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TEACHING HOSPITAL

Approach to Neurocognitive Disorders with Acute/Subacute and Insidious Onset

Neuropsychiatry: A Comprehensive Update 2025

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Founding Member, Mass General Brigham

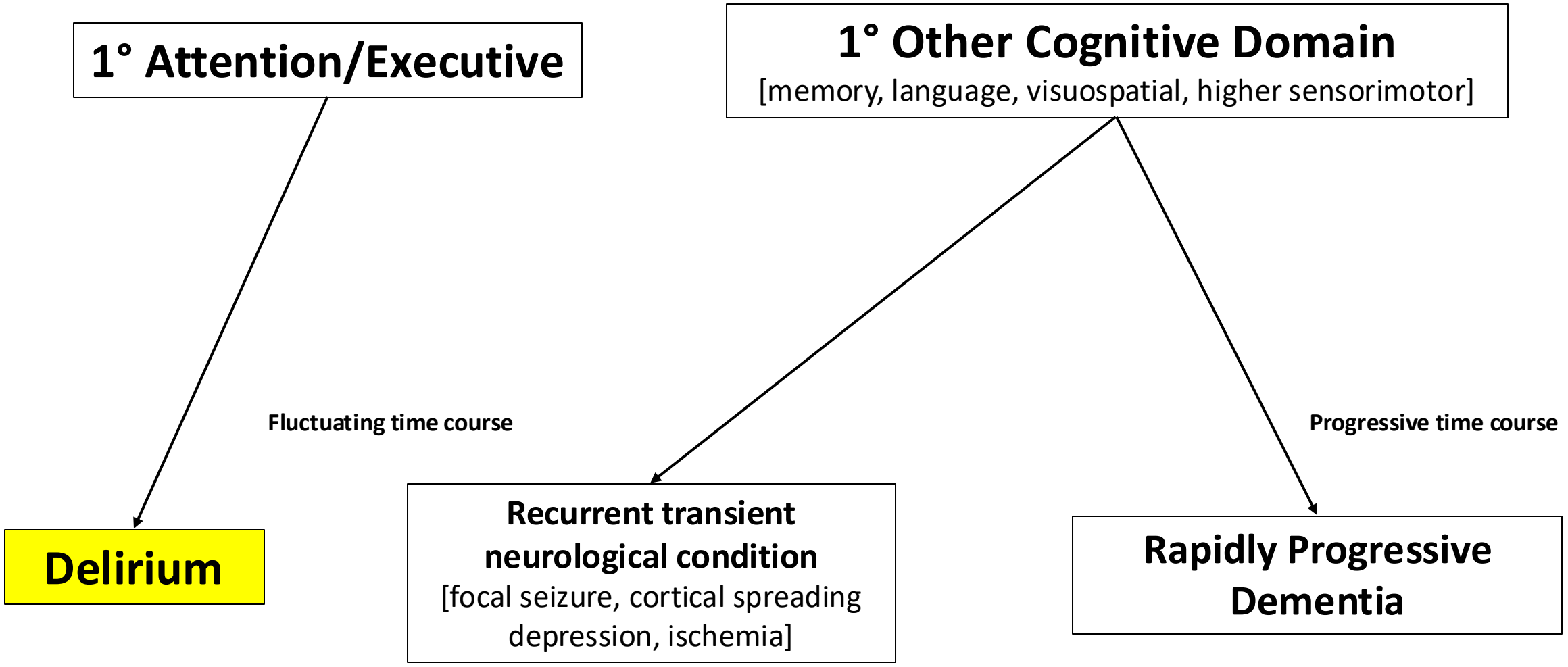
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Neither I nor my spouse has a relevant financial relationship with a commercial interest to disclose.

Goals

- To recognize the value of localization and time course in the diagnostic process of neurocognitive disorders.
- To understand distinguishing features of common conditions in the differential diagnoses of: (1) acute/subacute onset cognitive dysfunction; and (2) insidious onset cognitive dysfunction.
- To identify atypical features that should prompt a more extended work-up and/or consultation with a specialist.
- To review the value of differentiating between syndrome, severity and neuropathology in neurodegenerative conditions causing cognitive dysfunction.

Acute/Subacute Onset Cognitive Dysfunction



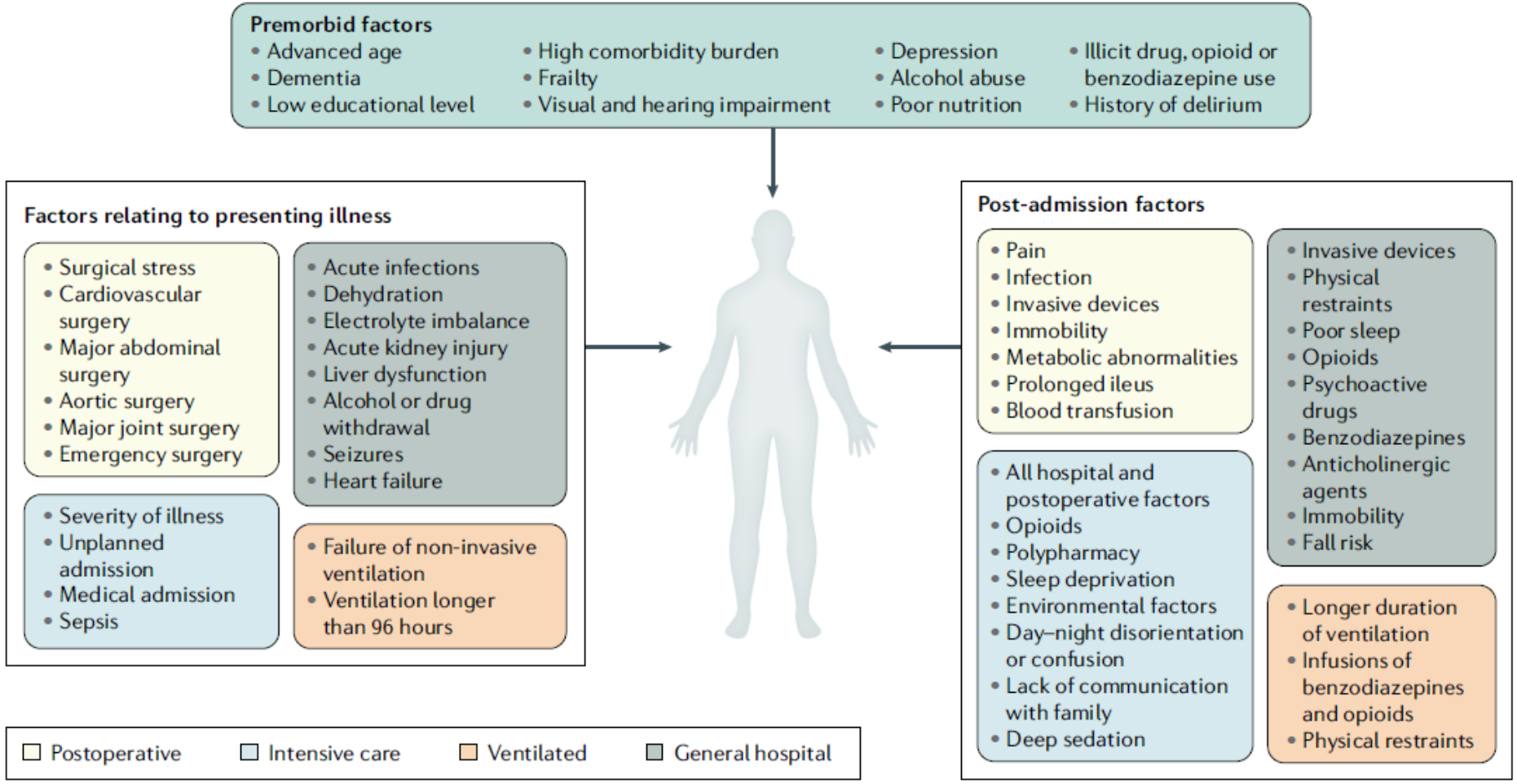
Delirium

- **Primary disturbance in attention: inability to maintain a coherent stream of thought.**
- **Fluctuating course with respect to attention and alertness; disrupted circadian rhythm.**
- **Absence of other localizing neurological signs.**
- **Tremulousness, myoclonus, asterixis, visual hallucinations (variably).**
- **Can be "hypoactive," "hyperactive," (with psychomotor agitation and sympathetic hyperactivity), or mixed.**



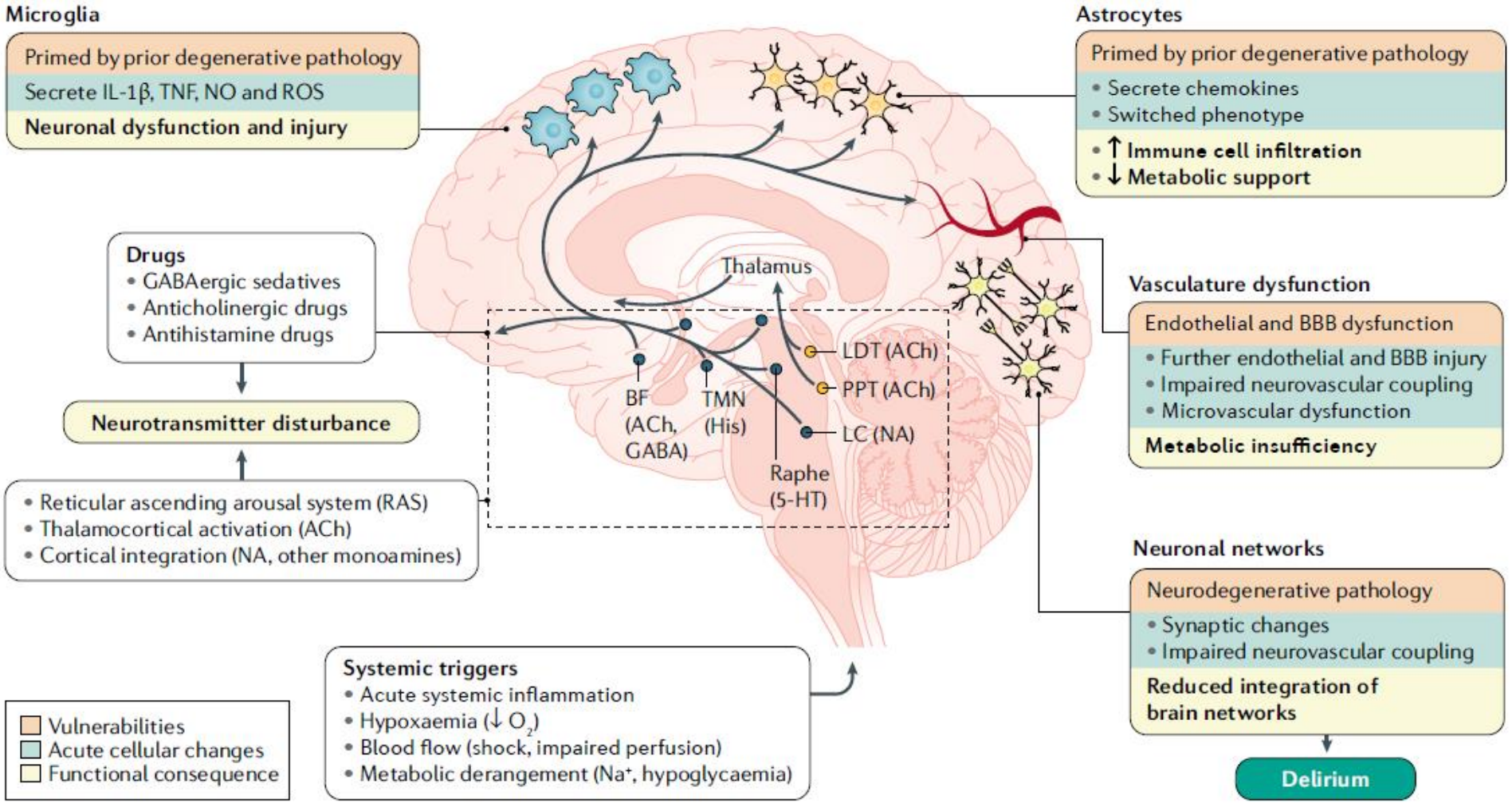
Delirium

- **Very common:** ~10-15% medical/surgical inpatients, ~25-45% hospitalized cancer patients, ~60% ICU patients, ~80% patients receiving mechanical ventilation, ~80-90% terminally ill palliative care patients.



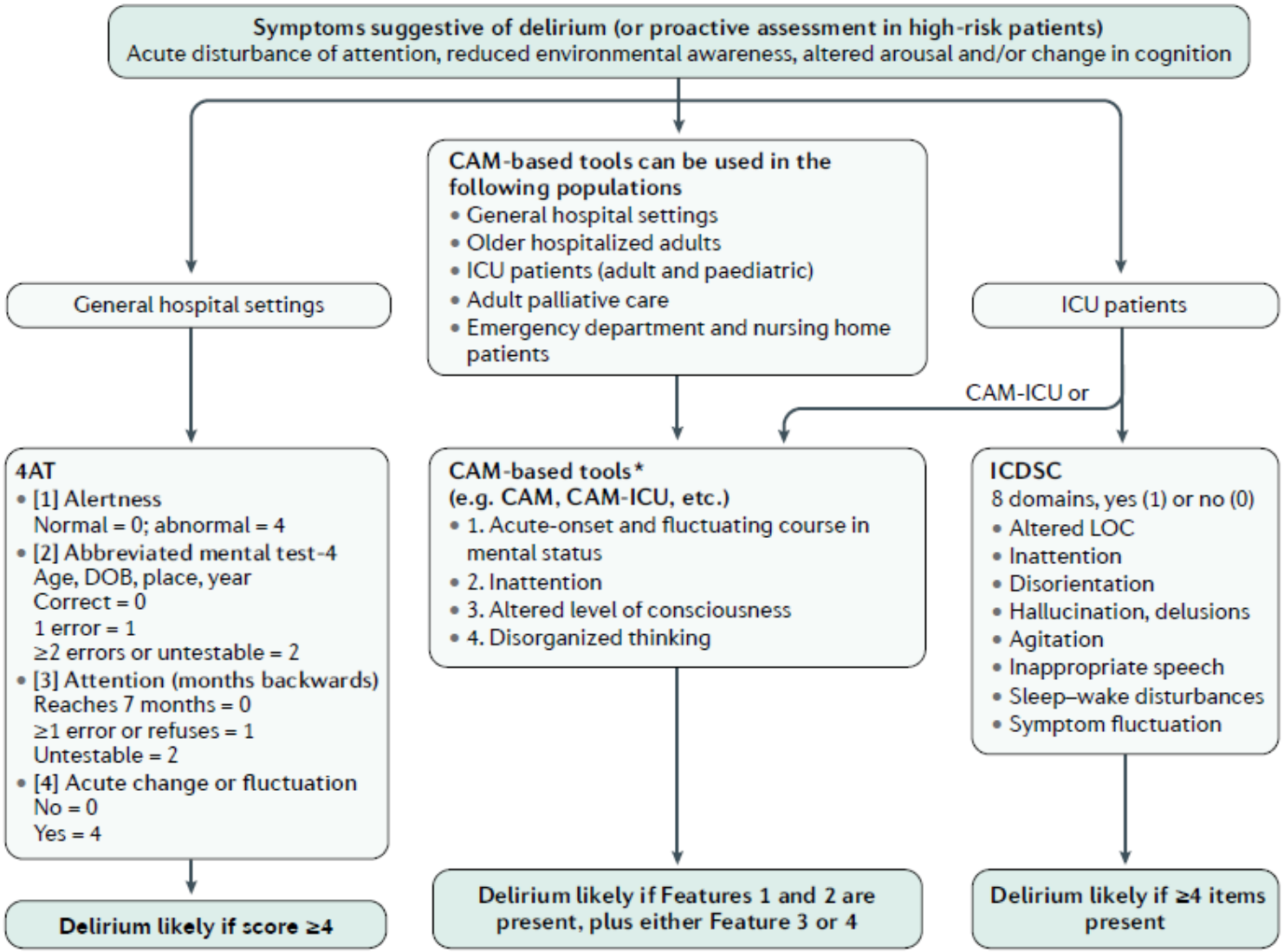
Wilson *Nat Rev Dis Primers* 2020;6:90

Delirium: Pathophysiology



Wilson *Nat Rev Dis Primers* 2020;6:90

Delirium: Screening



Wilson *Nat Rev Dis Primers* 2020;6:90

Delirium: Evaluation

- **Basic evaluation: metabolic, toxic, infectious causes**
  - Physical and neurological examinations; vitals, pulse oximetry
  - CBC, electrolytes, glucose, BUN, creatinine, LFTs, urinalysis and culture; drug levels; blood, urine toxicology
  - Chest x-ray, ECG

- **Evaluation dictated by preliminary findings**
  - Lumbar puncture for unexplained fever, nuchal rigidity, or suspected infection with unknown source
  - Neuroimaging (CT or MRI for focal findings or evidence of trauma)

- **Evaluation for persistent unexplained delirium**
  - Expanded lab workup (e.g., thyroid function, B12, ammonia, blood gas
  - EEG
  - MRI brain
  - Lumbar puncture



Delirium: Prevention and Treatment

Box 2 | **Delirium prevention in different health-care settings**

Consensus guidelines[241,262] make a number of recommendations for delirium prevention in various health-care settings.

General settings

Multicomponent interventions

- Early recognition of high-risk factors (age >65 years, dementia, hip surgery and high acuity)
- Daily screening for delirium
- Environmental orientation (sensory, auditory, dentures, time, events, family visits and music)
- Maintain normal hydration
- Regulation of bladder and bowel function
- Early establishment of normal diet
- Correction of metabolic disorders
- Cardiorespiratory optimization (with provision of oxygen if appropriate)
- Early identification of infection
- Effective treatment of pain
- Daily mobilization
- Avoidance of antipsychotic drugs
- Avoidance of benzodiazepines
- Reduced nocturnal disturbances to promote sleep
- Early removal of devices (intravascular and airway devices)
- Avoidance of physical restraints
- Sleep promotion (eye mask and earplugs)

Pharmacological interventions

- None with high-level evidence

Intensive care and high acuity units, intubated and non-intubated patients

Non-pharmacological interventions (as above, consider also)

- Early recognition of high-risk patients (age >65 years, high acuity, sepsis, shock, dementia and ventilation)
- Light sedation
- No benzodiazepines
- Early mobilization
- Promotion of day–night routine
- Environmental awareness and orientation
- Removal of devices (intravascular and airway devices)

Pharmacological interventions

- Some suggestive evidence but not recommended by consensus guidelines

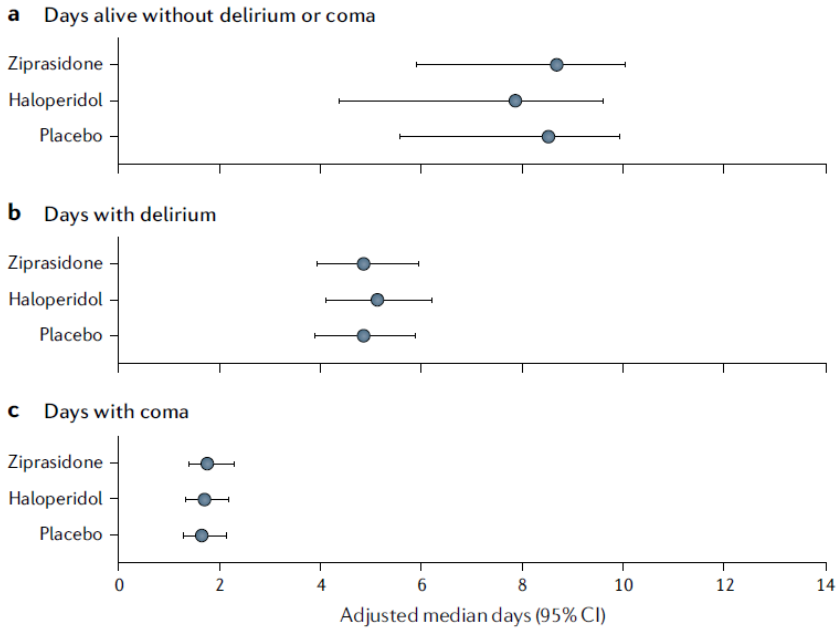
Treat the underlying etiology

- Discontinue non-essential potential contributing medications

- Thiamine supplementation for patients with evidence of nutritional deficiency

- Identify and manage withdrawal states

- Consider low-dose, short-term antipsychotic (haloperidol, risperidone, ziprasidone, olanzapine, quetiapine) for patients with potential to harm self or others despite non-pharmacological interventions.



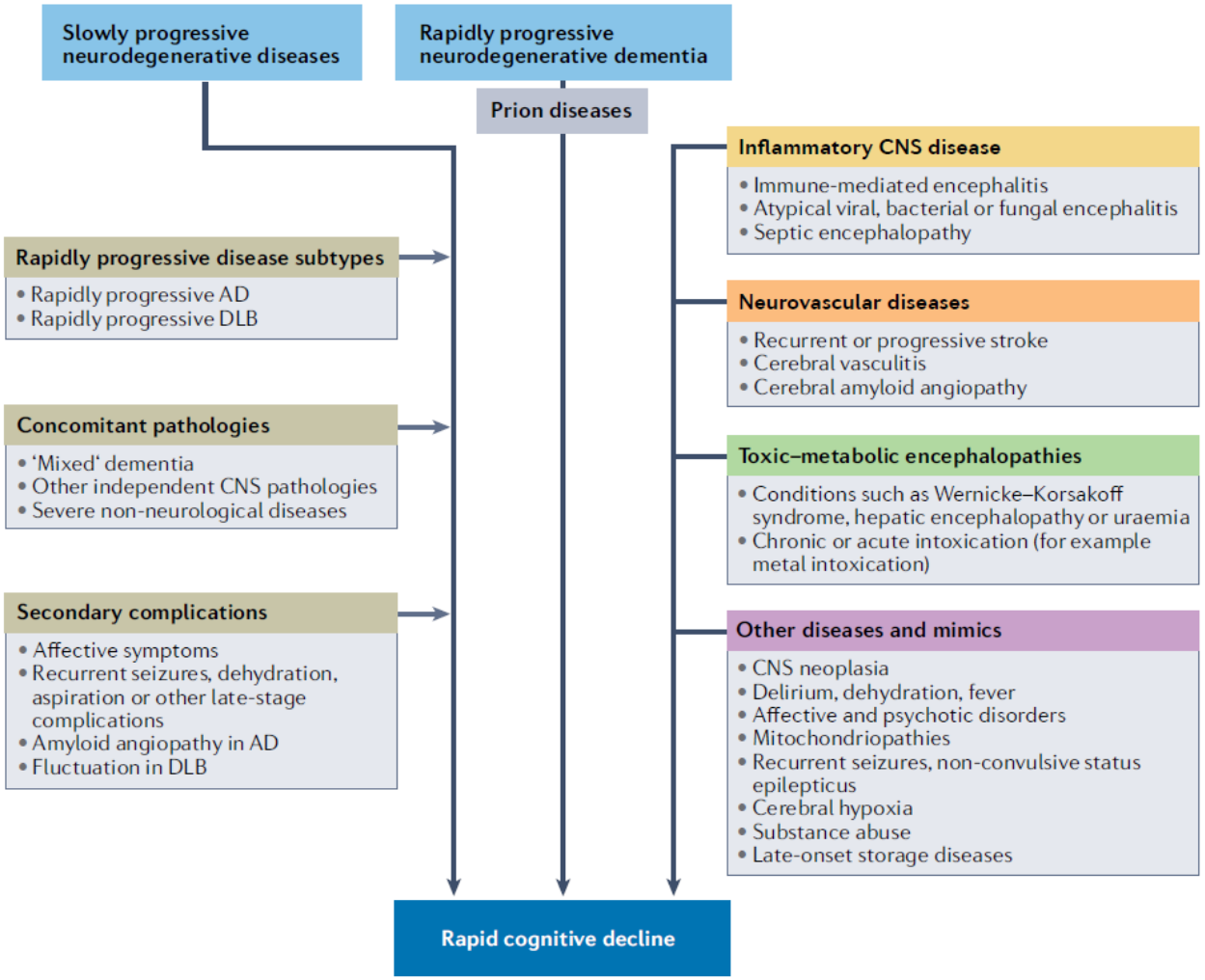
Wilson *Nat Rev Dis Primers* 2020;6:90 Girard *N Engl J Med* 2018;379:2506

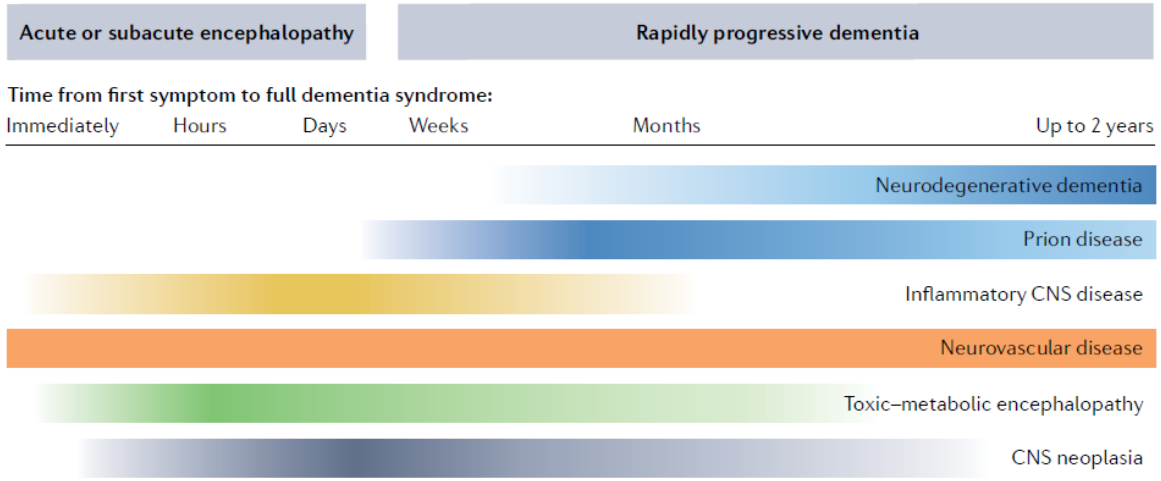
Clues of a primary neurological etiology (subacute presentations)

- **Primary domain of impairment in a cognitive domain other than attention.**
- **Neurological signs (other than asterixis/myoclonus).**
- **Steadily progressive time course.**
- **Pertinent abnormalities on neuroimaging, EEG, CSF.**

There is great value in developing and employing a time-efficient bedside mental status and general neurological examination to gain comfort with what is normal vs abnormal.

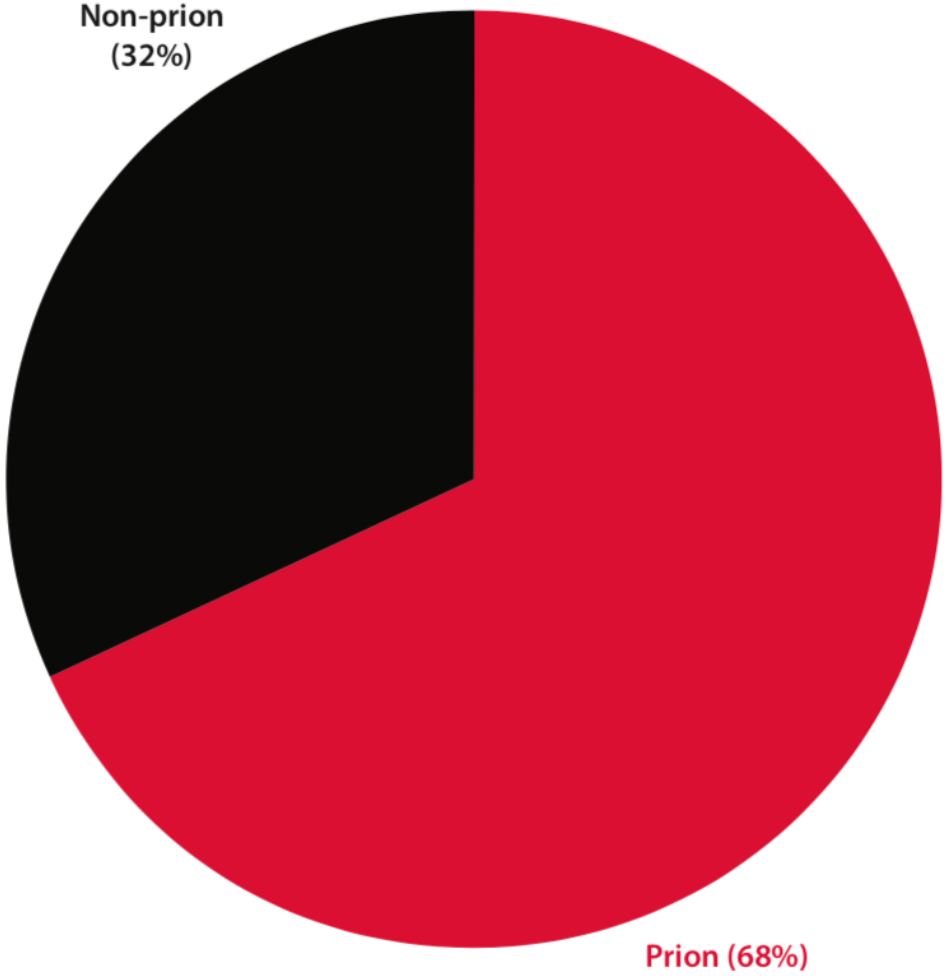
Rapidly Progressive Dementia

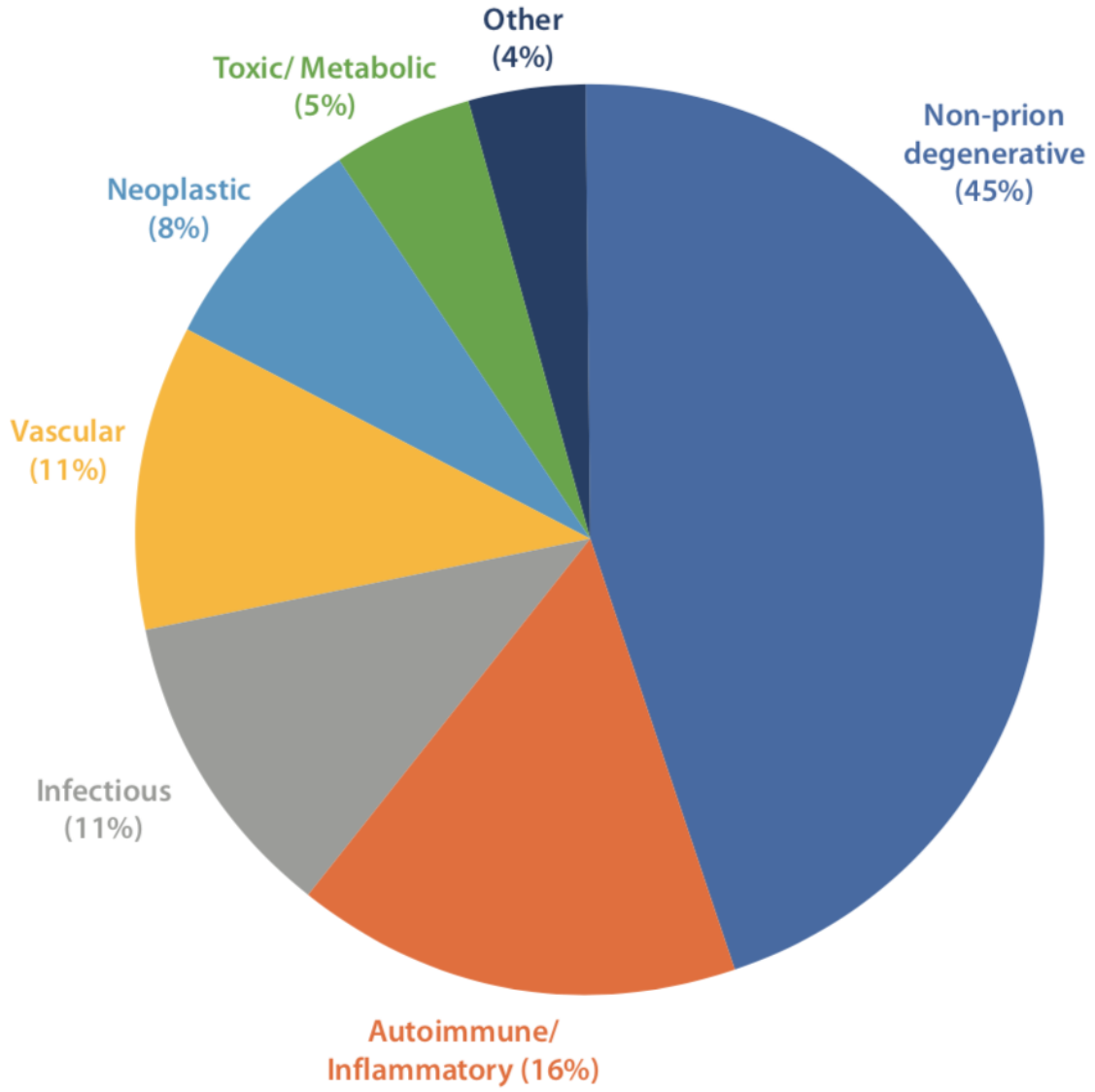




Hermann and Zerr *Nat Rev Neurol* 2022;18:363-76.

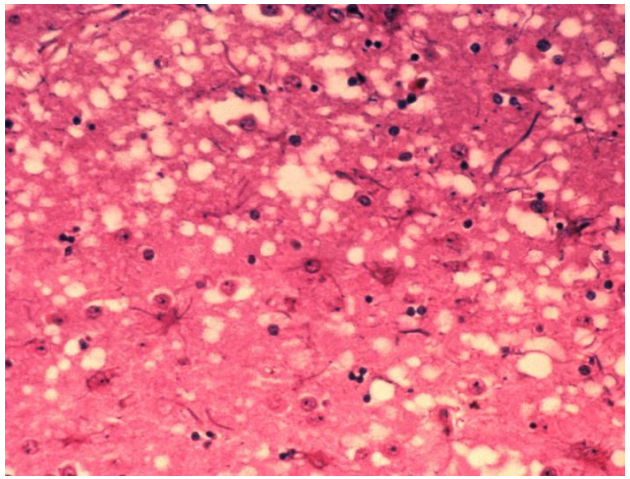
RPD: Prion vs. Non-prion





Prion disease

- **Sporadic Creutzfeldt-Jakob disease (sJCD) is the most common; incidence 1-2 per 1,000,000 per year.**
- **Rapidly progressive deterioration in cognition and behavior with higher cortical signs; myoclonus occurs in >90% of cases; pyramidal or extrapyramidal motor signs (>50%), cerebellar signs (>50%) are also common.**
- **Neuropsychiatric features: apathy ➔ akinetic mutism, depression; less commonly euphoria, emotional lability, anxiety, psychotic features.**
- **Molecular variants defined by amino acid at codon 129 of prion protein gene (M or V) and type of pathological prion (1 or 2) influence clinical presentation.**

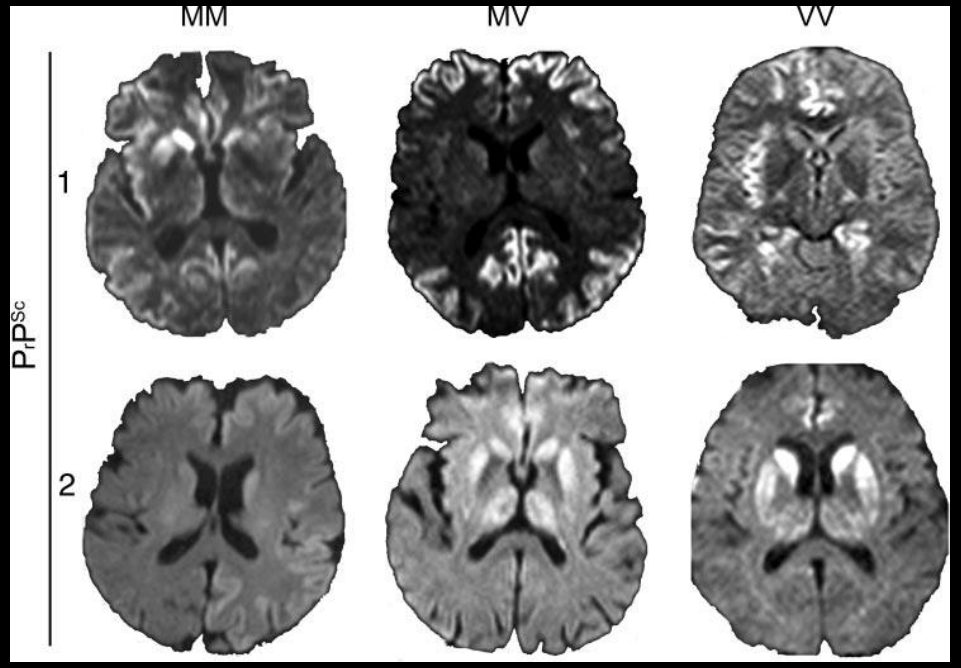




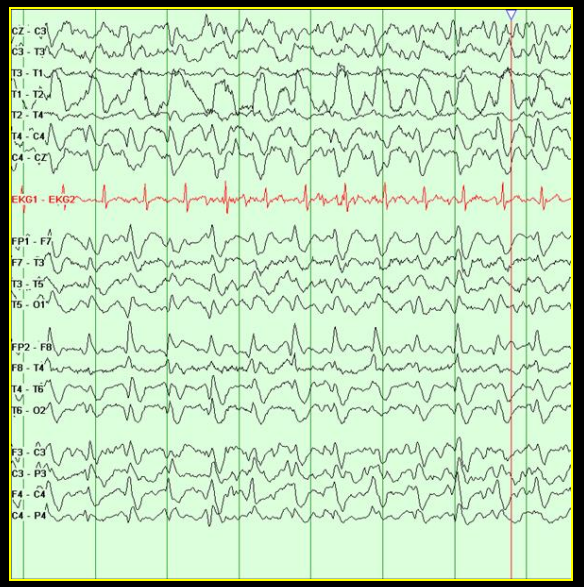


CJD biomarkers

DWI restriction ~90-95% sensitive, ~90-99% specific



Periodic sharp wave complexes ~65% sensitive, ~90% specific



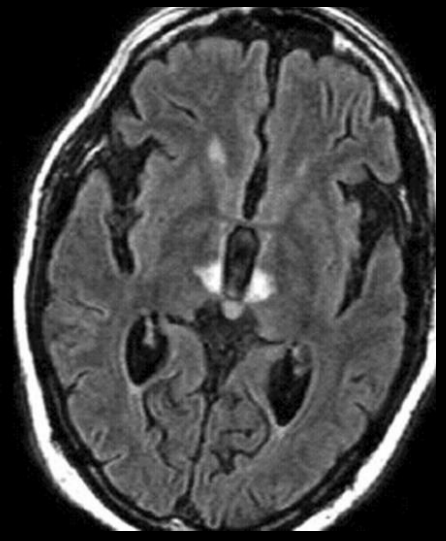
- Real-time quaking-induced conversion (RT-QuIC) assay amplifies detection of PrP(CJD); CSF or olfactory mucosa brushings; sensitivity ~90-96%, specificity ~99-100%
- Supportive but non-specific: elevated CSF 14-3-3 protein; highly elevated CSF total tau

Meissner *Neurology* 2009;72:1994-2001.
Lattanzio Acta Neuropathol 2017;133:559-78

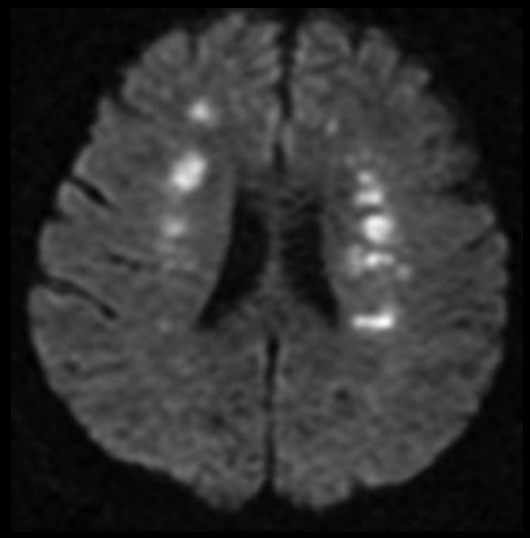
Vascular cognitive impairment



Microvascular disease
"Subcortical" dementia



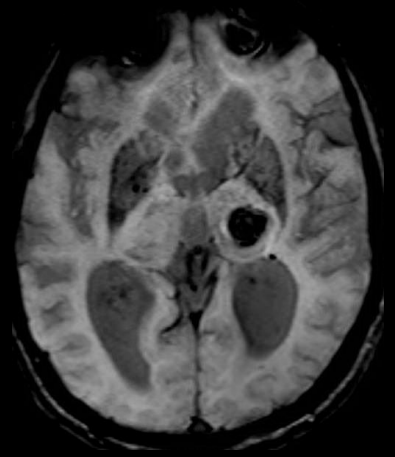
Strategic infarcts



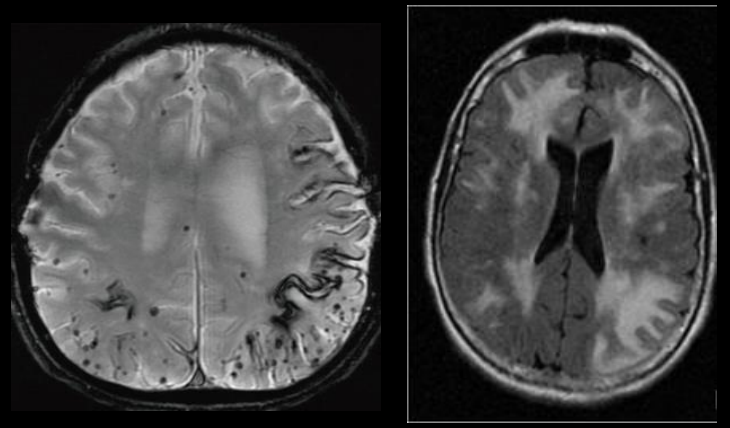
Multifocal/diffuse emboli
(May present as delirium)



Subdural hematomas

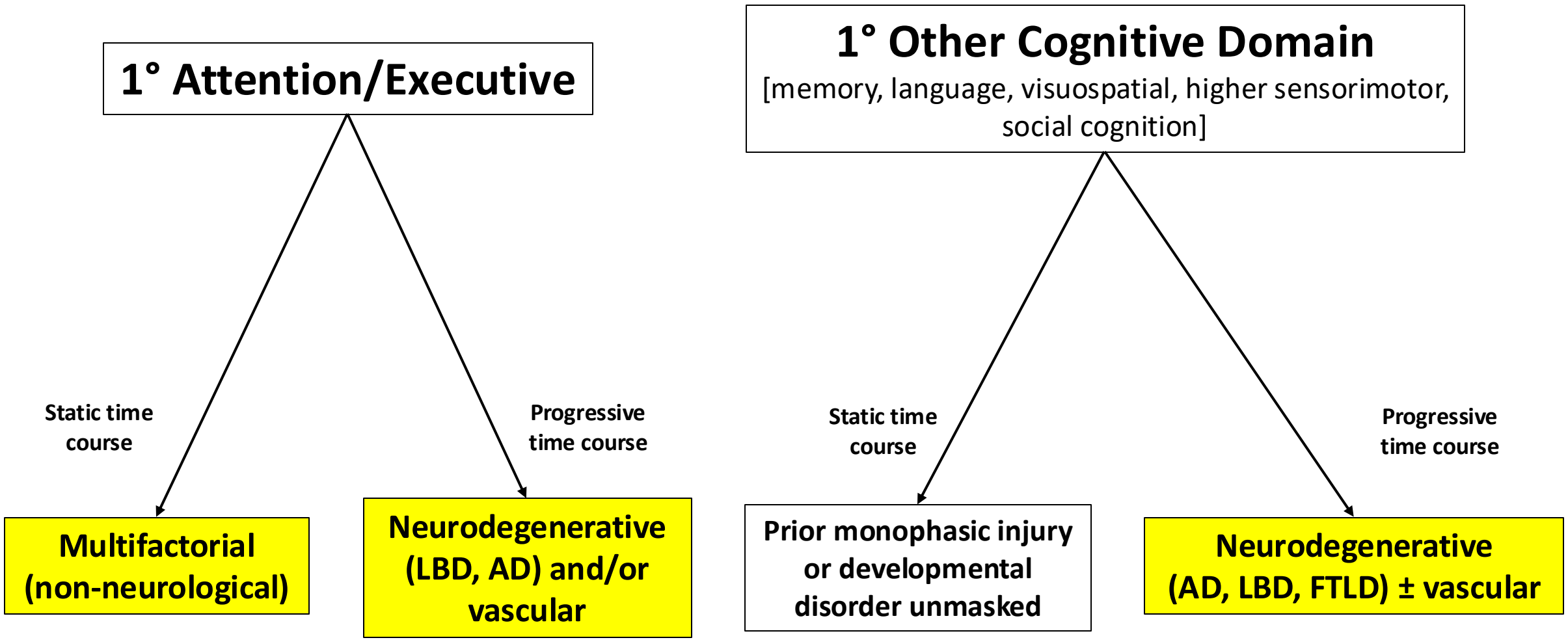


Intraparenchymal hemorrhage (IPH)

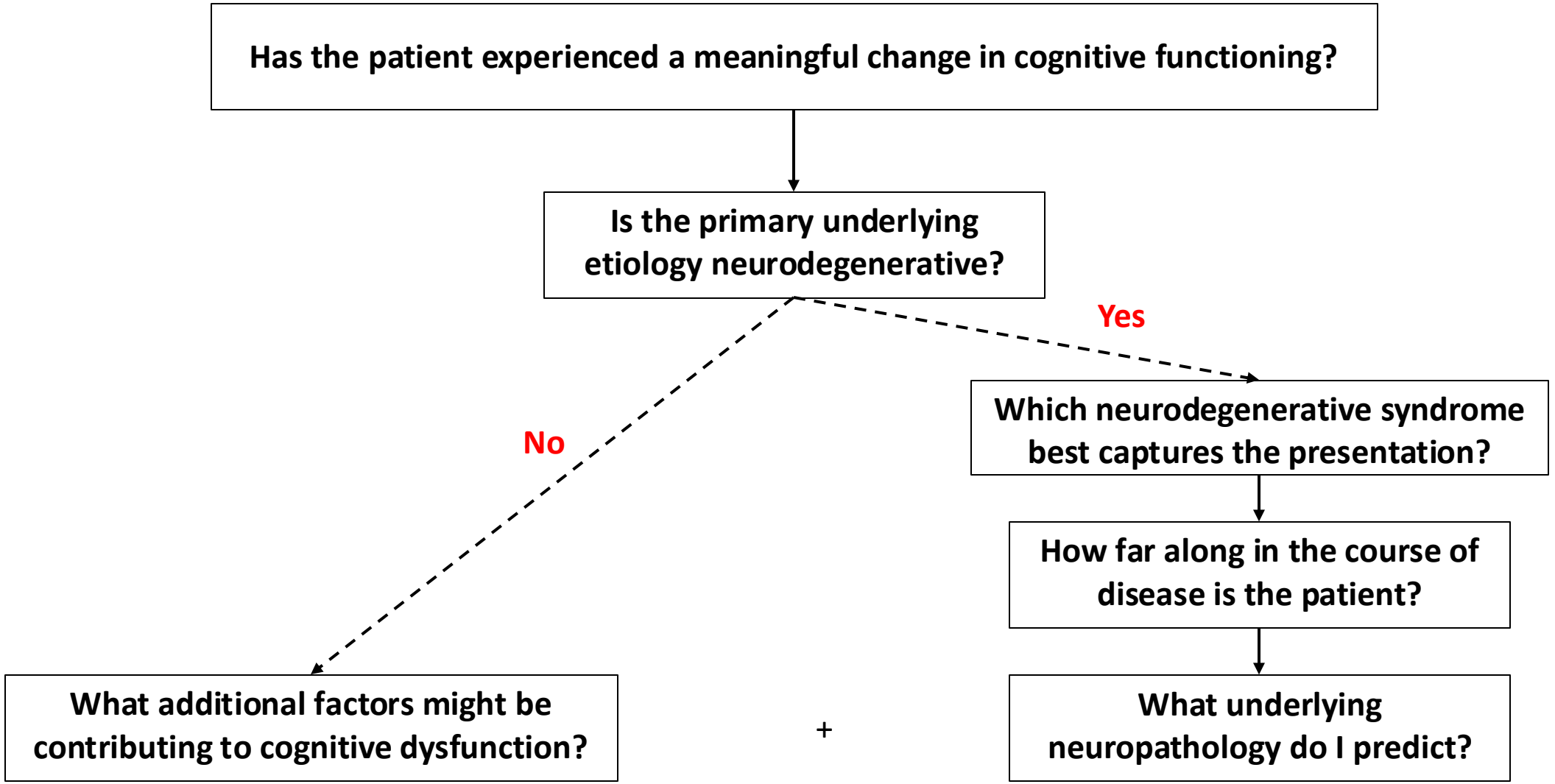


Cerebral amyloid angiopathy (CAA)

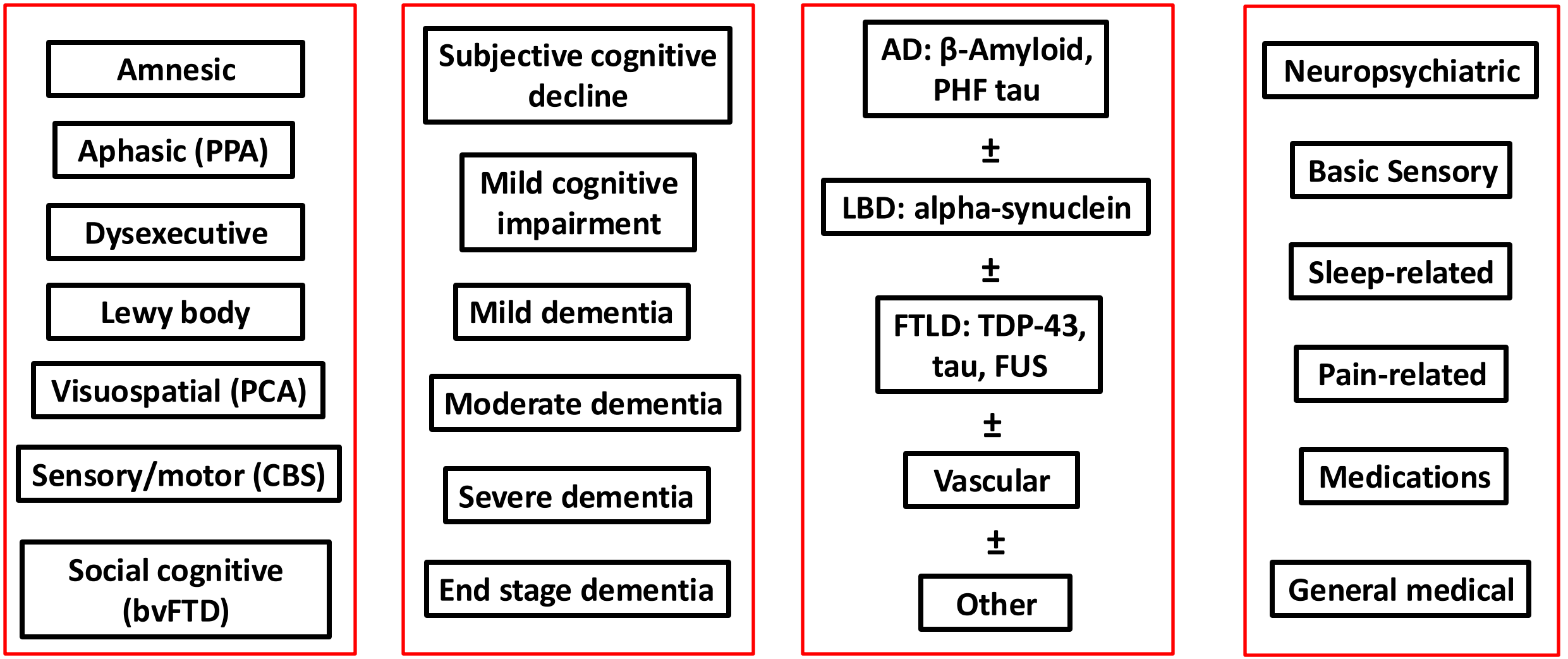
Insidious Onset Cognitive Dysfunction



Initial Assessment: Questions



Formulation: Degenerative Cognitive Disorders



Syndrome *Stage* *Neuropathology* *Contributing Factors*

Initial Assessment

History

- Cognitive Symptoms
- Usual Activities
- Behavioral/Emotional Symptoms
- Sleep/Fluctuations
- Motor/Sensory
- Autonomic/Pain

+

- Developmental, Occupational, Social, and Family Histories

- Cognitive Examination
- Neuro Examination

- **Cognitive Profile**
- **Time Course**
- **Severity**
- **Associated Features**

Initial Assessment

History

- Cognitive Symptoms
- Usual Activities
- Behavioral/Emotional Symptoms
- Sleep/Fluctuations
- Motor/Sensory
- Autonomic/Pain

+

- Developmental, Occupational, Social, and Family Histories

- Cognitive Examination
- Neuro Examination

- **Cognitive Profile**
- **Time Course**
- **Severity**
- **Associated Features**

Challenges

- **Variable reliability of self-report**
- **Variable reliability of informant report**
- **“Memory” is frequently not (episodic) memory.**
- **Impaired attention can affect processing in other domains.**

Initial Assessment

History

- Cognitive Symptoms
- Usual Activities
- Behavioral/Emotional Symptoms
- Sleep/Fluctuations
- Motor/Sensory
- Autonomic/Pain

\+

- Developmental, Occupational, Social, and Family Histories

- Cognitive Examination
- Neuro Examination

- **Cognitive Profile**
- **Time Course**
- **Severity**
- **Associated Features**

Challenges

- **Evaluations are often cross-sectional.**
- **Subjective worsening often does not equal objective worsening.**
- **Standard brief cognitive examination measures may lack sensitivity early in the disease course.**

Initial Assessment

History

- Cognitive Symptoms
- Usual Activities
- Behavioral/Emotional Symptoms
- Sleep/Fluctuations
- Motor/Sensory
- Autonomic/Pain

\+

- Developmental, Occupational, Social, and Family Histories

- Cognitive Examination
- Neuro Examination

- **Cognitive Profile**
- **Time Course**
- **Severity**
- **Associated Features**

Challenges

- **Variable lifestyles/responsibilities at baseline**
- **Imperfect correlation between standard brief cognitive measures and functional severity of illness**

HPI: Usual Activities

Type	Elements/Examples
Advanced ADLs **Compromised in MCI**	**Performance at work** **Participating in group/community activities** **Leisure activities (intellectual, social)**
Instrumental ADLs **Loss of independence in mild dementia**	**Driving** (and other forms of transportation in the community) **Taking prescribed medications** **Managing finances** **Shopping for groceries and completing errands in the community** **Completing household chores, preparing meals** **Using the telephone and computer**
Basic ADLs **Loss of independence in moderate and severe dementia**	**Tending to personal hygiene and grooming** Bathing and/or showering Dressing Toileting Functional mobility Self-feeding

Recommended scale: **Activities of Daily Living Questionnaire** (Johnson et al. *Alzheimer Dis Assoc Disord* 2004;18:223-30)

Initial Assessment

History

- Cognitive Symptoms
- Usual Activities
- Behavioral/Emotional Symptoms
- Sleep/Fluctuations
- Motor/Sensory
- Autonomic/Pain

\+

- Developmental, Occupational, Social, and Family Histories

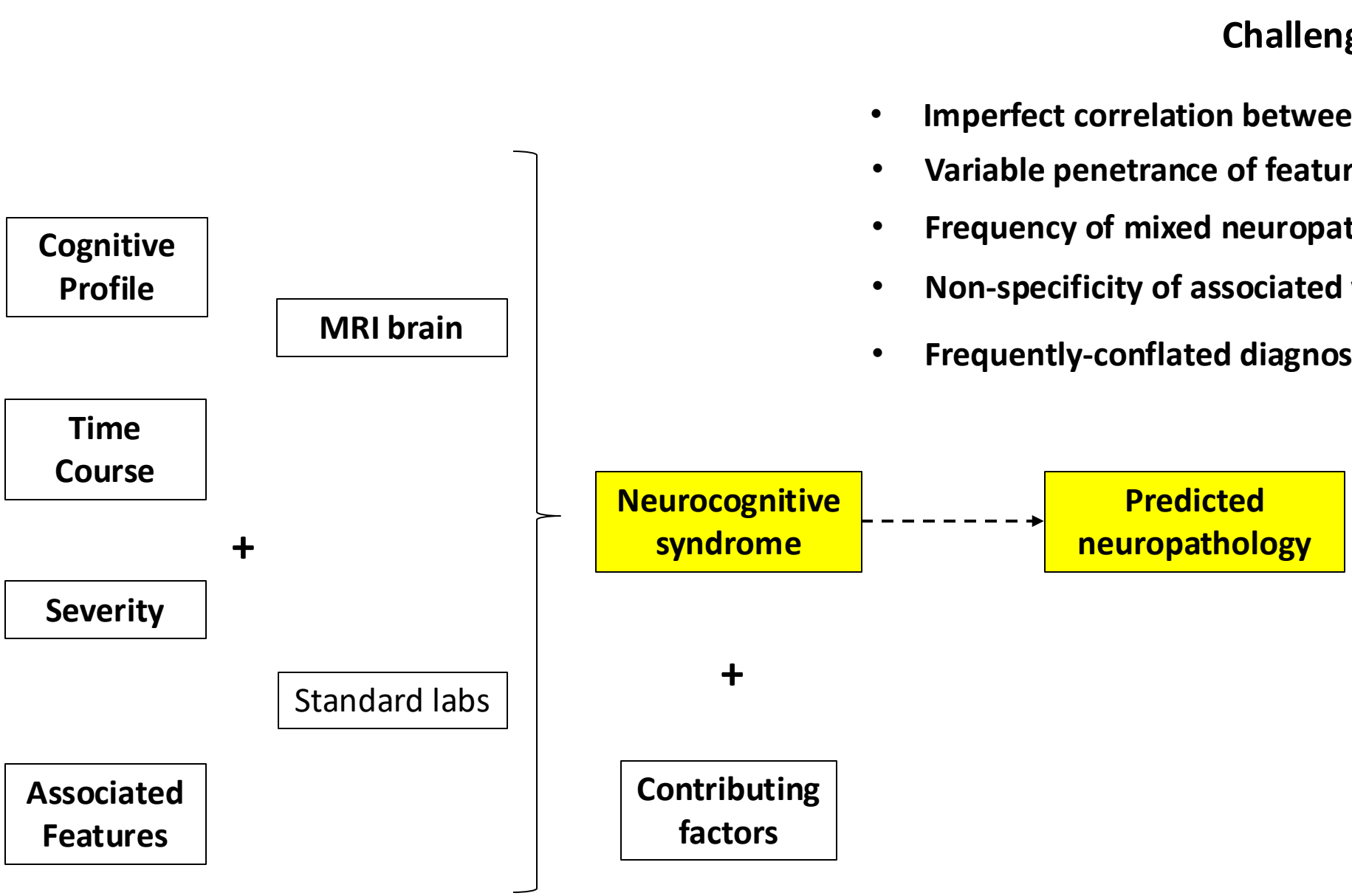
- Cognitive Examination
- Neuro Examination

- **Cognitive Profile**
- **Time Course**
- **Severity**
- **Associated Features**

Challenges

- **Variable reliability of self-report**
- **Variable reliability of informant report**
- **Time limitations**

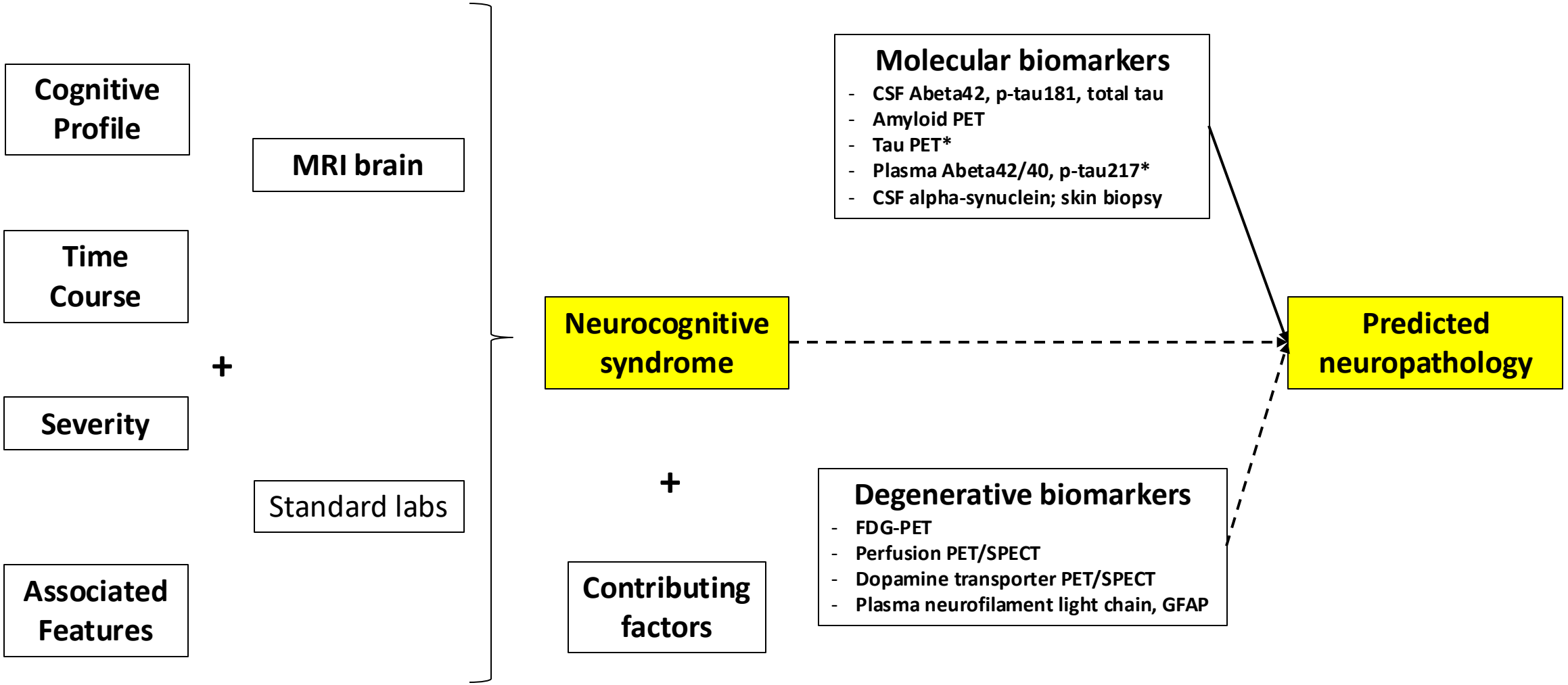
Initial Assessment



Challenges

- Imperfect correlation between syndrome and pathology
- Variable penetrance of features early in the disease course
- Frequency of mixed neuropathology
- Non-specificity of associated vs. contributing factors
- Frequently-conflated diagnostic terms

Initial Assessment



How will the information impact the care of the patient?

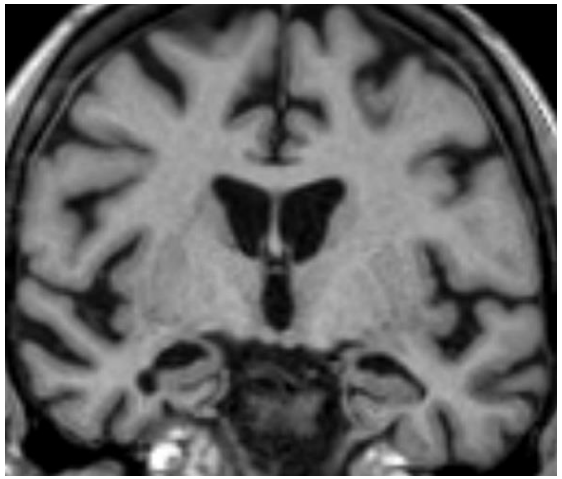
Amnesic MCI/Dementia

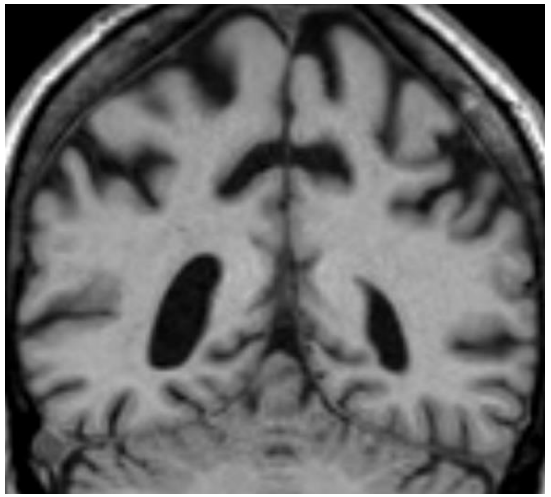
History + Examination

Progressive primary amnesia
± attention/executive, language, visuospatial

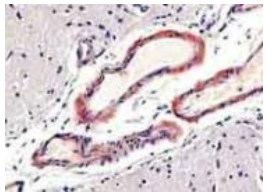
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Irritability, anxiety, apathy, depression,
paranoia, poor insight





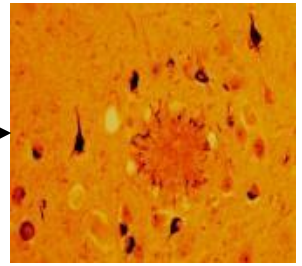
Vascular disease



±

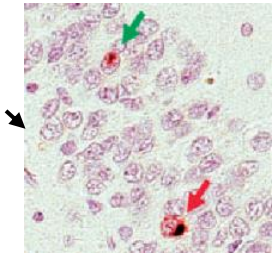
Alzheimer disease

PPV ~80-90% in late-onset amnesic dementia



±

Limbic-predominant Age-related TDP-43 Encephalopathy (LATE)



Dysexecutive MCI/Dementia

History + Examination

Primary attention, executive, visuospatial
± memory, language

+

Visual hallucinations and/or dream enactment and or fluctuations in attention/alertness and/or parkinsonism

±

Anxiety, depression, apathy, delusions, dysautonomia, anosmia

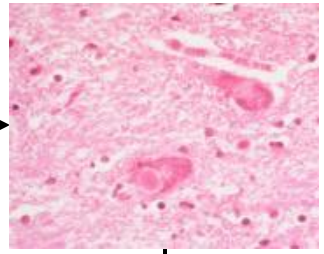
PPV ~80-90% for diffuse neocortical Lewy bodies

Vascular Disease



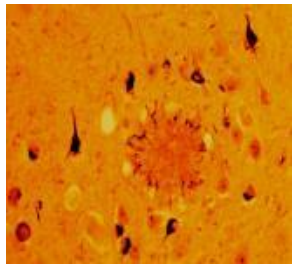
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Lewy body disease



AD co-pathology in ~60-70% of cases

Alzheimer Disease



Non-progressive attention/executive dysfunction

Stress

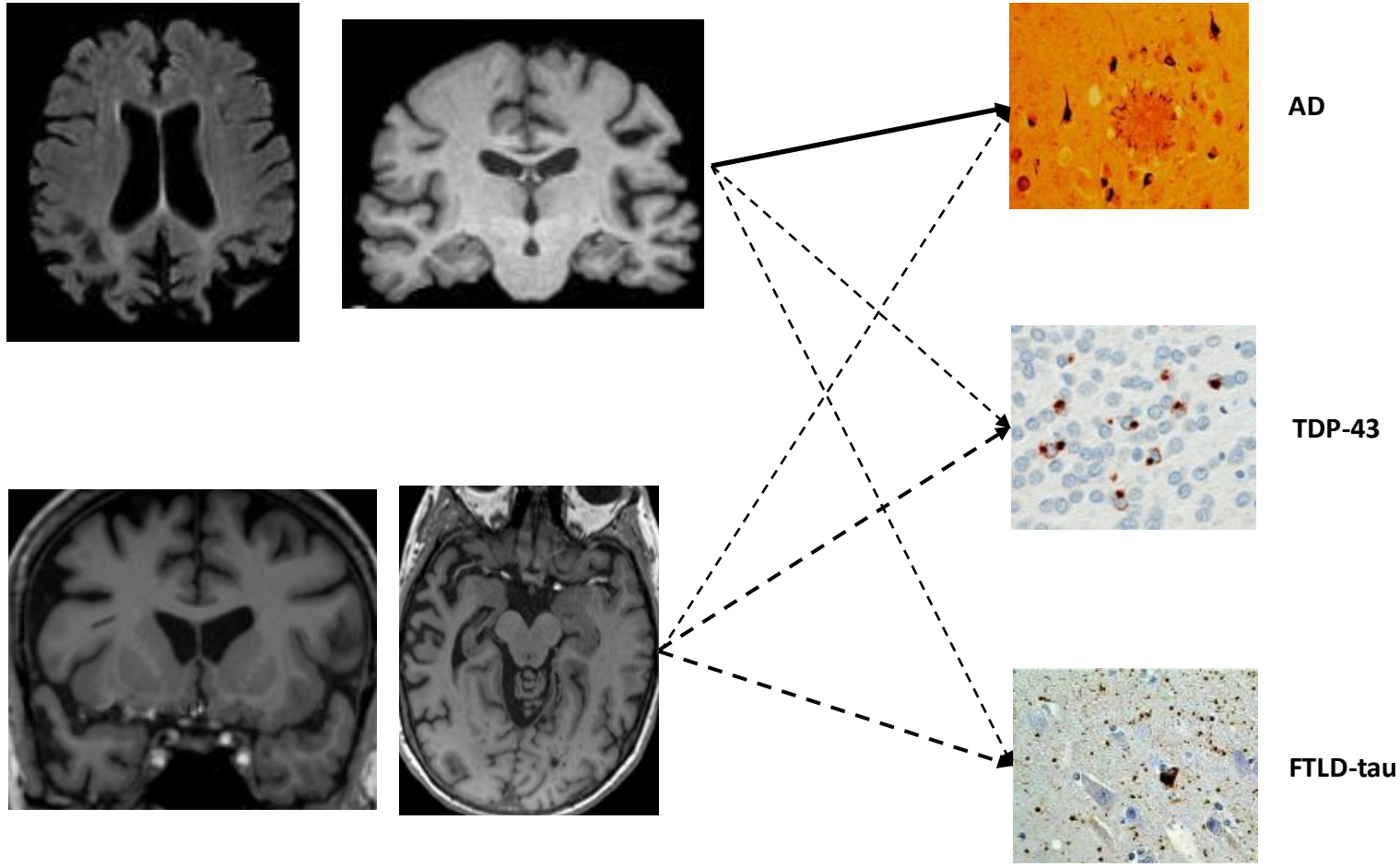
- **Psychiatric illness**
- **General medical illness**
- **Chronic pain**
- **Poor sleep**
- **Medications**
- **Nutritional deficiency**

+ **Aging** **±** **Genetic and/or Developmental factors**

Less Common Neurocognitive Syndromes

AD-spectrum:
- Posterior cortical atrophy
- Logopenic variant PPA
- Dysexecutive/behavioral AD

FTLD-spectrum:
- Behavioral variant FTD
- Semantic variant PPA
- Nonfluent/agrammatic variant PPA
- Primary progressive apraxia of speech
- Corticobasal syndrome
- PSP syndrome



Atypical Features

- **Rapid progression over days to weeks**
  - Consider admission to the hospital for expedited work-up
  - Prion disease, autoimmune/inflammatory conditions high on the ddx

- **Non-amnesic cognitive profile**
- **Young age of onset (< 65 years old)**

} **Frequently FTLD or atypical presentation of AD**

- **Family history suggesting autosomal dominant inheritance**
  - Mutations in *APP*, *PSEN1*, *PSEN2* associated with AD
  - Mutations in *C9orf72*, *MAPT*, *GRN* associated with FTLD

- **Atypical associated medical or neurological symptoms and/or signs**

Accurate diagnosis provides the foundation for longitudinal care

	SCD/ Preclinical	MCI	Mild dementia	Mod. dementia	Sev. dementia
Symptomatic pharmacotherapy (cognition)	-	+/- (off-label)	+	+	+/-
Disease modifying pharmacotherapy	?	+++	++	-	-
Cognitive rehabilitation therapy	-	++	+	-	-
Compensatory strategies, brain health habits, vascular risk factors	+++	++	+	-	-
Safety	-	+	+++	+++	+
Advance directives/planning	+	+++	+++	++	++
Care arrangements/Caregiver support	-	+	++	+++	+++
Clinical therapeutic research (if interested)	+++	+++	++	-	-

Thank you





- BWH Center for Alzheimer Research and Treatment:
  617-732-8085; BWHmemory@partners.org

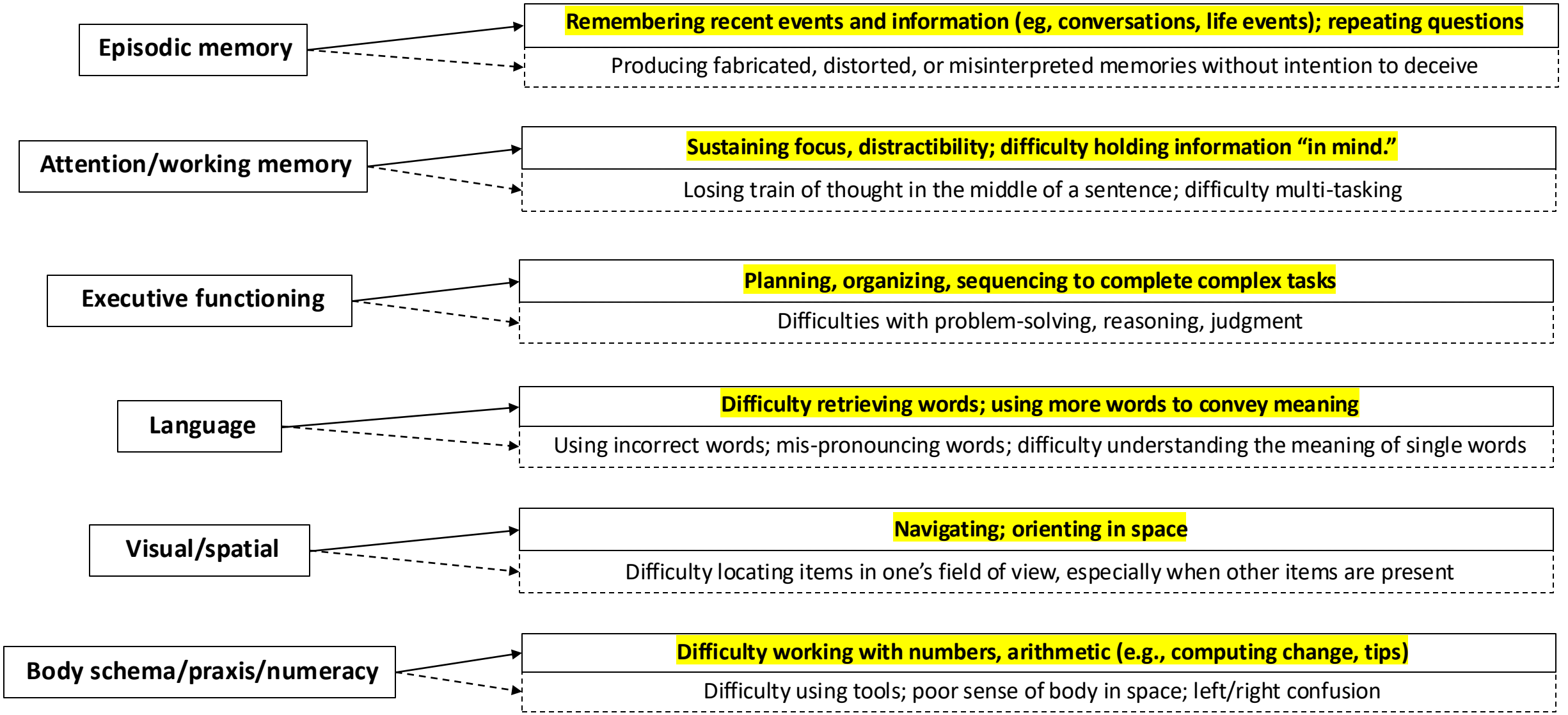
- MGH FTD Unit: 617-726-5571; MGHFTDunit@partners.org

MGH FTD Unit

Notes/References: Delirium risk medications

- **High risk:**
  - **Benzodiazepines**
  - **Opiates**
  - **Dihydropyridines (e.g., amlodipine, nifedipine)**
  - **H1 antagonists**
- **Moderate risk:**
  - **H2 antagonists**
  - **Anticholinergics (including but not limited to tricyclic antidepressants)**
  - **Anti-Parkinsonian agents**
  - **Corticosteroids**
  - **Antimuscarinics**
- **Some risk:**
  - **Selected antimicrobials, anticonvulsants, antineoplastic agents, cardiac drugs, salicylates, NSAIDs, stimulants**

HPI: Cognitive Symptoms



HPI: Other Features

Behavioral/Emotional Symptoms

Mood; ability to derive pleasure from usual sources; motivation; anxiety; appetite

False beliefs; bipolar-spectrum symptoms; PTSD-spectrum symptoms; disinhibition, obsessive-compulsive or perseverative behaviors, sympathy/empathy, food behaviors

Neuropsychiatric Inventory-Questionnaire (Kaufer 2000)

Sleep/Fluctuations

Schedule; insomnia (early, middle, late); snoring/breathing; dream enactment; daytime energy level; napping, dozing; episodes of prolonged staring and/or disorganized speech

Restless legs symptoms; other movements in sleep; vivid dreams

Mayo Sleep Questionnaire (Boeve 2011)
Mayo Fluctuations Scale (Fermin 2004)

Motor/Sensory

Walking, balance; tremors; fine manual dexterity; basic vision, hearing, smell/taste; visual hallucinations, illusions

Speech, swallowing; handwriting; stiffness; eye movements; episodic muscle contractions; fasciculations; extracampine (presence) hallucinations; motion hallucinations; auditory or tactile hallucinations

Queen Square Visual Hallucinations Inventory (Williams 2008)

Autonomic/Pain

Orthostatic lightheadedness; constipation, loose stools; urinary frequency, urgency; pain

Rhinorrhea; excessive salivation, sweating; temperature regulation; erectile function

NACC/UDS Autonomic Symptoms Checklist

Cognitive Examination: Goals

- Goal of determining whether there are **changes above and beyond those attributable to normal aging**, considering baseline intellect/education.
  1. **Survey major cognitive domains**, testing hypotheses generated from the history (MMSE alone is not sufficient; MoCA, SLUMS, ACE-III may be sufficient in 'typical' cases, particularly if supplemented).
  2. Standard evaluation is geared towards discriminating between common conditions and identifying atypical features, corroborating evidence from history.
  3. Flexible evaluations employed in specific atypical situations (e.g., primary dysfunction in a domain other than memory, attention/executive functioning).
  4. Global scores on selected measures can provide a gauge of severity but should always be considered with functional status.
- Billing possible using Medicare CPT code 96116, neurobehavioral status exam

If time doesn't permit a detailed cognitive examination/interpretation, refer to a specialist (e.g., neuropsychologist or cognitive neurologist) for initial assessment.

Brief Cognitive Instruments: Comparison

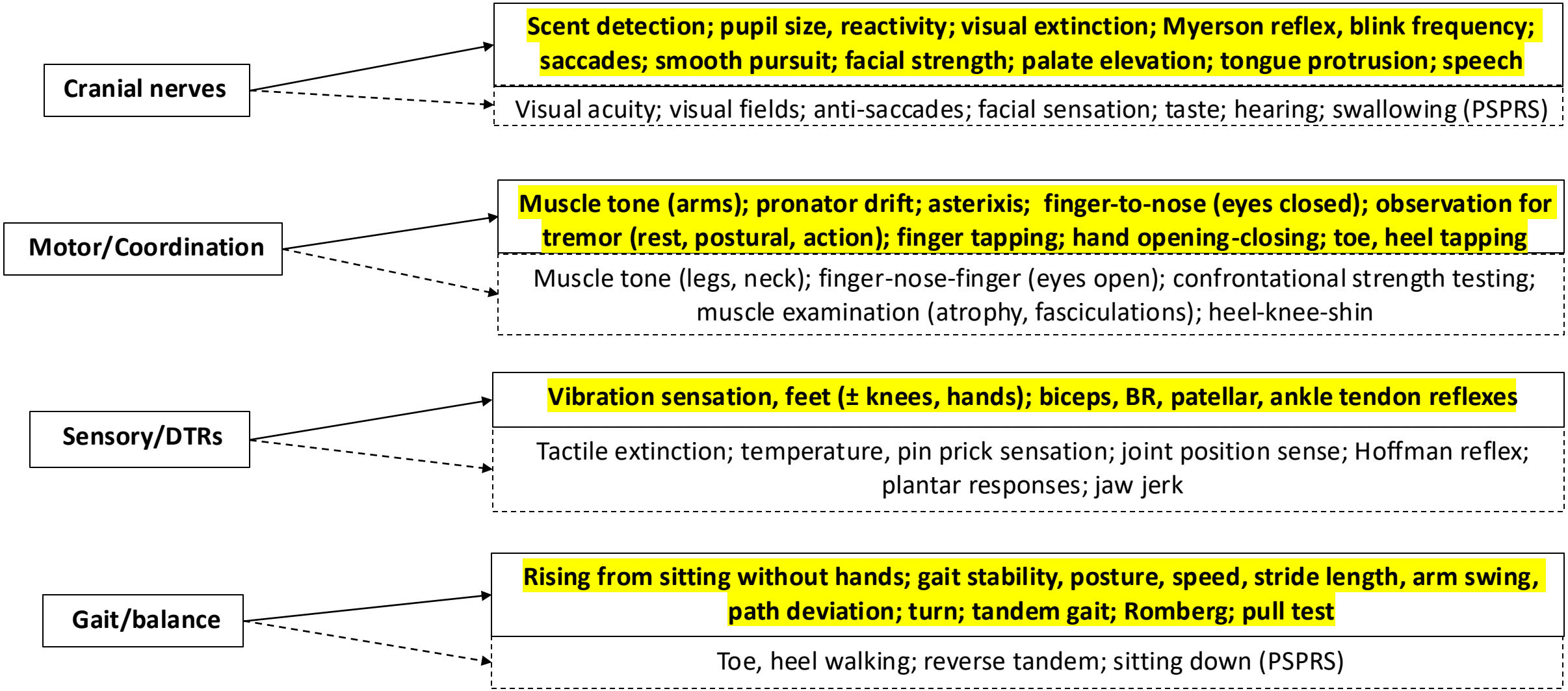
	MoCA	MMSE	ACE-III	SLUMS
Memory	++	+	++	++
Attention/Executive	++	+	+	+
Language	+	+	++	+
Visual/Spatial	++	+	+++	++
Time efficiency	++	+++	+	++
Typical range: MCI*	~19-25	~25-29	~82-89	~21-26
Typical range: Mild dementia*	~14-18	~20-24	~62-81	~12-20

*Most applicable in typical (amnesic) Alzheimer disease

Standard and Flexible Cognitive Examination

Episodic memory	**MoCA 5-item word list**	Supra-span word list tests (e.g., CERAD word list, HVLT); visual tests (e.g., BVMT-R, 3 words/3 shapes)
Attention/working memory	**MoCA trail making, digit span, vigilance, serial 7s, sentence repetition**	Trail Making Test parts A and B; oral trail making
Executive functioning ± Social Cognition	**MoCA clock drawing (qualitative), phonemic fluency, abstraction; Luria motor series**	FAB similarities, conflicting instructions, go/no go, prehension behavior; Rey-O figure copy; Reading the Mind in the Eyes Test
Language	**MoCA naming, sentence repetition; 15-item Boston Naming Test; category fluency (animals)**	NACC/UDS FTLD module: word reading, semantic word-picture matching, semantic associates, sentence repetition; Sherman pictures; BDAE: commands, complex ideational material, oral agility; irregular word spelling; writing
Visual/spatial	**MoCA cube copy, clock drawing test; pentagons copy; letter cancellation (multiple target sizes)**	BORB overlapping figures, overlapping letters; VOSP number location, incomplete letters; Navon figures; Sherman pictures; Face-noise pareidolia; Famous faces
Body schema/praxis/numeracy	**Limb apraxia testing (transitive); interlocking fingers**	Graphesthesia, stereognosis testing; in between fingers test; BDAE body part identification

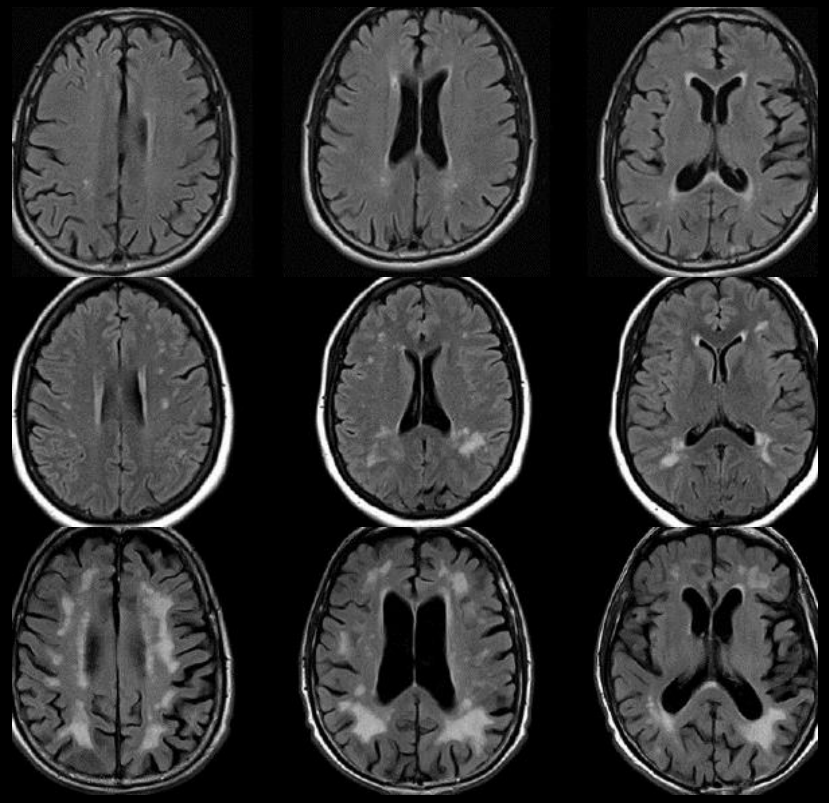
General Neurological Examination

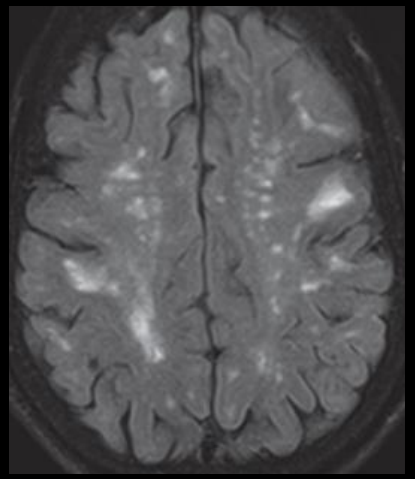


Standard Imaging: Vascular Disease

T2/FLAIR hyperintensities

- Location:
  - Small vessel ischemic disease: periventricular (ependymal loss, ischemic demyelination), subcortical (lipohyalinosis), juxtacortical (arteriole atherosclerosis)
  - Cerebral amyloid angiopathy: centrum semiovale
- Severity (Fazekas Scale):



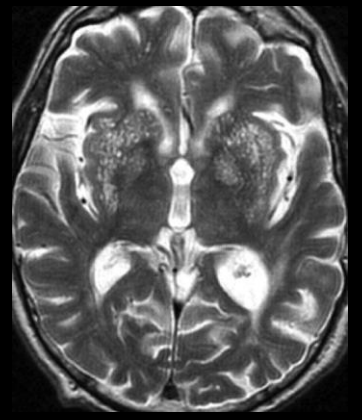


Cerebral amyloid angiopathy

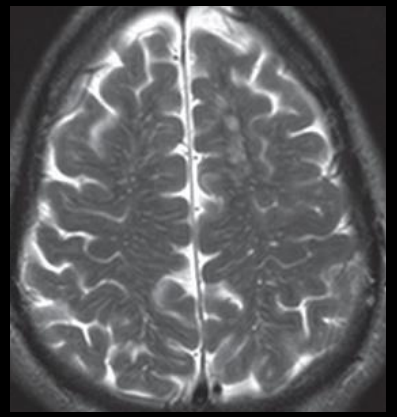
Charidimou *Lancet Neurol* 2022

Dilated perivascular spaces

- Hypertensive vasculopathy: basal ganglia
- Cerebral amyloid angiopathy: centrum semiovale



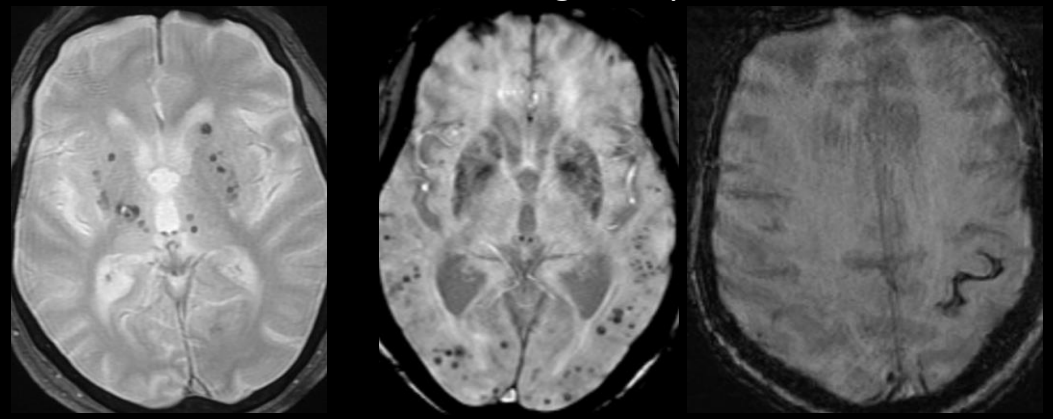
Fergus *Stroke* 2010



Charidimou *Lancet Neurol* 2022

Susceptibility

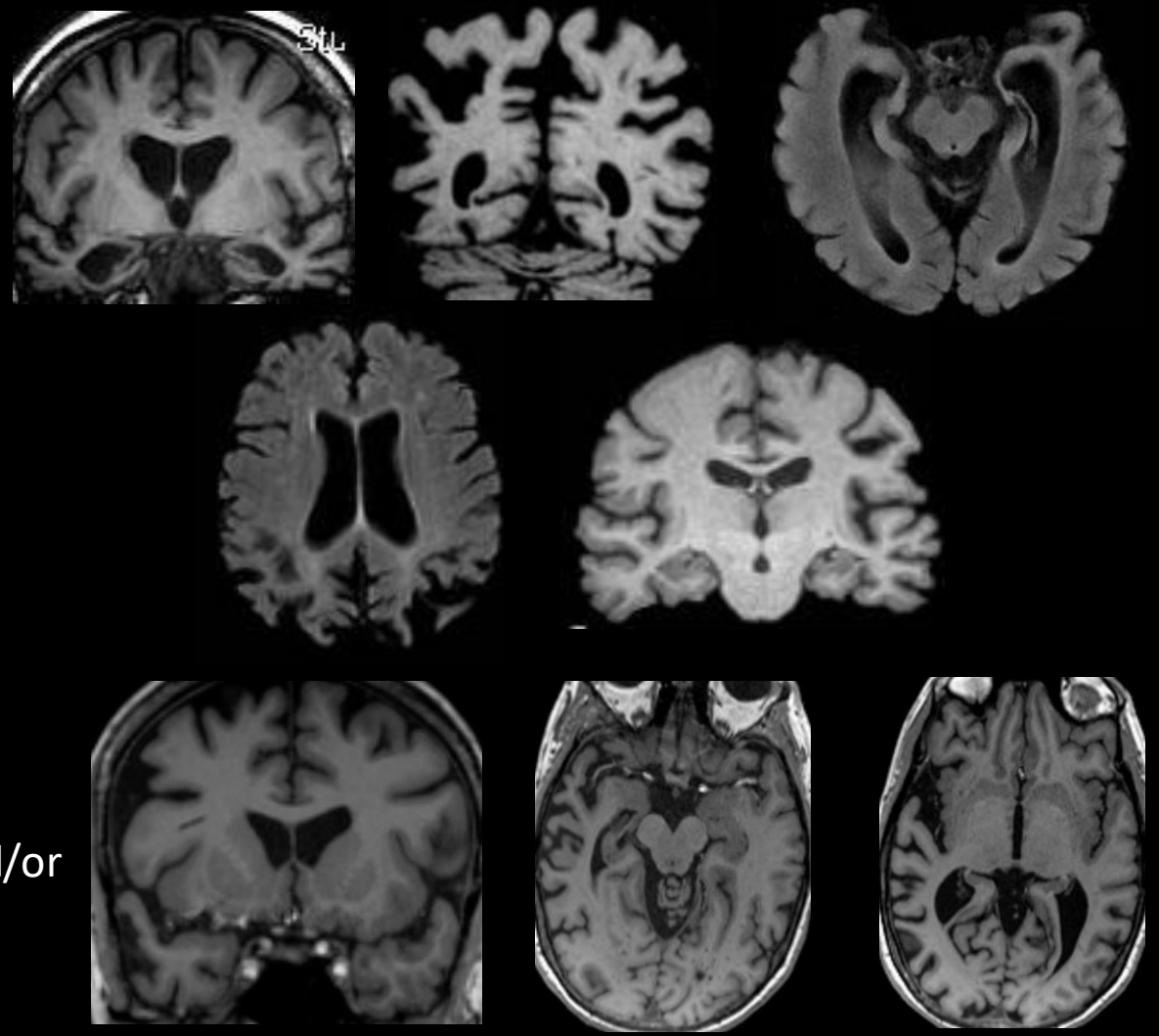
- HTN: subcortical > cortical microhemorrhages
- CAA: cortical microhemorrhages, superficial siderosis



Standard Imaging: Atrophy

High resolution T1 imaging (e.g., SPGR, MPRAGE); 3d reconstruction

- Typical (amnesic) AD: early atrophy in medial temporal, posterolateral temporal, parietal cortices.
- Atypical (non-amnesic) AD: early atrophy in posterolateral temporal, parietal ± dorsal frontal, occipital cortices
- Atypical, non-AD: early asymmetrical atrophy in frontal and/or temporal lobes



Labs: Non-molecular biomarker

Labs	Utilities/Comments
Standard: Comprehensive metabolic panel, TSH, B12, CBC	**Abnormalities are rarely the principal cause of cognitive dysfunction, but may contribute; note eGFR**
Also pertinent: Hgb A1c, lipid profile, homocysteine, 25-OH vitamin D, PT, PTT	**Consider ordering if recent results not available**
Situation-specific (blood): thiamine; treponemal Abs; HIV 1/2 Ab/Ag; rheumatologic labs; autoimmune encephalopathy panel	**Informed by social history, general medical illness, time course**
Situation-specific (CSF): protein, glucose, cell counts; IgG index, oligoclonal bands; autoimmune encephalopathy panel; cytology, flow cytometry,, IL-10; VDRL, viral PCRs/cultures, bacterial, mycobacterial, fungal stains/cultures, BioFire array; 14-3-3	**Informed by history, time course, associated symptoms/signs; usually conducted inpatient**

Labs: Molecular Biomarker and Genetic

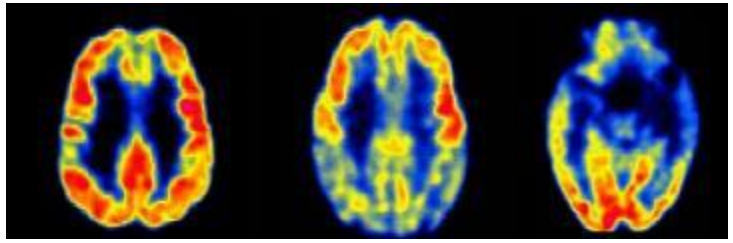
Labs	Utilities/Comments
CSF: Abeta42, total tau, p-tau181; alpha-synuclein RT-QuIC*; IgH gene arrangement, *MYD88* analysis	CSF amyloid and tau has comparable diagnostic accuracy to amyloid PET
Plasma p-tau217, Abeta 42/40*	Increasingly used in clinical research; need more validation for clinical use
Skin biopsy: alpha-synuclein	Useful in Parkinson disease, dementia with Lewy bodies, multiple system atrophy
Apolipoprotein E (*APOE*) genotype	Useful for risk stratification for patients receiving amyloid-lowering immunotherapies; not sensitive or specific for AD
Genetic: Amyloid Precursor Protein (*APP*), Presenilin 1 (*PSEN1*), Presenilin 2 (*PSEN2*) mutations	Useful when family history suggests an autosomal dominant pattern of inheritance
Genetic: Progranulin (*GRN*), Microtubule-associated protein tau (*MAPT*) mutations; *C9orf72* repeat expansion	Most common autosomal dominant gene mutations associated with FTLD

Appropriate use criteria, CSF AD biomarkers: Shaw *Alzheimers Dement* 2018

Extended Imaging: Neurodegeneration

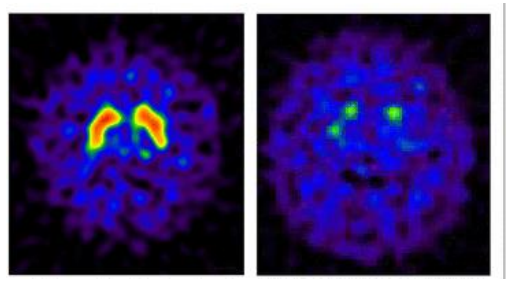
Modalities	Utilities	Limitations
^{18}F-fluorodeoxyglucose (FDG) PET	- Discriminate syndromic FTD, AD, DLB with some predictive value for underlying neuropathology - Discriminate degenerative from non-degenerative cognitive impairment (negative predictive value)	- Lack of molecular specificity - Potential for false-positive results (e.g., asymptomatic *APOE4* carriers) - Variable insurance coverage for non-Medicare patients and indications other than discriminating FTD from AD
^{18}F-fluorodopa PET dopamine transporter (DaT) imaging	- Discriminate degenerative from non-degenerative (e.g., vascular, medication-induced) parkinsonism	- Lack of molecular specificity - Does not discriminate between neurodegenerative conditions causing parkinsonism

FDG-PET



Normal | AD syndromes | FTD syndromes

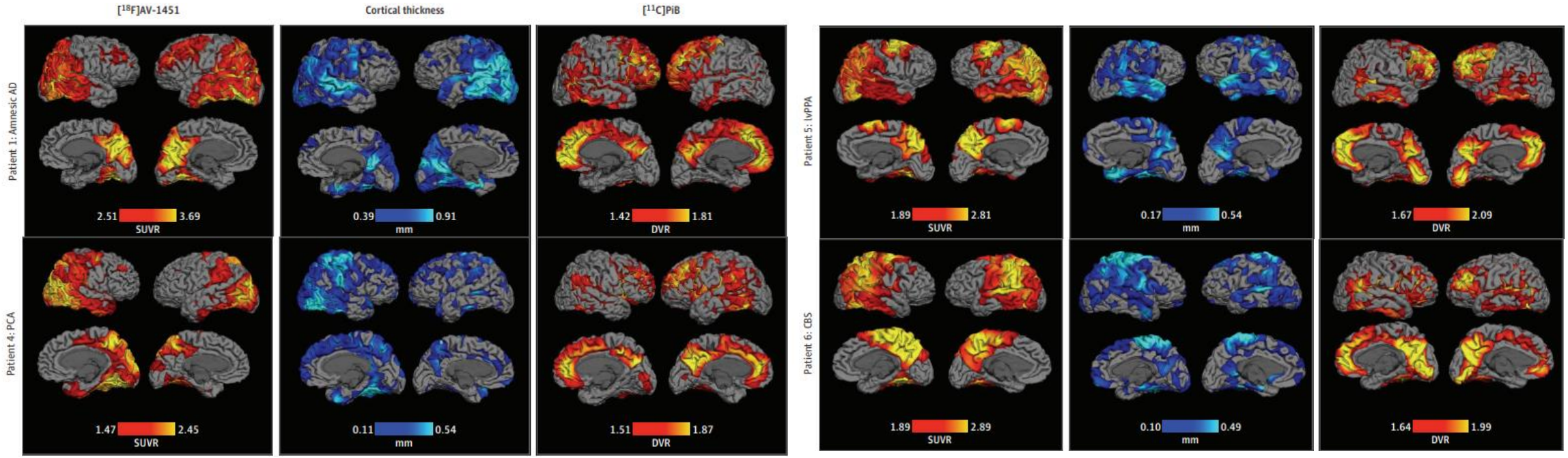
Dopamine transporter imaging



Normal | Degenerative

Extended Imaging: Molecular Pathology

Modalities	Utilities	Limitations
^{18}F-Amyloid PET (florbetapir, florbetaben, flutemetamol)	- Detect fibrillar beta-amyloid with high sensitivity and specificity against neuropathological gold standard). - FDA-approved and covered by Medicare	- Elevated fibrillar beta-amyloid does not equate to a diagnosis of AD (necessary but not sufficient)
^{18}F-Tau PET (Flortaucipir)	- Provides information about not only molecular pathology but also topography, pertinent to disease stage and phenotype. - Substantially elevated uptake in neocortical regions is highly predictive of elevated beta-amyloid.	- FDA-approved but not covered by insurance



Appropriate use criteria, amyloid PET: Johnson *Alzheimers Dement* 2013

Additional Studies, Referrals

Studies, Referrals	Utilities/Comments
Neuropsychology	Establish, clarify cognitive profile; longitudinal time course; time to wait for evaluation is frequently long
Audiology	Hearing correction liberates attention, working memory resources
Ophthalmology, Neuro-ophthalmology	Evaluate basic vision in cases of visual hallucinations, higher visual deficits
Electroencephalogram (EEG): routine, long-term ambulatory	Evaluate paroxysmal symptoms; AD increases risk of focal seizures; useful in Lewy body disorders d/t fluctuations and inattention
Polysomnogram ± Sleep Medicine referral	Evaluate for obstructive sleep apnea; RBD
Electromyogram, nerve conduction studies (EMG/NCV) ± Neuromuscular referral	Evaluate for motor neuron disease
Autonomic testing (Autonomic neurology referral)	Evaluate for dysautonomia
Direct admission to inpatient neurology service	Expedite workup for rapidly progressive dementia