Easy Diagnosis of Dementia in the Office

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Dementia Definitions

- Mild Cognitive Impairment (MCI)
- MCI-Vascular
- Cognitive impairment ND
- Alzheimer’s
- Vascular dementia
- Other dementias
Mild Cognitive Impairment
Evolution of terms

Earlier MCI Criteria

- Memory complaint (collateral is best)
- Memory impairment for age
- Preserved general cognitive function
- Intact activities for daily living
- Not demented
Mild Cognitive Impairment

Not all MCI converts to AD and other cognitive impairments seen that progress to other dementias

Dementia DSM-IV

Gradual and continued decline
**Dementia DSM-IV**

A1: Memory impairment or one or more of...

A2: Aphasia, apraxia, agnosia, dysexecutive

B: These deficits cause social or occupational dysfunction and not due to other neurological, medical or delirium condition

C: Gradual and continued cognitive decline

D: Other systemic neurological and psychiatric disease excluded

E: AD should not be diagnosed during delirium

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**Cognitive Testing**

*Overview and scope of the challenge*

- Mental Status
- Cranial Nerves
- Motor System
- Reflexes
- Sensation
- Coordination
- Gait

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7/9/2009
A paradigm shift. New concepts - “90% of the brain involved in cognition”

**Neurocognitive Domains**

**Hierarchical Requirement**
- Attention
- Aphasias
- Frontal Network Systems
- Amnesias
- Anosognosia and neglect syndromes

**Testing order unimportant**
- Agnosia
- Apraxia
- Aprosodia
- Visuospatial function
- Acalculia
- Alexia and agraphia
- R/L orientation and body part naming
- Miscellaneous group
**Cognitive Compass**

1. General attentional systems
2. Left hemisphere network
3. Right parietofrontal network
4. Hippocampal limbic network
5. Prefrontal and subcortical network
6. Occipitotemporal network
Cognition Overview

- Cerebral Networks
- Many present with dysmemory
- Increasing array of neurodegenerative syndromes
- Increasing array of sub-syndromes
- Complexity of mixed dementias
- Most have multiple components

Dementia: functional, neurotransmitter maps

*Frontal serotonergic, posteriorly cholinergic deficiency*
Clinical Dementia Subtypes

Frontotemporal lobe disorders
- Behavioral variant (3 subtypes)
- Progressive Non fluent aphasia (2 subtypes)
- Extrapyramidal (2 subtypes)

Alzheimer’s disease
- Frontal variant
- Posterior variant (Balint’s Syndrome)
- Primary progressive aphasia

Cognitive Vascular Disorders (multiple subtypes)

Progressive Lewy Body disease

Dementia Subtypes

- Argyrophilic dementias
- Prionopathies and other transmissible diseases
- Demyelinating diseases
- Huntington’s and PSP
- Toxic dementias (solvents, heavy metals)
- Cancer and paraneoplastic disorders
- Hydrocephalus
- Urbach Wiethe Disease (lipoid proteinosis)
**Vascular Cognitive Disorder**

Cognitive Impairment – no stroke
- Brain at risk stage (risk factors only)
- TIA and CITS

Cognitive impairment - subcortical infarct
- Strategic infarct - caudate, thalamus, BG
- Leukoaraiosis
- Watershed infarction

Cognitive impairment - cortical infarct
- L angular gyrus, R temporal lobe, Frontal

Cognitive impairment - subtentorial stroke
- Brainstem and Cerebellum

Multiple infarcts
- Vascular dementia
Mixed VCI-AD

- Consider pattern and severity of cognitive impairments
- Consider the size and location of infarcts including symptomatic infarcts, silent infarcts and leukoaraiosis
- Consider severity of hippocampal atrophy and pattern of atrophy (frontal versus parietal)
- To what extent can infarcts explain cognitive impairment
- If VBI cannot adequately explain the cognitive impairment, consider that AD is also present.

- Note: Not possible by NINDS-AIREN criteria but ADDTC has a category for this subgroup.
Mixed VCI-AD

- Decline in memory is strongly associated with AD
- Decline in executive function strongly associated with CVD


Cerebrovascular risk factor
Leukoaraiosis

- Small vessel stroke risk: OR 2.9
- Hemorrhage risk (tpa, oral anticoagulation)
- Increased vascular mortality
- Cognitive decline (executive)
- Dementia risk
- Mood / depression risk
- Gait and balance disorder
- Urinary incontinence

Neumann-Haefelin et al. Stroke 2006;37:2463-2466
Classification Systems

• The current definition of dementia, is memory centered
•Does not reflect the predominant executive dysfunction of the VaD (vascular disorder) subtypes
•Does not include minor cognitive deficits due to VaD
• VCI-ND been recommended, i.e., cognitive deficits that do not meet criteria for dementia but impair tasks such as household chores, eating, managing money.
• A substantial number of such VCI-ND may nevertheless go onto become demented [1]


Vascular Dementia Diagnosis

• Evidence of dementia or cognitive impairment
• Evidence of vascular brain injury (VBI)
• Presumptive evidence of a causal relationship between cognitive impairment and VBI

Criteria (Second generation)
• Hachinski
• NINDS-AIREN
• ADDTC
• DSM-IV
• ICD-10
Relative Risk (RR) and Population Attributable Risk

• Population attributable risk for dementia for untreated HTN ~40% even though RR is small.
• Expected AD cases of 106 million in 2050
• Of these 106 million, 23 million could be AVOIDED completely if we can delay the start of the disease by 2 years. (Starting in 2010).

AD-VaD

• The discovery of vascular risk factors for AD does not negate neurodegenerative processes.
• Clinical dementia is a mixture of degenerative and vascular processes which may be impossible to untangle

**Vascular Risk Factors and Dementia**

- HTN
- DM
- Elevated cholesterol
- Smoking tobacco
- Atrial fibrillation
- Angina
- Leukoaraiosis
- APOE 4
- Homocysteine

**MMSE: Executive function absent**

**Orientation** (10 items)

**Attention** and Calculation (serial 7’s)

**Memory**
- Registration
- Recall

**Language**
- Naming, repetition, reading, writing

**Praxis (ideational): Three stage command**

**Visuospatial:** Copy intersecting pentagons
Montreal Cognitive Assessment: MOCA

Neuropsychological Tests
CTMT: Trail 5

- Scoring in seconds
- Individual Trails
- Sum of the 5 Trails
- T scores
- Percentiles
- z scores
- Stanines
- Quotients

Frontal Systems Behavioral Scale

- Executive dysfunction
- Apathy
- Disinhibition
- Before/After options
- Lickert Scale
- 46 questions
- T scores ≥ 65 impaired
- T scores 60-64 marginal
### BRIEF: BRI, MI and GEC

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**FRSBE**
Frontal Network Syndromes

subsystems, 1st and 2nd order

- Executive
- Impersistance
- Environmental autonomy
- Perseveration

Frontal Network Syndromes
General Medical Dementia Causes

- Hepatic encephalopathy
- Uremic encephalopathy
- Sleep apnea, snoring
- Medications
- Anticholinergics >600 drugs we currently use

Minimal Hepatic Encephalopathy

1. Ammonia elevation
2. Manganase deposition in BN
3. Increased astrocytic peripheral type benzodiazepine receptors (PTBR)
4. Allopregnanolone production: affinity GABA-A
5. Increased GABA ergic tone
6. Octopamine (false neurotransmitters)
7. Endozepine 4 (endogenous benzo) accumulate
8. Serotonergic abnormalities (dyssomnia)
9. Endogenous Opioids increased
10. Mercaptan accumulation
**Hemodynamic TIA’s**

- Maximal medical treatment failure
- MRA: R ICA occlusion
- MRP: R hemisphere hypoperfusion
- Intracranial reperfusion by EC/IC bypass (COSS trial)

**A New Understanding**

- Memory
- Executive
- Degenerative e.g. AD
- Vascular Cognitive Disorder
Aphasias, Dysarthria

- Fluency
- Comprehension
- Repetition
- Naming
  - Example: Transcortical motor aphasia misdiagnosed as MS

Memory Testing

Memory domains
- Immediate memory
- Delayed memory
- Working memory

Two modalities
- Auditory
- Visual

Task formats
- Recall
- Recognition
Memory testing at bedside

1. Working memory (Immediate memory).
   • Reverse digits
2. Verbal and non verbal (short term memory)
   • Register 3 words and 3 shapes, test recall 5 min.
3. Remote memory
   • Recite last 3 presidents or 3 important personal dates (graduations)
Frontal Network Testing

- Luria’s motor sequence test
- Word List (FAS) generation
- Abulia. Poverty of action and speech.
- Similarities/differences and proverbs
- Environmental autonomy (imitation, utilization behavior)
- Interference control (Go-No-Go)
- Disinhibition
- Impersistence
- Perseveration

Apraxias

- Melokinetic. Thumb - finger opposition test
  Compare R + L (only if ≥ 4/5 power)
- Buccolingual. Lick your lips, blow up your cheeks
- Ideomotor apraxia (clumsy action with pen or eating utensils).
- Ideational. Fold piece of paper in half, write your name and place inside a file or book
**Agnosias**

- Object agnosia. Cannot name 3 objects by visual inspection, but can by touch or sound.
- Achromatopsia (different hues or colors).
- Simultanagnosia (and Balint’s Syndrome): CTPT, identify all 3 persons or analog time telling.
- Optic ataxia. Touch under visual guidance.
- Optic apraxia. Look R/L up, down to command.
- Prosopagnosia: Does not recognize family or friends by visual appearance.

**Neglect Syndromes**

- Tactile. Simultaneous stimulation of both arms.
- Auditory: Simultaneous stimulation of both ears.
- Visual: Simultaneous stimulation of both fields.
- Motor: Bisect 10 cm line.
Anosognosia

- Recognizes weakness
- Underestimation
- Complete denial of deficit or illness
- Asomatognosia
- Misoplegia

Aprosodias

*As per family, speech has become flat monotone*

- Receptive, expressive global as with aphasias
- Cannot comprehend intonations (happy/sad)
- Cannot repeat altered intonation (happy/sad)
- Chinese Mandarin “Ma” (horse, numbness, mother, curse)
Visuospatial

- Copy 2D image of examiner’s flower.
- Copy a 3D image representation of examiner’s cube.
- Intersecting pentagons

Disconnection Syndromes

- Alien hand syndrome. The one hand interferes with the other during routine tasks
- Alexia without agraphia. Can write but not read
- Pure word deafness. Hears environmental sounds but not spoken speech.
R/L orientation and finger ID

• Gerstmann’s Syndrome
• Angular Gyrus Syndrome
• Simple
• Complex

Alexia, agraphia, acalculia

• Alexia without agraphia. Can write but not read
• Alexia with agraphia
• Hemialexia
• Semantic alexia
Miscellaneous

- Amusia – may be receptive (poor appreciation of music or expressive unable to play/sing.
- Allesthesia. During neurological examination, transfers perceived tactile stimuli from L to R
- Autoscopy. During interview reports out of body experience
- Synesthesia. Activation of one sensory system induces perceived sensation in another
- Geographical disorientation or planotopagnosia

Denying blindness or weakness
Anton’s syndrome and Anosognosia
Neuroimaging of cognition
From coma to cognitive fitness

These are our paraclinical tools
- PET Brain (PIB)
- Diffusion tensor imaging
- Molecular imaging
- functional MRI (mirror neuron systems)
- MR spectroscopy (Min hepatic encephalopathy)

Multimodality MR imaging: DWI, MRA, MRV, MR Perfusion, MR Spectroscopy, f-MRI, DTI
**White matter lesions on MRI**

- Cerebrovascular (HTN, Atrial Fib, DM, Homocysteine)
- Alzheimer’s
- APOE 4 status
- Trauma
- Migraine
- AIDS dementia
- Psychiatric (Bipolar, Schizophrenia)
- CADASIL
- Wilson’s, Hallevorden Spatz
- Dystonia
- Neuroacanthocytosis
- Fragile X associated tremor and ataxia
- Susac’s syndrome
- Myotonic dystrophy type 1 and 2
- Hypoglycemic encephalopathy
- Leucodystrophies (Metachromatic, Krabbe)
- Multiple Sclerosis
- Autoimmune vasculitic (SLE, Sjogren’s)

**Hydrocephalus**
Watershed lesions
Frontal behavioral syndromes, simultanagnosia and “Man in the Barrel Syndrome”
USF Cognitive Neurology Registry
AD visuospatial variant

USF Cognitive Neurology Registry
Posterior Cortical Atrophy Syndrome
**DTI: L Corticospinal Tract Disruption**

**PET Brain with PIB**

- PET images of normal left, 3 MCI patients and AD patient right. PIB binds to A beta deposits with high affinity and detected by PET.
Serotonin receptor (5HT1A) imaging distinguishes amnestic MCI from mild AD

- Upregulation in hippocampal serotonin metabolism in a-MCI
- Contrasts to dramatic down regulation in later stages of AD
- A controls, B-MCI, C-AD
- Selective receptor density modification occurs earlier than neuronal loss in AD
- 5HT1A antagonist 18 F MPPF

Truchot L et al. Neurology 2007;69:1012-1017

Neuroimaging: AD and VaD

- More WM changes and less medial temporal lobe atrophy seen in VaD compared to AD
- Some overlap with white matter changes
- White matter changes (leukoaraiosis) – 2 types
- Separated from ventricles more specific for VaD
- Periventricular leukoaraiosis – non vascular? Occurs in healthy adults and dementias.
Clinical Assessment

1. Cognitive Syndromes
2. Neuropsychiatric Syndromes
3. Elementary Neurological Syndromes
4. Cerebrovascular and cardiovascular Syndromes
5. General Medical Syndromes
6. Then combine with neuroradiological and laboratory assessment
7. Attempt pathophysiology

Randomized Controlled Trials
Treatment for VaD

• Galantamine (1): ADL and NP symptoms improved
• Donepezil (2): MMSE and ADL improved
• Memantine (2): MMSE and CGI-C improved
• Rivastigmine: Ach deficit due concomitant AD?
• Perindopril: 34% decrease in dementia and 45% decrease in cognitive decline
• Simvastatin: Telephonic interview for cognitive status
**Exercise and Brain Health**

Exercise best moderate intensity
- Improves learning and memory
- Improves executive functioning
- Alleviates depression
- Delays age related cognitive decline
- Reduces risk of neurodegeneration