Cognitive Impairment

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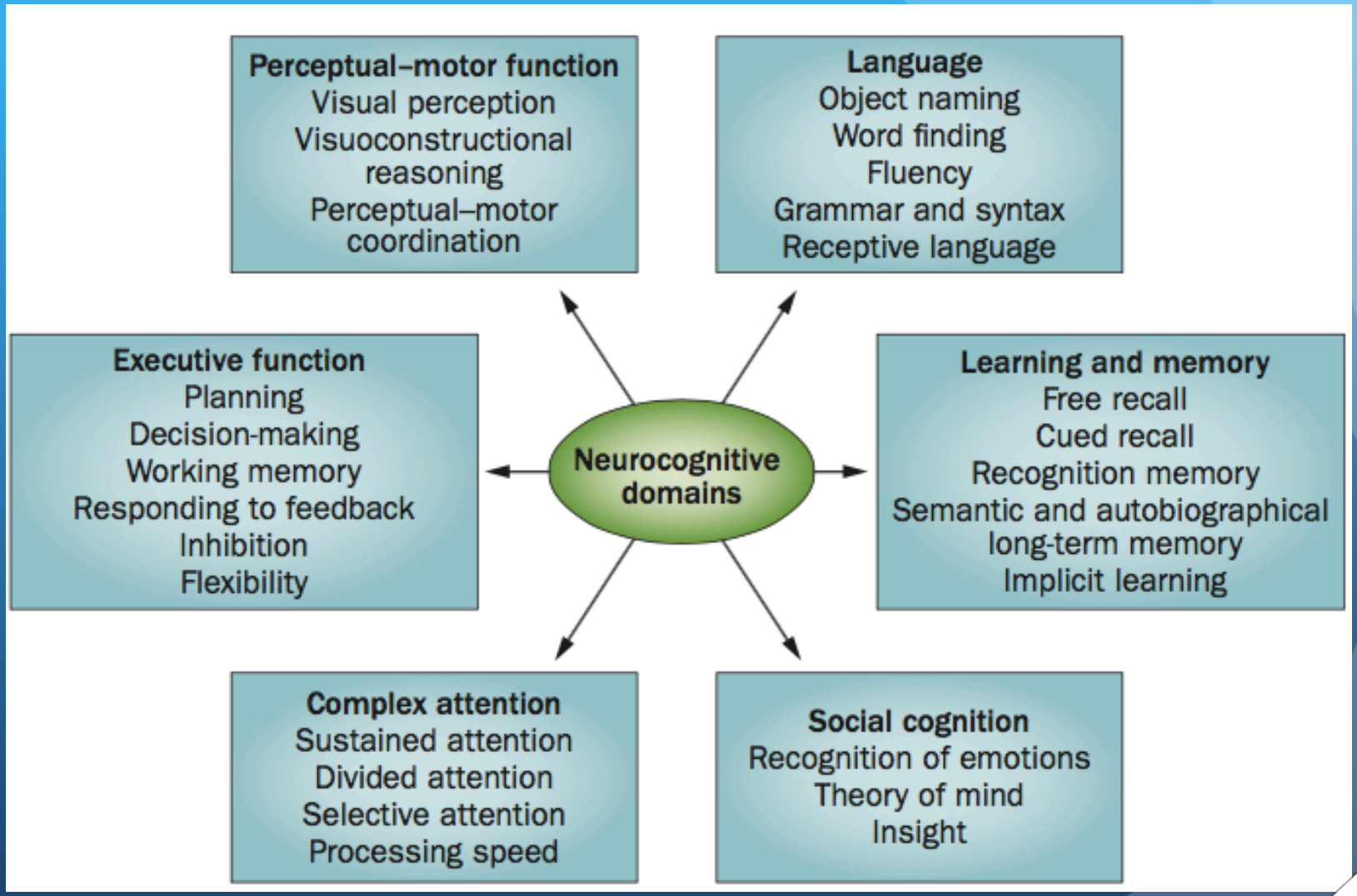
Neurology

- New DSM criteria focus on cognitive domains rather than memory alone

Neuro-Cognitive Domains



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Mild Cognitive Impairment

Box 2 | Diagnostic criteria for mild neurocognitive disorder

A. Evidence of modest 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 mild decline in cognitive function; and
   2. A modest impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

B. The cognitive deficits do not interfere with capacity for independence in everyday activities (that is, complex instrumental activities of daily living such as paying bills or managing medications are preserved, but greater effort, compensatory strategies, or accommodation may be required).

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 (for example, major depressive disorder or schizophrenia).

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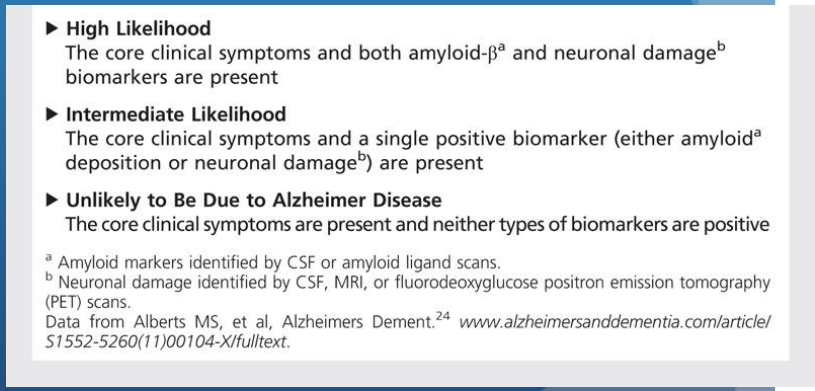
MCI

- Increased risk of developing dementia (AD)
  - 3 – 15%
- Prevalence 2 % - 20% (depending on the study)
- 20% of patients with diagnosis of MCI return to normal on follow up
- Biomarkers:
  - CSF tau levels and amyloid levels
  - Hippocampal volumes



▶ **High Likelihood**
The core clinical symptoms and both amyloid-β[a] and neuronal damage[b] biomarkers are present

▶ **Intermediate Likelihood**
The core clinical symptoms and a single positive biomarker (either amyloid[a] deposition or neuronal damage[b]) are present

▶ **Unlikely to Be Due to Alzheimer Disease**
The core clinical symptoms are present and neither types of biomarkers are positive

[a] Amyloid markers identified by CSF or amyloid ligand scans.
[b] Neuronal damage identified by CSF, MRI, or fluorodeoxyglucose positron emission tomography (PET) scans.
Data from Alberts MS, et al, Alzheimers Dement.[24] *www.alzheimersanddementia.com/article/S1552-5260(11)00104-X/fulltext.*

Continuum Neurology 2013: Mild Cognitive Impairment

Dementia or Major Neurocognitive Disorder

Box 3 | Diagnostic criteria for major neurocognitive disorder (or dementia)

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.

Specify:

- Without behavioural disturbance: if the cognitive disturbance is not accompanied by any clinically significant behavioural disturbance
- With behavioural disturbance (specify disturbance): if the cognitive disturbance is accompanied by a clinically significant behavioural disturbance (for example, psychotic symptoms, mood disturbance, agitation, apathy, or other behavioural symptoms). For example, major depressive disorder or schizophrenia

Nature Reviews Neurology (2014): 10: 634-642

Epidemiology

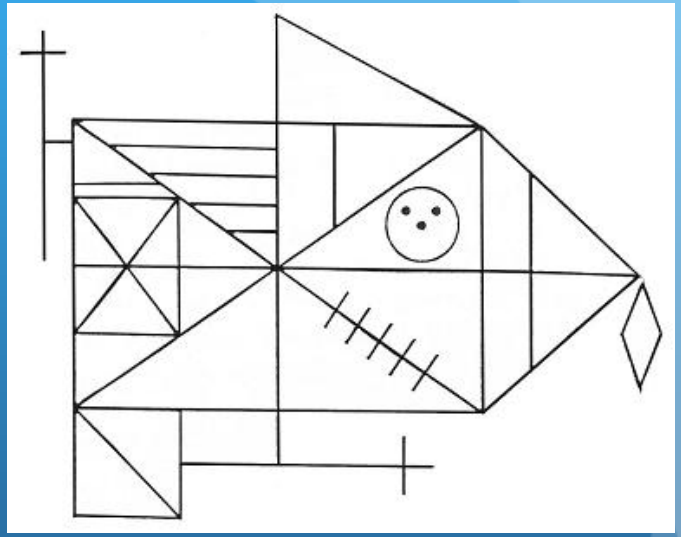
- Prevalence
  - 1-2% at age 65
  - 10-15% at age 85
  - Estimated prevalence to be doubled in the next 20 years
- Impact
  - Costs ($15 billion/year in 2008)
  - Increased demand for LTC beds
  - Informal care giving

History

- Collateral, collateral, collateral
  - Try interviewing them separately
- Details about onset and early symptoms
  - Gradual/insidious vs. abrupt
- Course
  - Gradual progression vs. stepwise
- Characterize cognition
  - Memory, judgment, reasoning, language, visuospatial abilities, behaviour/personality
- Functional abilities
  - Basic ADLs and IADLs
  - Driving and safety
  - Medications
- Social History
- Vision and Hearing

Physical

- Mental Status Exam
- Neurologic Exam
  - Frontal release signs, Balint Syndrome
- Cognitive Tests
  - MMSE
  - MOCA
  - Clock Drawing
  - Rey-Osterreith figure copying
  - Addenbrooke's
  - Boston naming test
  - Frontal Battery Assessment
  - Trail A/B
  - CERAD



Reproduced from: Euromicro Conference, 2000. Proceedings of the 26th

Work up

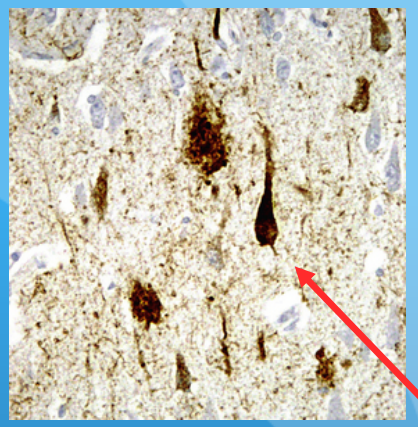
- Neuropsych testing if unusual presentation
- B12, Thyroid
- HIV, CNS inflammatory work up if suspicious
- Structural imaging – CT or MRI
- Biomarkers
  - No guidelines
  - FDG PET – AD vs FTD

Etiological Classification

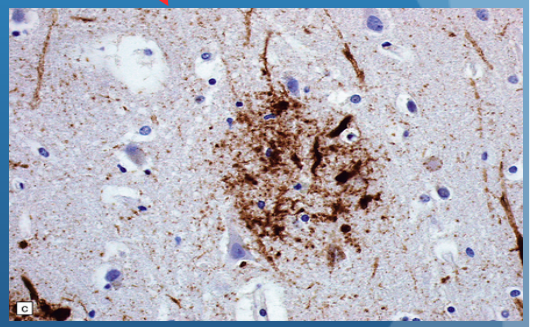
- Alzheimer
- Vascular
- Frontotemporal
- Lewy Body Dementia
- Other causes
  - Parkinsonism, HIV, Prion Disease, Huntingtons, Alcohol related, Neurosyphillis

Alzheimer Disease

- Most common cause of dementia (80%)
- Genetics
  - Sporadic forms
    - ApoE
  - Early onset forms (Autosomal Dominant)
    - Amyloid precursor protein
    - Presenilin 1 (PSEN1)
    - Presenilin 2 (PSEN2)
- Pathology (Tauopathy)
  - Neurofibrillary tangles – neuronal cytoplasmic inclusions
  - Neuritic (Amyloid – β) plaques – extracellular structures
  - Cell loss in nucleus basalis of meynert – cortical cholinergic projections



Neuritic plaques and tangles



Reproduced from:
Neuropathology, A reference text of CNS pathology

AD

- Biomarkers
  - CSF
    - Increased tau and decreased ß-amyloid (combined sens 80% and spec 90%)
  - Imaging
    - Generalized cortical atrophy, selective hippocampal and amygdalar atrophy, compensatory enlargement of ventricles
    - PET studies – Biparietal hypometabolism
- Treatment
  - Non-pharma
  - Pharmacological
    - Cholinesterase Inhibitors
    - NMDA antagonist

Posterior Cortical Atrophy

- 78% pathologically AD
- 5 – 10% of young onset AD
- Progressive loss of visual processing and posterior brain functions; atrophy of parietal, occipital and occipitotemporal cortices
- Symptoms: Reading, driving, navigating and identifying objects

Vascular Cognitive Impairment

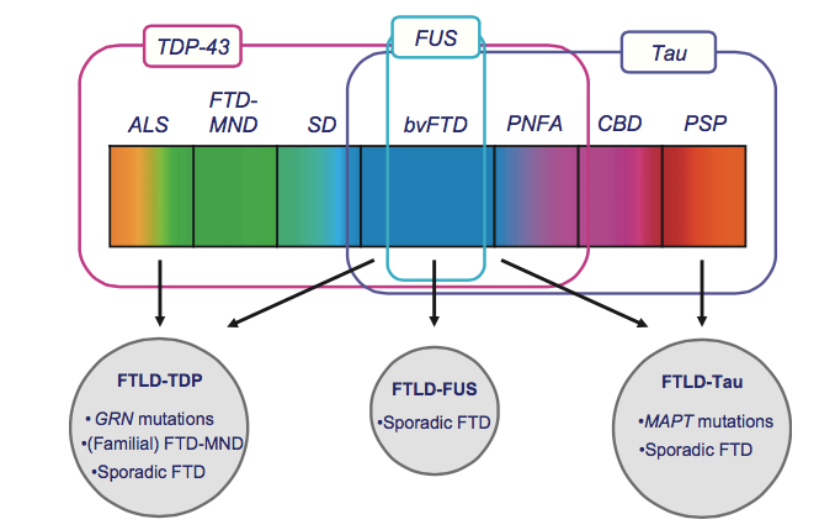
- Second most common after AD (10%); 1/3 of post stroke patients
- Pathology
  - Arteriolosclerosis
  - Atherosclerosis
  - Amyloid angiopathy
- Genetics
  - CADASIL
- Demographic Factors
  - Age
- Lifestyle Factors
  - Low Education
  - Diet
  - Lack of Physical Activity
  - Smoking
- Depression
- Physiologic Factors
  - Hypertension
  - Hyperglycemia
- Vascular risk factors
  - Coronary Artery Disease
  - Stroke
  - CKD
  - Atrial Fiberillation

Vascular Cog

- Clinical Features
  - Cognitive symptoms variable include attention, information processing and executive functioning
  - Non-cognitive features
  - VAS-cog
- Higher mortality
- Imaging
  - Sufficient CVA on imaging to account for cog impairment
  - Atrophy (both generalised and hippocampal)
- Management
  - Prevention: Smoking cessation, physical activity, hypertension treatment, diet etc.

Frontotemporal Lobar Degeneration

- Common cause if onset < 60 years
- Prevalence: 2.5 – 15.1 cases per 100,000 adults
- Most cases are sporadic
- 50% are familial
- 3 Main mutations
  - GRN (Progranulin)
  - MAPT
  - C9orf72



J Neurol Neurosurg Psychiatry 2011: 82: 476-486

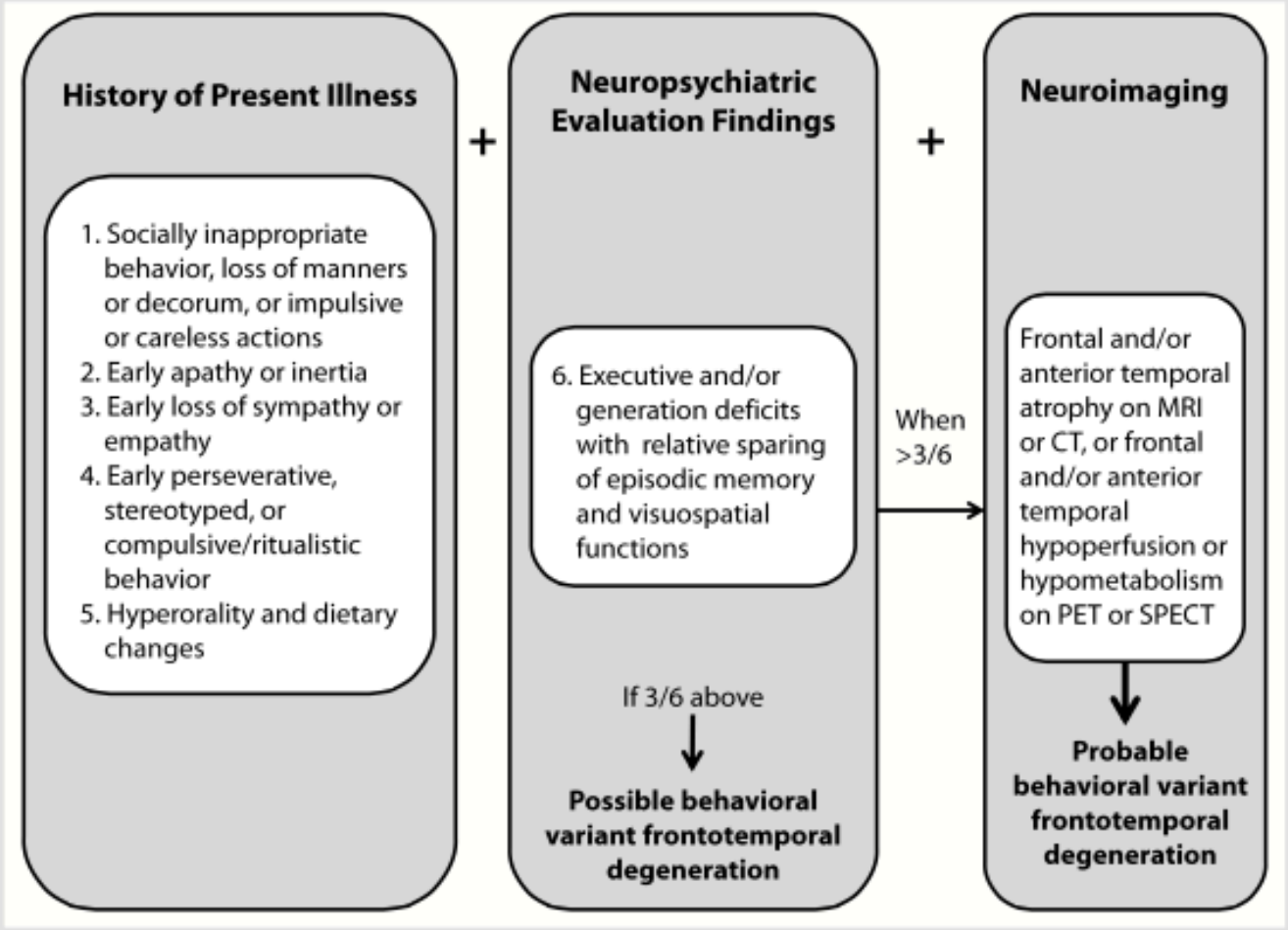


FIGURE 9-1 The diagnostic process for behavioral variant frontotemporal dementia (bvFTD) according to Rascovsky and colleagues.[1] Note the change from the 1998 Neary and colleagues[8] criteria away from the use of supportive criteria for the equivalent of probable cases in order to diagnose early-stage possible bvFTD and the dropping of blood pressure lability and early incontinence from the list of features. As in accompanying text, clinicians can also consider the bvFTD diagnosis in patients who have onset after age 65, but are encouraged to keep Alzheimer disease high on the differential.

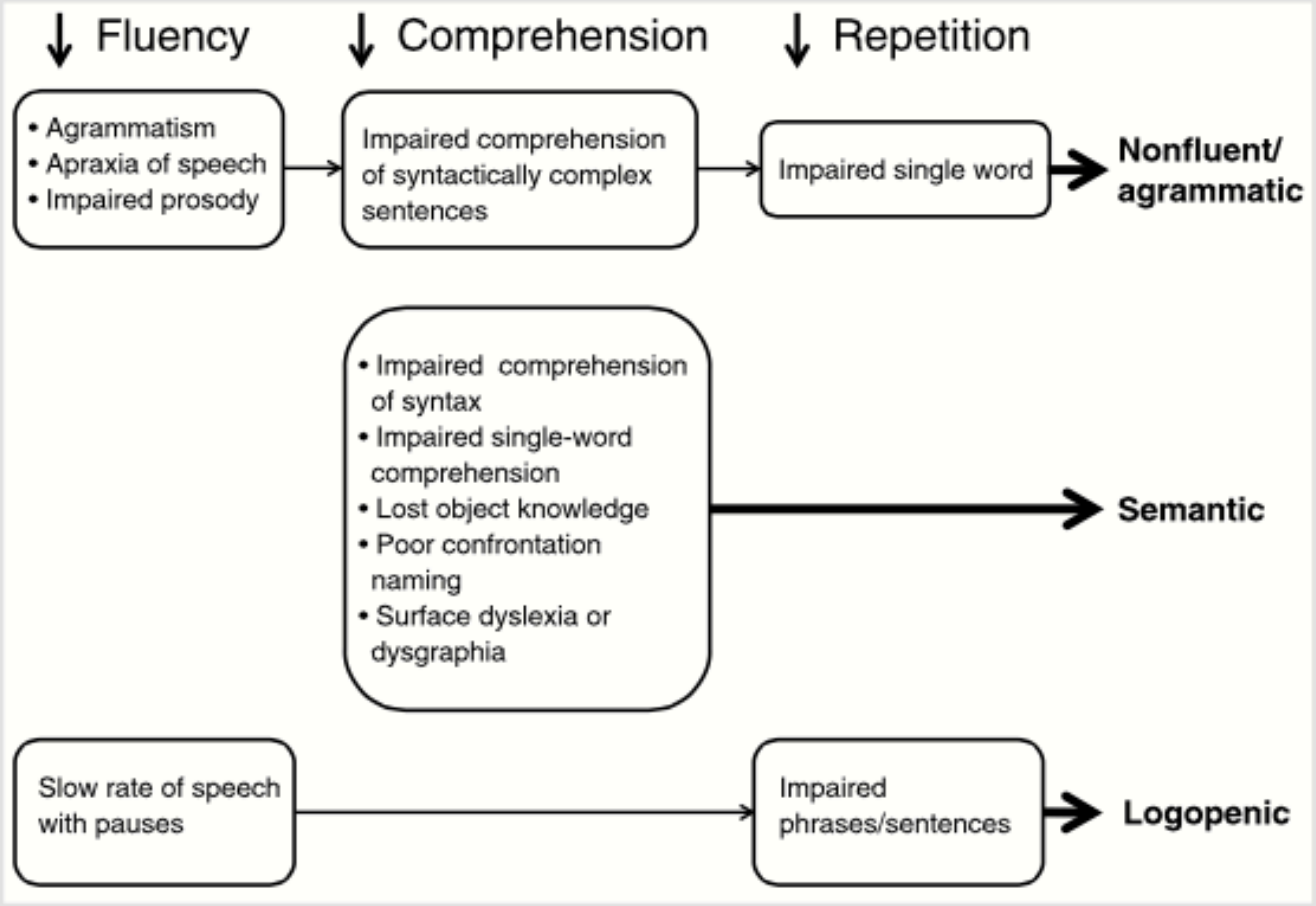
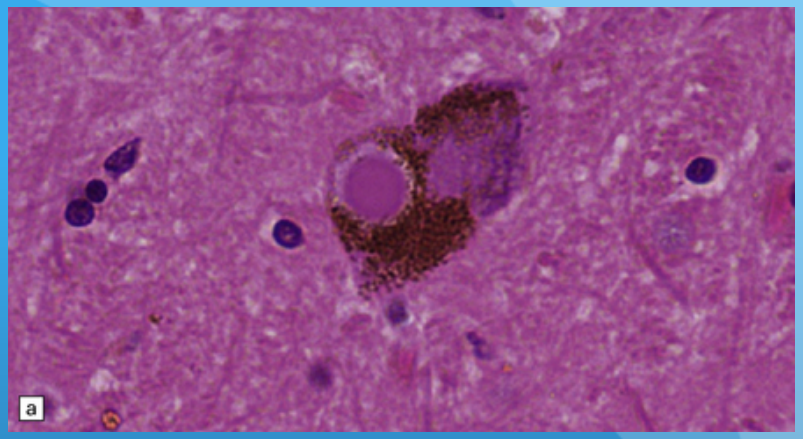


FIGURE 9-4 The diagnostic process for three variants of primary progressive aphasia as written by Gorno-Tempini and colleagues,[2] based upon characteristics of fluency, comprehension, and repetition. Alzheimer disease remains high on the differential for semantic dementia and logopenic progressive aphasia.

- Variants
  - Behavioral variant FTD (50%)
  - Primary progressive aphasia (PPA)
    - Semantic PPA
    - Logopenic PPA
    - Non-fluent/agrammatic PPA
- FTD-MND
  - Same clinicopathological spectrum
  - Rapid progressive course: mean survival 3 years
- Imaging
  - Frontal and temporal lobe atrophy on CT or MRI
  - Asymmetrical hypometabolism
- Management
  - SSRIs for carb craving
  - Clomipramine
  - SLP/OT/PT

Lewy Body



From Neuropathology: A reference text of CNS pathology

- Epidemiology
  - Prevalence 4.2 – 7.5%
  - Men > Women
- Pathology
  - α- Synuclein neuronal inclusions
- CSF synuclein lower in DLB
- Imaging
  - Loss of parieto-occipito white matter integrity
  - Reduced dopamine uptake in caudate and putamen
  - Hypometabolism of occipital lobes on FDG-PET

Table 1 Revised criteria for the clinical diagnosis of DLB (2005)

1. Central feature (essential for a diagnosis of possible or probable DLB)
Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function.
2. Core features (two core features are sufficient for a diagnosis of probable DLB, and one for possible DLB)
Fluctuating cognition with pronounced variations in attention and alertness
Recurrent visual hallucinations that are typically well formed and detailed
Spontaneous features of parkinsonism
3. Suggestive features
REM sleep behaviour disorder
Severe neuroleptic sensitivity
Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging.
4. Supportive features
Repeated falls and syncope
Transient, unexplained loss of consciousness
Severe autonomic dysfunction, e.g., orthostatic hypotension, urinary incontinence
Hallucinations in other modalities
Systematised delusions
Depression
Relative preservation of medial temporal lobe structures on CT/MRI scan
Generalised low uptake on SPECT/PET perfusion scan with reduced occipital activity
Abnormal (low uptake) MIBG myocardial scintigraphy
Prominent slow wave activity on EEG with temporal lobe transient sharp waves
5. A diagnosis of DLB is less likely
In the presence of cerebrovascular disease evident as focal neurologic signs or on brain imaging
In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
If parkinsonism only appears for the first time at a stage of severe dementia
6. Temporal sequence of symptoms
DLB should be diagnosed when dementia occurs concurrently or within one year of parkinsonism (if it is present).

Continuum Neurology (2016): Dementia with lewy bodies

Case

- 77 F, husband gave history over telephone hiding from the basement
- Baseline personality of “life of party”
- Diagnoses of depression and anxiety – treated with citalopram
- Memory loss and behavioral changes X 3 years
- Physically violent behavior, sang continuously, lost her way in familiar places, needs to be prompted to dress appropriately and brush teeth
- O/E: Euphoria, MMSE 28/30, postural tremor.
- Imaging: Severe atrophy of temporal lobes

Case 2

- 65 M accountant, 2 year hx of memory complaints
- Not noticed by colleagues or wife.
- PMHx: Htn
- Normal neuro exam, MMSE 29/30, normal clock drawing
- Normal MRI
- Dx?
- Comprehensive neuropsych testing showed memory 1.5 SD below normal
- Progression: 2 years later, trouble with IADLs and retired from job, MMSE 25/30
- Dx?

Questions?

Thanks!