Dementia (aka) Neurocognitive Disorders

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Disclosures

• I have no relationships with industry to disclose
Neurocognitive Domains

Perceptual–motor function
- Visual perception
- Visuoconstructional reasoning
- Perceptual–motor coordination

Language
- Object naming
- Word finding
- Fluency
- Grammar and syntax
- Receptive language

Executive function
- Planning
- Decision-making
- Working memory
- Responding to feedback
- Inhibition
- Flexibility

Learning and memory
- Free recall
- Cued recall
- Recognition memory
- Semantic and autobiographical
  long-term memory
- Implicit learning

Complex attention
- Sustained attention
- Divided attention
- Selective attention
- Processing speed

Social cognition
- Recognition of emotions
- Theory of mind
- Insight

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At the end of this talk…

• You will know the early signs and features of Alzheimer’s Disease, as well as:
  – Frontotemporal Dementia (FTD)
  – Vascular Dementia (VaD) (formerly ‘multi-infarct dementia’)
  – Dementia with Lewy Bodies (DLB)

• You will have an elementary understanding of behavior changes beyond just memory impairment

• Brain-Behavior Correlates
How common is dementia, anyway?

• Between the ages of 60 and 65, what percentage of the population is ‘demented?’

• The prevalence of dementia doubles (approximately) every 5 years after age 65

• Roughly half of all people who survive to 90+ have dementia (…and half do not)
According to DSM-IV, Dementia was defined as Short Term Memory Impairment plus at least one:

- Aphasia (language deficits: word-finding…sentence construction)
- Agnosia (recognizing people or objects)
- Apraxia (motor coordination problems: fine motor to gross motor)
- Executive Dysfunction (impaired complex problem solving)
DSM-V: Major Neurocognitive Disorder

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual–motor, or social cognition) based on:

1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and

2. A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

B. The cognitive deficits interfere with independence in everyday activities (that is, at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).

C. The cognitive deficits do not occur exclusively in the context of a delirium.

D. The cognitive deficits are not better explained by another mental disorder.
In Alzheimer’s Disease, Memory is the initial presenting problem.

We will spend a few minutes talking about Alzheimer’s.

Later, we will come back and contrast other forms of dementia with Alzheimer’s.
So with Alzheimer’s Disease...

“Posterior Cortical Dementia”
Typical Progression of Symptoms...

- ST Memory Impairment
- Forgetfulness, frustration, repeat self
- ‘Insidious’ onset…early on hard to distinguish from normal
- Progresses to difficulty with complex tasks that rely on ST memory (tinkering, bill-paying, cooking) Executive Function
- Word-finding deficits become more prominent Aphasia
- Recognizing once-familiar objects, situations Agnosia
- Fine motor, then gross motor problems Apraxia
- Slowly progressive: 7-10 years life expectancy after dx
  - exception: familial AD cases are rare, but often result in early onset [before age 60] and more rapid progression
Now Let’s compare AD to non-AD dementias

• Frontotemporal Dementia:
  – An umbrella term that captures more than 20 different neurodegenerative diseases.
FTLD: Personality change comes in two major types

**Disinhibition Syndrome:**
- Impulsive
- Quick to anger
- Irritable / giddy
- Can make cruel comments, unempathic
- Sometimes sexually inappropriate
- Can be violent

**Apathy Syndrome:**
- Impaired problem-solving
- Amotivation
- Lacking Curiosity
- Indifferent
- Emotional Blunting
- Lacking Spontaneity
- Neglect Hygiene
- Often Lose weight
- Can become incontinent

**Dorsolateral Prefrontal Cortex**

**Orbitofrontal Cortex**
FTD is an umbrella term, describing numerous diseases, including...

What these dementias share is frontal cortical involvement, an earlier age of onset (50’s and 60’s), personality change, and in some cases significant language deficits.

- Frontotemporal Dementia, behavioral variant (FTDbv)
- Corticobasal Syndrome
- FTD with Motor Neuron Disease (FTD/MND)
- Pick’s Disease
- Primary Progressive Aphasia (PPA)
  - 3 variants
- http://www.theaftd.org/
FTD: Challenge in Diagnosis

- Memory may be intact, even as they fail to function
- Early age of onset (50’s and 60’s)
- MMSE often normal or near normal
- Structural MRI and EEG frequently normal
- Apathy Syndrome is often mistaken for severe depression (but they lack depressed mood)
  - Poor response to antidepressants (they need structure!)
- Disinhibition Syndrome is often mistaken for bipolar disorder, psychosis, or antisocial personality
  - Yet most appropriate medication may be an antidepressant (to help with frustration tolerance)
- If undiagnosed, impossible for family to prepare appropriately
FTD: Making the diagnosis

- Screen with instrument that has executive testing (Montreal Cognitive Assessment…not MMSE)
- Other Frontal-specific screens (EXIT-25, Royal; FBI, Kersetz,)
- Neuropsychological testing…if you can get it
- Consider *functional* neuroimaging, like SPECT (fuel metabolism, not shape)
- Consult with a geriatric psychiatrist
- They need supervision and structure, need prompting
- Education for the family and caregivers very important
- http://www.theaftd.org/
What is Functional Neuroimaging?

Brain SPECT

NORMAL AGING

ALZHEIMER’S

PICK’S
Why is diagnosis so important in FTD?

- We cannot change the disease course
- But the family *desperately* needs to understand what is happening
- Prognosis in FTD is grave, it *progresses more rapidly than other dementias*
- The personality change can be devastating
- Families are often are puzzled and hurt by the patient’s behavior
- Families typically personalize everything, which is exactly what we need to train them *not* to do
- With the proper diagnosis, families can take appropriate steps
- Steps are taken to get the loved one into a more highly structured environment (either through enhanced home services or through placement)
Switching to Vascular Dementia

Perhaps the 2nd most common cause of dementia

Vascular Dementia used to be called "Multi-Infarct Dementia"

'Multi-infarct' described a 'step-wise' loss in function

Step-wise loss from discrete vascular events

Gradual decline from progressive accumulation of small vessel ischemic disease
Vascular Dementia

- The same factors that contribute to cardiovascular disease and peripheral vascular disease can cause ‘cerebrovascular disease’
- Deficits can vary, depending on the location of the vascular disease (subcortical, cortical)
- In addition to the dementia features of AD…
- may present with clumsiness, slurred speech, gait changes, exaggerated reflexes, pseudo bulbar palsy (“emotional incontinence”), focal weakness
- MRI will show prominent ‘white matter ischemic changes’ in the brain
The Frontal Lobes may be most vulnerable to vascular injury, So it is not uncommon for vascular dementia to present with personality change, such as disinhibition or apathy

Interventions are the same as FTD, prevention is the same as prevention of heart disease, stroke
Dementia with Lewy Bodies (DLB)

- Also called “Diffuse Lewy Body Disease”
- Lewy Bodies are protein accumulations within cell cytoplasm (“alpha-synuclein inclusion bodies”)
- Lewy Body pathology is at the root of Parkinson’s disease (PD)
- In Parkinson’s Disease, Lewy Bodies are limited to the subcortex
- In DLB, the Lewy Bodies arise throughout the brain
- So the deficits do not respond as well to PD treatments (dopamine replacement)
- Clinicians “Rule of One Year:” if Parkinsonism and dementia onset within the same year, most likely this is DLB
International Consensus Consortium for Dx of DLB

- Progressive cognitive decline (like AD)
- Two of the following:
  - Fluctuations in alertness (“delirium-like”)
  - Spontaneous features of Parkinsonism
  - Well-formed visual hallucinations
- Some supporting features:
  - Falls, fainting spells, extreme sensitivity to antipsychotics (esp. potent D2 blocking agents like Haldol)
# Pharmacotherapy for Dementia

## Cholinesterase Inhibitors

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Pearls</th>
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<tbody>
<tr>
<td>Donepezil</td>
<td>Aricept</td>
<td>Reversible selective acetylcholinesterase inhibitor. SEs: GI distress, insomnia, muscle cramps.</td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>Exelon</td>
<td>Same as above for donepezil.</td>
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<tr>
<td>Galantamine</td>
<td>Razadyne</td>
<td>Added postulated mechanism of modulation of nicotinic receptors.</td>
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## NMDA Receptor Antagonist

| Memantine    | Namenda    | Blocks Glutamate Receptors on neuronal cell surface. |
Screening: MOCA and Minicog

The Montreal Cognitive Assessment “MOCA”

The “MiniCog”

Register 3 words

Recall 3 words
And, as always, clinical complexity exists
Summary

• This has been a general overview of 4 major dementia syndromes
• Dementias are not all the same- some do not present with memory impairment as the initial sign/symptom
• The diagnosis of dementia is clinical
• In some cases, proper treatment can inform pharmacotherapy
• More importantly, appropriate diagnosis can expedite behavioral and environmental interventions, inform prognosis, enhance family understanding, and reduce patient and family suffering