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td>Speech</td>
<td>Incoherent</td>
<td>Dysphasia</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td>Psychomotor behavior</td>
<td>Lethargic/agitated</td>
<td>Normal</td>
<td>Variable</td>
<td>Variable</td>
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<tr>
<td>Physical illness</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
<td>Usually absent</td>
</tr>
</tbody>
</table>
Depression Reported in Older People

BRIGHT Screen – WDHB

Total Sample Positive Responses

- Help with personal hygiene
- Difficulty with getting around indoors
- Need help dressing lower body
- Difficulty Making Decisions
- Poor memory interferes with daily life
- Help with bath or shower
- Shortness of Breath when walking
- Have good health
- Feeling Depressed
- History of Falls
- Help with ordinary housework

Is it Depression? DSM IV Criteria

Depressed mood and or loss of interest or pleasure (pervasive for 2 weeks)

&

4 of the following (3 with both depressed mood and loss of interest or pleasure)

Physical
1. Sleep disorder
2. Appetite/weight change
3. Fatigue
4. Psychomotor retardation/agitation

Psychological
1. Low self-esteem/guilt
2. Poor concentration/indecisiveness
3. Thoughts of death/suicidal ideation
4. Depressed mood
5. Loss of interest/pleasure
RISK FACTORS

- History of depression
- Substance abuse
- Residence in ARC
- Changes in physical health status
- Frequent somatic (physical) complaints
- Psychosis e.g. delusional/paranoid thoughts, hallucinations
- Recent losses or crises e.g. death of spouse, friend, pet, retirement, anniversary dates, move to another
- Diseases: e.g. respiratory, cardiac, stroke, cancer
- Chronic pain
Systemic and Metabolic Issues

- Infection
- Anaemia
- Hyponatraemia
- Hypercalcaemia
- Hyperthyroidism
- Hypoglycaemia
- Congestive heart failure
- Kidney failure
- Hypothyroidism
- COPD
Medications

- steroids
- narcotics, sedatives/hypnotics
- benzodiazepines
- antihypertensives
- beta-blockers
- Antipsychotics
- immunosuppressives
- cytotoxic agents
Depression Assessment

• Obtain/review medical history and physical/neurological examination

• Assess for cognitive dysfunction

• Assess level of functional disability
Cornell Scale for Depression in Dementia

Patient's name: ________________________________
Date: ________________________________
Location: ________________________________

A. Mood-related signs
1. Anxiety (anxious expression, ruminations, worrying) a 0 1 2
2. Sadness (sad expression, sad voice, tearfulness) a 0 1 2
3. Lack of reactivity to pleasant events a 0 1 2
4. Irritability (easily annoyed, short tempered) a 0 1 2

B. Behavioral disturbances
5. Agitation (restlessness, handwringing, hairpulling) a 0 1 2
6. Retardation (slow movements, slow speech, slow reactions) a 0 1 2
7. Multiple physical complaints (score 0 if gastrointestinal symptoms only) a 0 1 2
8. Loss of interest, less involved in usual activities (score only if change occurred acutely—in less than 1 month) a 0 1 2

C. Physical signs
9. Appetite loss (eating less than usual) a 0 1 2
10. Weight loss (score 2 if greater than 5 lb in one month) a 0 1 2
11. Lack of energy (fatigues easily, unable to sustain activities) (score only if change occurred acutely—in less than one month) a 0 1 2

D. Cyclic functions
12. Diurnal variation on mood (symptoms worse in the morning) a 0 1 2
13. Difficulty falling asleep (later than usual for this person) a 0 1 2
14. Multiple awakenings during sleep a 0 1 2
15. Early morning awakening (earlier than usual for this person) a 0 1 2

E. Ideational disturbances
16. Suicide (feels life is not worth living, has suicidal wishes, or makes suicidal attempt) a 0 1 2
17. Poor self-esteem (self-blame, self-deprecation, feelings of failure) a 0 1 2
18. Pessimism (anticipation of the worst) a 0 1 2
19. Mood-congruent delusions (delusions of poverty, illness, or loss) a 0 1 2

Total score: **

Other Depression Scales:

- BASDEC Cards
- Geriatric Depression Screen
  (both sensitivity of 71%)
- Many others!
Geriatric Depression Scale: Short Form

*Choose the best answer for how you have felt over the past week:*

- Are you basically satisfied with your life? **YES / NO**
- Have you dropped many of your activities and interests? **YES / NO**
- Do you feel that your life is empty? **YES / NO**
- Do you often get bored? **YES / NO**
- Are you in good spirits most of the time? **YES / NO**
- Are you afraid that something bad is going to happen to you? **YES / NO**
- Do you feel happy most of the time? **YES / NO**
- Do you often feel helpless? **YES / NO**
- Do you prefer to stay at home, rather than going out and doing things? **YES / NO**
- Do you feel you have more problems with memory than most? **YES / NO**
- Do you think it is wonderful to be alive now? **YES / NO**
- Do you feel pretty worthless the way you are now? **YES / NO**
- Do you feel full of energy? **YES / NO**
- Do you feel that your situation is hopeless? **YES / NO**
- Do you think that most people are better off than you are? **YES / NO**

Answers in **bold** indicate depression. Score 1 point for each bolded answer. A score > 5 points is suggestive of depression and warrants follow-up comprehensive assessment. A score > 10 points is almost always indicative of depression. Doing new
Intervention

• Monitor and promote
  – Nutrition
  – Elimination
  – Sleep/rest patterns
  – Physical comfort
    (especially pain control)

• Enhance physical function
  – Structure regular exercise/activity
  – Refer to physical, occupational, recreational therapies
  – Develop a daily activity schedule.
Depression Intervention

• support groups

• ascertain need for spiritual support and contact appropriate clergy

• relaxation therapies,

• music therapy.

• Enhance social support e.g. identify/mobilise a support person e.g. family, confidant, friends

• Maximise autonomy/personal control/self efficacy

• Identify and reinforce strengths and capabilities.
Anxiety can be a symptom of depression

People experience anxiety in different ways, but the following three elements are considered to be common symptoms:

1. A conscious feeling of fear and danger without the ability to identify immediate objective threats that could account for these feelings;

2. A pattern of physiological arousal and bodily distress that may include miscellaneous physical changes and complaints, such as heart palpitations, faintness, feeling of suffocation, breathlessness, diarrhoea, nausea or vomiting;

3. A disruption or disorganisation of effective problem-solving and mental control, including difficulty in thinking clearly and coping effectively with environmental demands.
Neurotransmitters

Serotonin - happiness

Noradrenalin – excitement and ‘get up and go’

Dopamine – reward, pleasure
Medications

Selective serotonin reuptake inhibitors (SSRIs). fluoxetine, paroxetine, citalopram, sertraline, fluoxetine

Serotonin and norepinephrine reuptake inhibitors (SNRIs). Venlafaxine

Tricyclic antidepressants. Imipramine, nortriptyline, amitriptyline, doxepin

• Norepinephrine and dopamine reuptake inhibitors (NDRIs). Bupropion

• Atypical antidepressants. Trazodone, mirtazapine

• Monoamine oxidase inhibitors (MAOIs)
Depression and Dementia

Kaplan-Meier cumulative risk curves for dementia by baseline depressive symptoms (sxs) status based on the 11-item version of the Center for Epidemiologic Studies Depression Scale score.

Depression effects up to 50% of people with dementia
Treatment of Depression for those with Dementia

- SSRI’s appear to decrease symptoms initially, but after 13-39 weeks there is no difference with controls

- SSRI’s are associated with increased falls even at low doses (increases 3-fold with higher doses)

- Citalopram has been specifically associated with QTc interval prolongation

Swartz, Curr Opin Psychiatry 2012, 25:542–550
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

Differentiation From Normal Aging

• Normal aging, particularly in “old old”, is itself associated with: (Salmon & Bondi, 2009)
  – mild brain atrophy and white matter changes
  – change in cognitive function: processing speed, executive function, learning efficiency, effortful retrieval, word-finding difficulties are common in normal aging, but cues successfully enable retrieval

• Norms for performance in cognitive testing often not established for “old old”.

• Limited education may also be another factor in older age groups
### IOM Report 2015

**Promoting Brain Health**

<table>
<thead>
<tr>
<th>Good Evidence For:</th>
<th>Some Evidence or Mixed:</th>
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<tr>
<td>Be physically active</td>
<td>• Being socially and intellectually active</td>
</tr>
<tr>
<td>Reduce and manage cardiovascular disease risk</td>
<td>• Getting adequate sleep</td>
</tr>
<tr>
<td>high blood pressure, diabetes, and smoking.</td>
<td>• Avoid delirium</td>
</tr>
<tr>
<td>• Management of conditions and medications that might</td>
<td>• medications, nutritional supplements, and cognitive training are mixed</td>
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<td>have a negative effect on cognitive function</td>
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**Promoting Brain Health**

- Promoting Brain Health
- Good Evidence For:
  - Be physically active
  - Reduce and manage cardiovascular disease risk
    - high blood pressure, diabetes, and smoking.
  - Management of conditions and medications that might have a negative effect on cognitive function
- Some Evidence or Mixed:
  - Being socially and intellectually active
  - Getting adequate sleep
  - Avoid delirium
  - medications, nutritional supplements, and cognitive training are mixed

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
- Thyroiditis
- B12/Folate
- Hepatic
History - Onset and Duration

**Gradual & chronic**
- Alzheimer’s Disease (AD)

**Rapidly progressive**
- Vascular Disease
- Hashimoto’s hypothyroid
  - Myxedematous 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 Apnoea 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
  – Anticholinergics
  – 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?
“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
Cognitive Impairment
Degenerative Sub-types

Cortical

Frontal Temporal Lobe

Alzheimer’s Disease
- Early Onset
- Late Onset

Lewy Body Dementia

Sub-Cortical – basal ganglia, Motor

Cortico-basilar

Semantic aphasia

Progressive Nonfluent Aphasia

Progressive Supranuclear Palsy

Parkinson’s Dementia

Huntington’s

CJD
Alzheimer’s Disease

- First Diagnosed in 1906
- Alois Alzheimer’s
- Considered relatively rare when first described
Alzheimer’s Disease Diagnosis

NIA-Alzheimer’s Assoc. workgroups on diagnostic guidelines for AD

• A minimum of two of the following:
  – Impaired ability to acquire and remember new information
    • repetitive questions or conversations, misplacing personal belongings, forgetting events or appointments, getting lost on a familiar route.
  – Impaired reasoning and handling of complex tasks, poor judgment
    • poor understanding of safety risks, inability to manage finances, poor decision-making ability, inability to plan complex or sequential activities.

AND...
Alzheimer’s Disease Diagnosis

NIA-Alzheimer’s Assoc. workgroups on diagnostic guidelines for AD

• A minimum of two of the following (continued):
  – Impaired visuospatial abilities
    • inability to recognize faces or common objects or to find objects in direct view, inability to operate simple implements, or orient clothing to the body.
  – Impaired language functions (speaking, reading, writing)
    • difficulty thinking of common words while speaking, hesitations; speech, spelling, and writing errors.
    • Changes in personality, behavior, or uncharacteristic mood fluctuations
    • agitation, impaired motivation, initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive or obsessive, socially unacceptable behaviours.
Imaging for Alzheimer’s Disease

- Extreme hippocampal and medial temporal lobe atrophy
- Severe global atrophy
Animals named in 1 min (mms>19) - CERAD data set

- Normal Controls, CS = 1, n = 386
- Alzheimer patients, CS = 0, n = 380
PET Scan beta amyloid deposits

Rowe, et al., J Nucl Med November 1, 2011 vol. 52 no. 11 1733-1740
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

No Dementia

Alzheimer’s Disease

Vascular Dementia

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>
AD Risk Factors

- Familial Relationship in 5% of cases – APOE gene
- Age
- Women have higher rate of dementia (live longer?)
- Low education (decreased reserve?)

Ott A et al. BMJ 1995;310:970-973
Vascular Dementia Treatment

- Cardiovascular Health
  - Hypertension Tx
  - Lipid Therapy
  - Anticoagulation

Cholinesterase Inhibitors

Roman, JAGS 51:S296–S304, 2003
Dementia with Lewy bodies (LB)

- DLB typically under-diagnosed in clinical samples (~5%), yet pathology studies suggest more common (~15%)
- Up to 40% of people with AD also have Lewy Bodies
- **Symptoms**
  - can range from traditional Parkinsonian effects
    - loss of spontaneous movement (bradykinesia)
    - rigidity (muscles feel stiff and resist movement)
    - tremor and shuffling gait
  - to effects similar to those of AD
  - *acute confusion & Hallucinations*
<table>
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<th>Lewy Body and Parkinson's Disease Dementia</th>
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<tbody>
<tr>
<td><strong>LBD</strong></td>
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<tr>
<td>• Cognitive Impairment</td>
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<tr>
<td>• Parkinson’s Dx occurs around the same time or after dementia dx</td>
</tr>
<tr>
<td>• Fluctuating Cognition</td>
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<tr>
<td>• Visual Hallucinations</td>
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<tr>
<td>• Varying alertness and attention</td>
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<tr>
<td>• Delusions</td>
</tr>
<tr>
<td>• Unexplained syncope</td>
</tr>
<tr>
<td>• Rapid eye movement sleep disorder</td>
</tr>
<tr>
<td>• Neuroleptic sensitivity</td>
</tr>
<tr>
<td>• Depression</td>
</tr>
<tr>
<td><strong>PDD</strong></td>
</tr>
<tr>
<td>• Cognitive Impairment</td>
</tr>
<tr>
<td>• Parkinson’s Dx for at least 1 year</td>
</tr>
</tbody>
</table>
Physical Exam

- Often have orthostatic hypotension
- Some Parkinsonian signs but usually not enough to meet the criteria for a diagnosis of Parkinson disease
- Mild gait impairment is relatively frequent
- Resting tremor occurs less frequently than in Parkinson disease
- Memory retrieval worse than memory storage
Lewy Body Dementia Treatment

• cholinesterase inhibitor first choice
  – rivastigmine may decrease psychiatric symptoms particularly apathy, anxiety, hallucinations, and delusions
  – Donepizil 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 behavior disorder
Fronto-temporal Lobe Dementia

- Behavioural Changes
- May not have memory issues
- Executive Function Disorders
Frontotemporal Lobe Dementia

• First 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
Fronto-temporal Lobe Dementia

- Specific atrophy
- Apraxia – late
- Marked personality change – early in the disease
- Memory impairment – late in the disease
- Little response to ACHase Inhibitors
- Pick inclusion bodies on pathology

Alzheimer’s Disease

- Diffuse atrophy
- Apraxia – early
- Subtle personality changes
- Memory Impairment – early in the disease
- Good response to ACHase inhibitors
- Neurofibrillary plaques and tangles
Frontal Lobe Battery

1. Similarities (conceptualization)
   • “In what way are they alike?” A banana and an orange

2. Lexical fluency (mental flexibility)
   • “Say as many words as you can beginning with the letter S, except proper nouns.”

3. Motor series “Luria” test (programming)
   • “fist–edge–palm.”

4. Conflicting instructions (sensitivity to interference)
   • “Tap twice when I tap once.” then “Tap once when I tap twice.”

5. Go–No Go (inhibitory control)
   • “Tap once when I tap once.” then “Do not tap when I tap twice.”

6. Prehension behaviour (environmental autonomy)
   • “Do not take my hands.”
FTD Variations

• progressive non-fluent aphasia (PNFA)
  – Hesitant, effortful speech
  – Speech 'apraxia'
  – Stutter
  – Anomia – unable to name common items
  – Sound errors in speech e.g. 'gat' for 'cat'
  – Using the wrong tense or word order

• Semantic aphasia

• Progressive Suprauclear Palsy (PSP)
  • Progressive lack of coordination,
  • Stiffness of the neck and trunk,
  • Difficulties with eye movement,
  • Slow movements
  • Cognitive dysfunction, and difficulty walking that can result in falls.

• Cortico-Basilar Dementia
Cortico-Basilar Dementia

- Degeneration of the fronto-parietal cortex and deeper brain regions, i.e. basal ganglia.

- Begins unilaterally, but eventually bilateral
- Symptoms parkinsonism such as poor coordination
- Akinesia, rigidity, disequilibrium and limb dystonia (alien limb)

- Cognitive and visual-spatial impairments, apraxia, hesitant and halting speech, myoclonus, and dysphagia

- CT or MRI asymmetric atrophy of the fronto-parietal lobe
Normal Pressure Hydrocephaly

- Gait apraxia
- Incontinence
- Memory impairment

**DX:**

50 ml CSF lumbar drain
Or 3-5 day continuous drain

Early dx increases potential recovery

http://www.thebarrow.org/Education_And_Resources/Barrow_Quarterly/205294
Thank You.