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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

APPROACH TO NEUROCOGNITIVE DISORDERS

IAN COULTER, MD

UNIVERSITY OF WASHINGTON

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

SPEAKER DISCLOSURES

✓ No conflicts of interest

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

Mark Duncan MD
Barb McCann PhD
Matt Iles-Shih, MD, MPH
Kari Stephens PhD
Jen Jepsen, PharmD
Justin C Bayley, DNP
Trudy Mossop MS
Betsy Payn MA PMP
Anna Ratzliff MD PhD
Esther Solano

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OBJECTIVES

1. Understand the basics of localization theory in behavioral neurology/neuropsychiatry

2. Grasp the descriptive hierarchy in neurodegenerative disorders

3. Develop an approach to diagnostic logic based on defining the initial symptom

4. Understand specific ancillary tests

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LOCALIZATION THEORY

- A patient presents with a symptom or set of symptoms
- Generate a set of hypotheses about what part(s) of the nervous system may be involved
- Use the exam to empirically challenge those hypotheses and yield a **“location”** or **“localization”**
- The historical features (speed of onset, evolution, exacerbating or alleviating factors) contextualized by the localization generate the differential diagnosis
- Ancillary testing (imaging, EEG, EMG, etc) probe the likelihood of different diagnoses in the differential

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AN OUTLINE OF AN APPROACH

- Establish the nature of the cognitive/behavioral syndrome
- **Localize the syndrome**
- Establish the time course

- A localized syndrome + time course yields a differential diagnosis

- Ancillary testing can probe this differential (does MRI show atrophy pattern in regions which you have localized to?)

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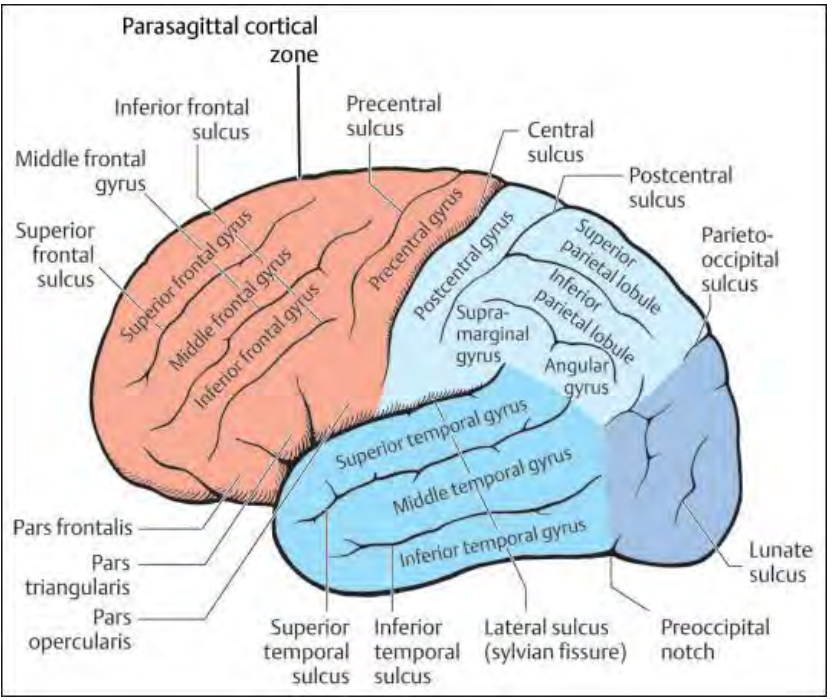
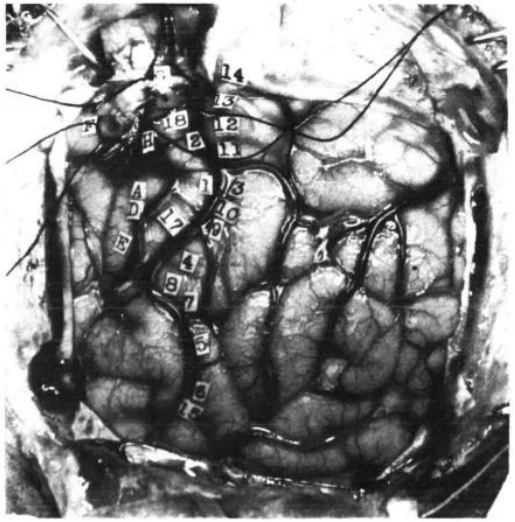
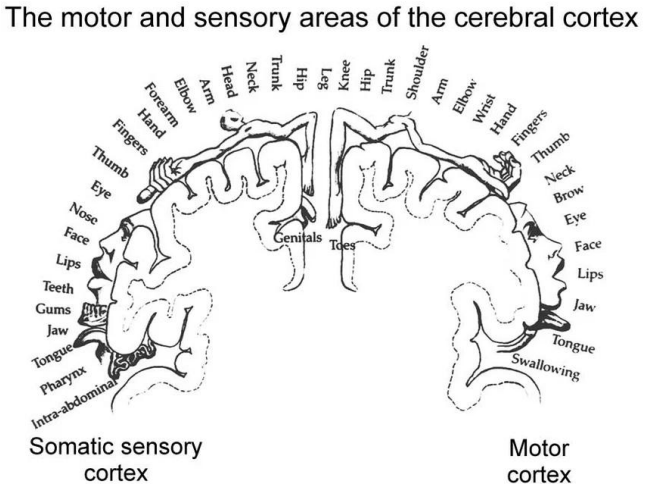
WHAT IS A “LOCATION”?

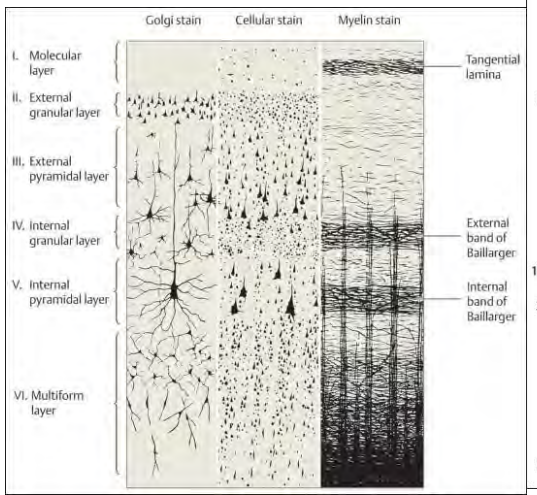


Gross (macroscopic)

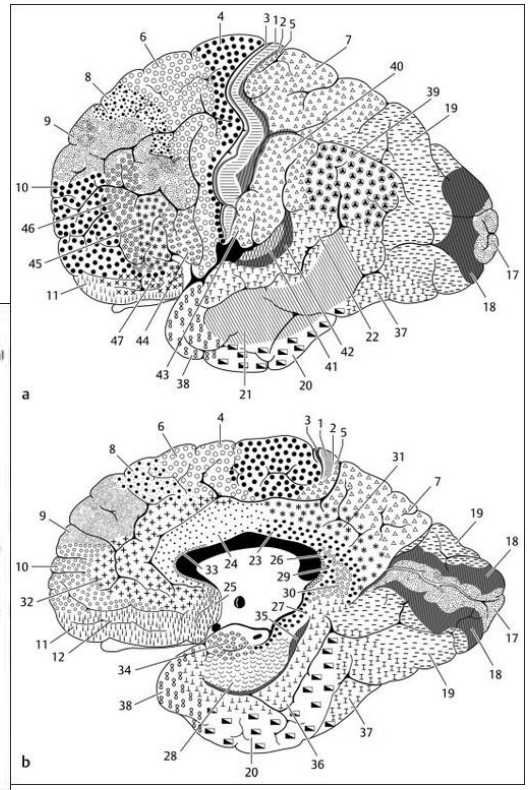


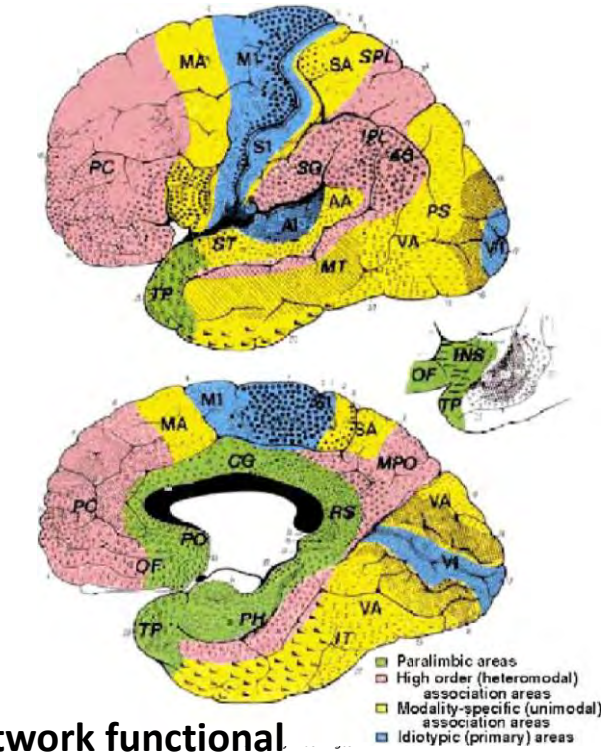


Modular functional



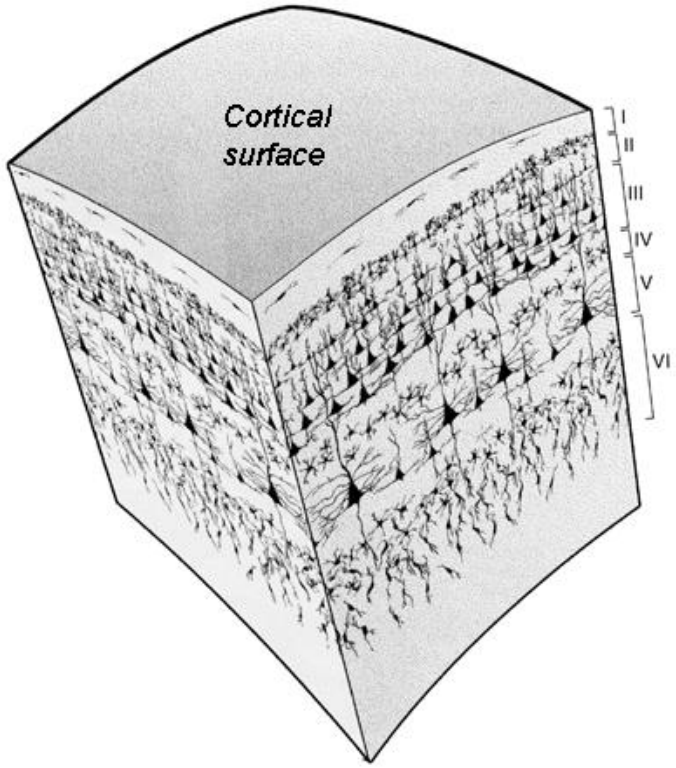
Cytoarchitectural (microscopic)

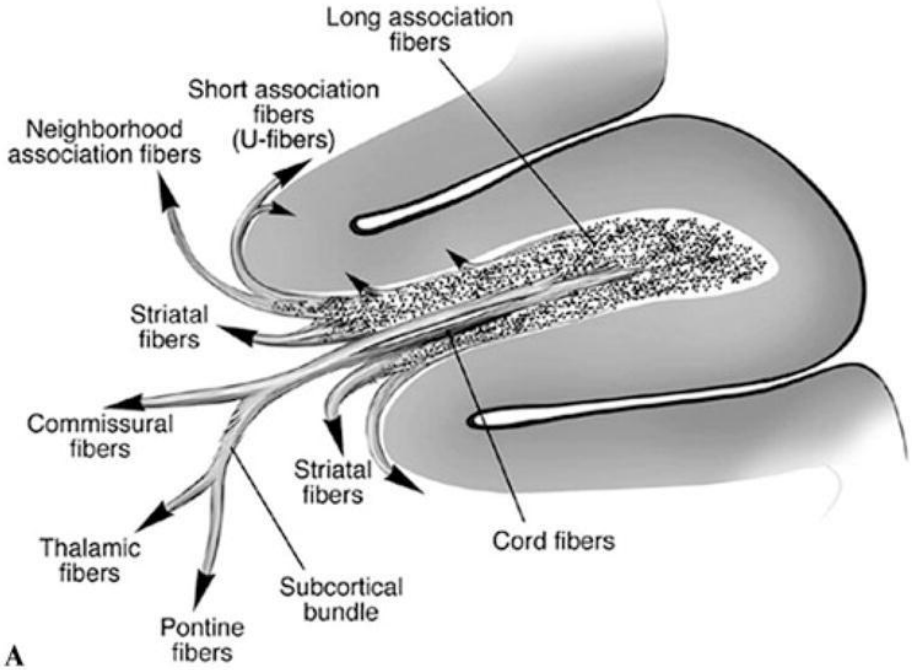


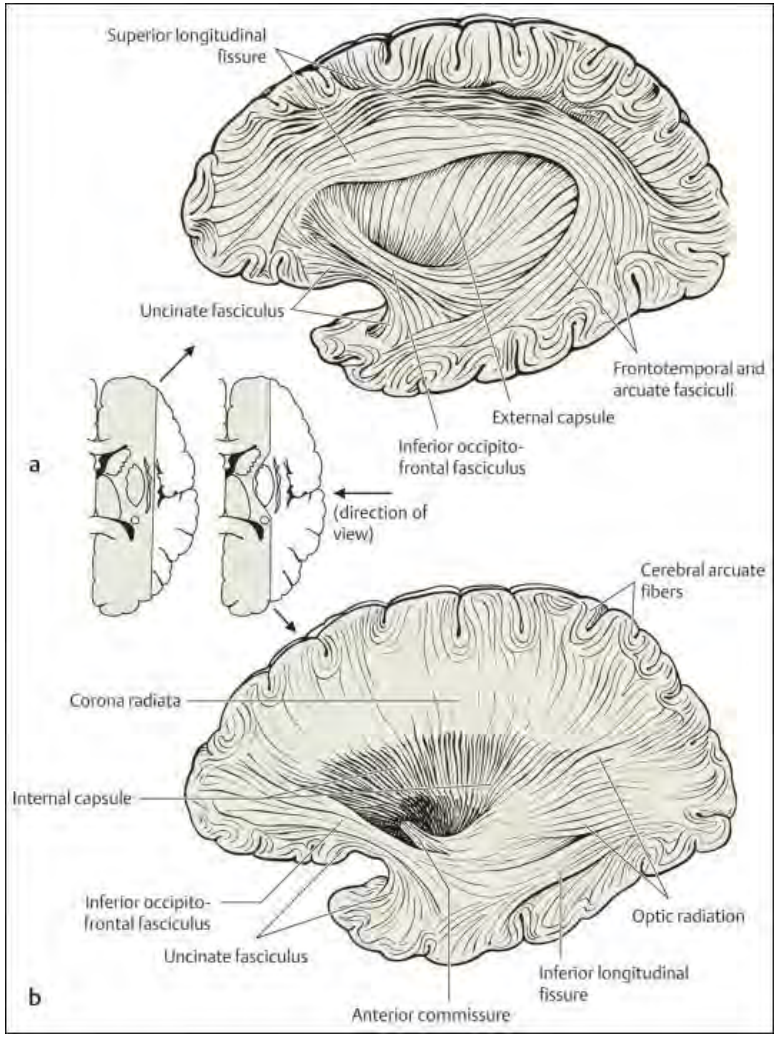


Anatomical network functional

THE NERVOUS SYSTEM IS ORGANIZED INTO NETWORKS OF INTERCONNECTED BRAIN REGIONS







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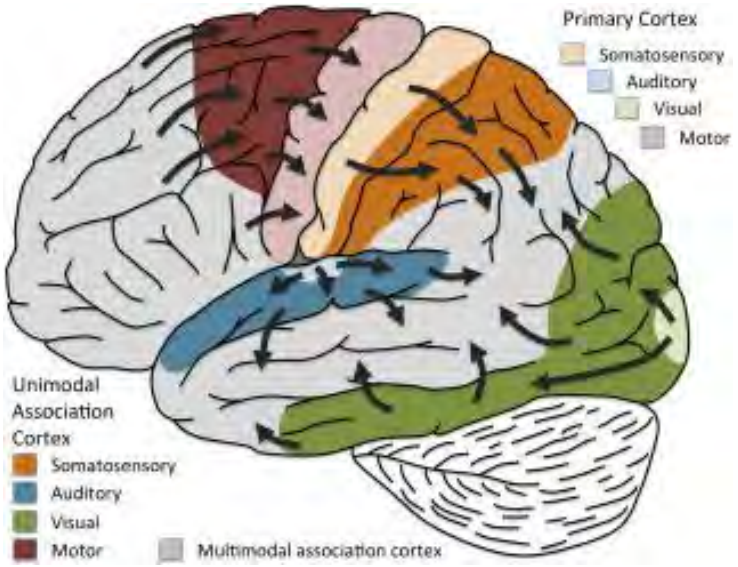
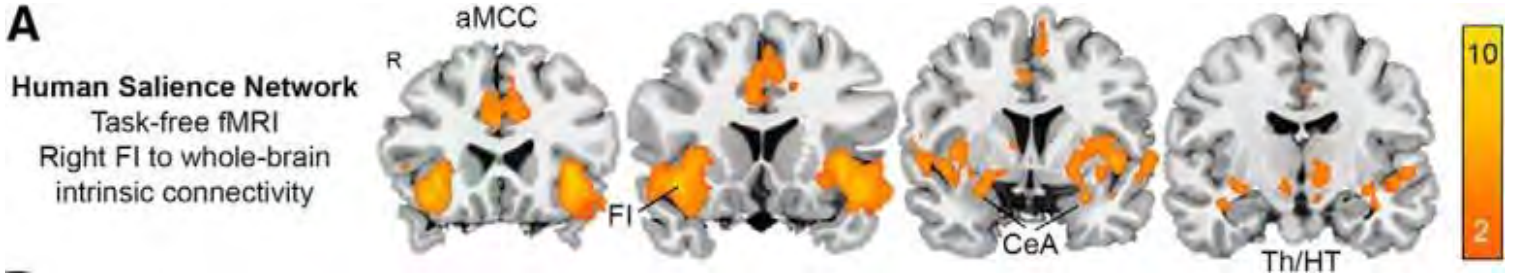
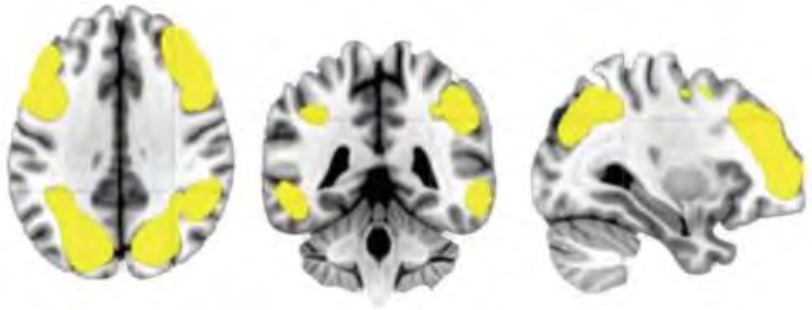
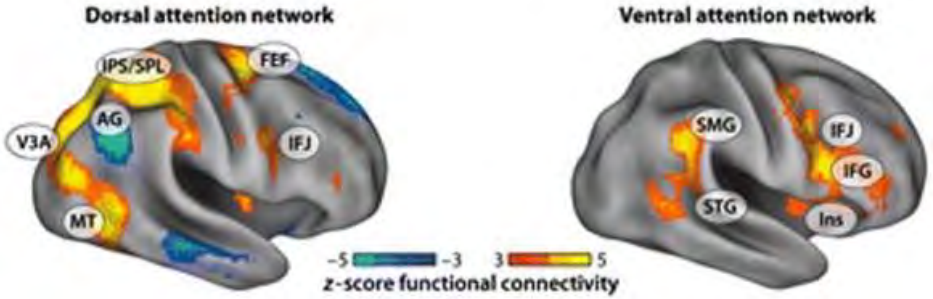
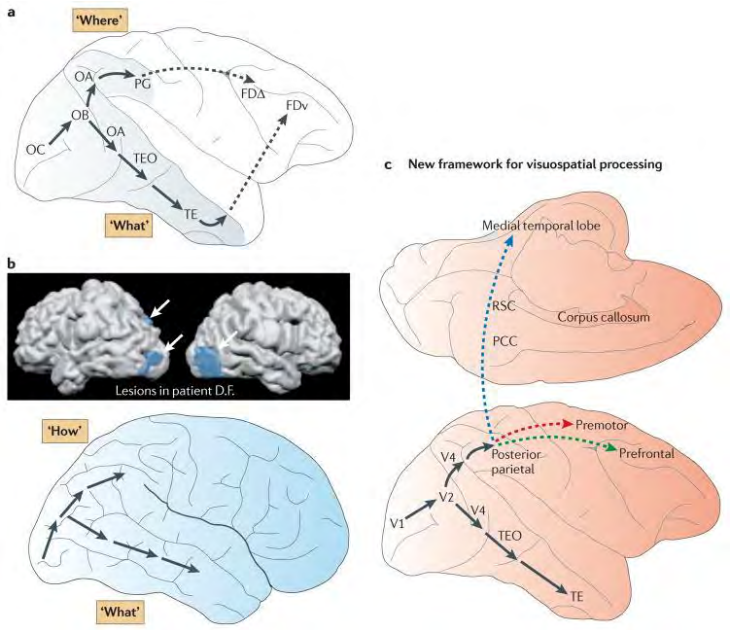


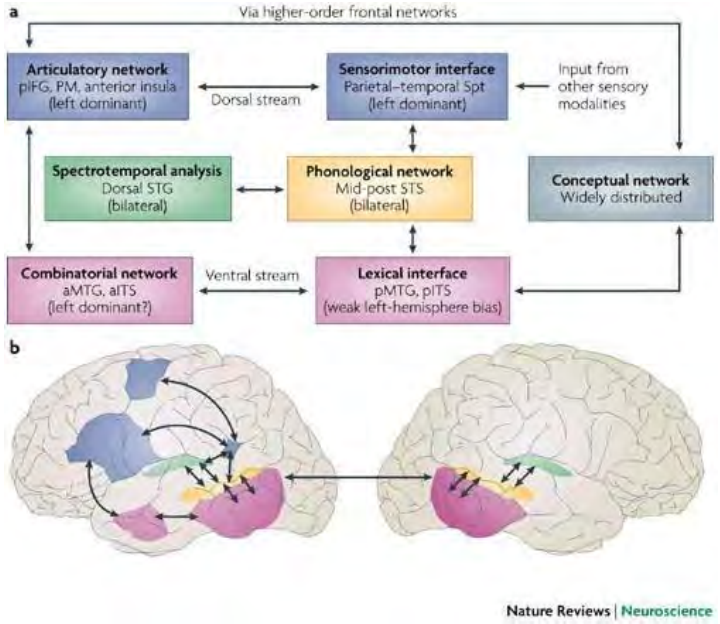


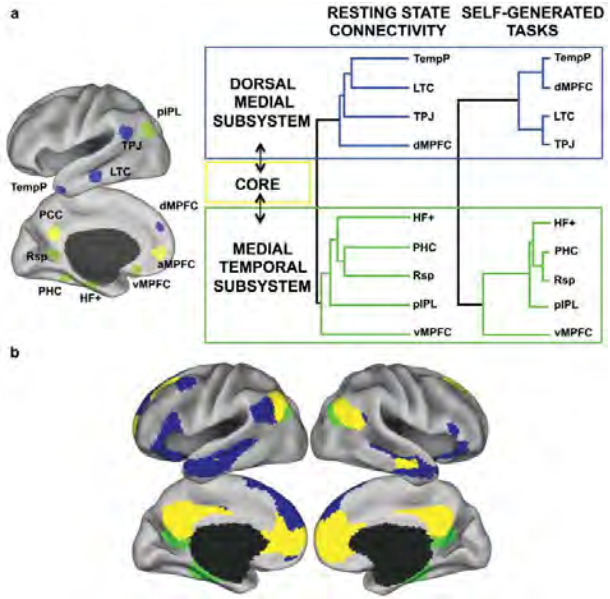
Central Executive Network



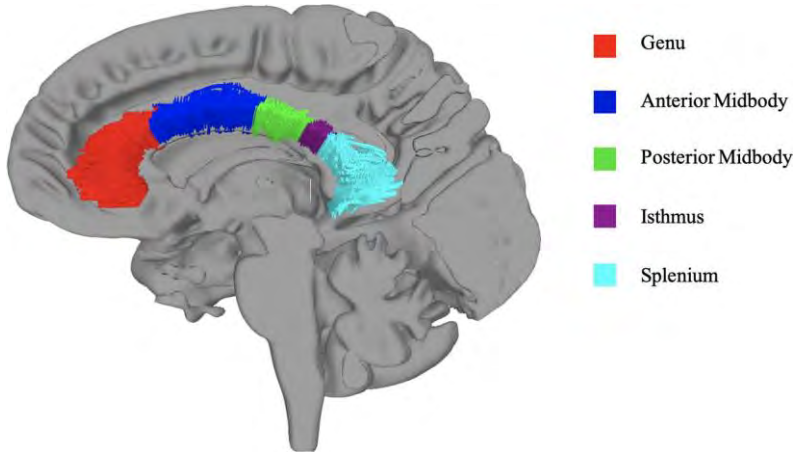


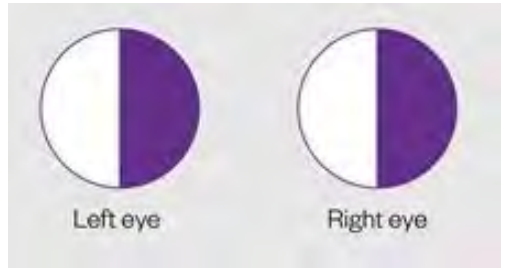


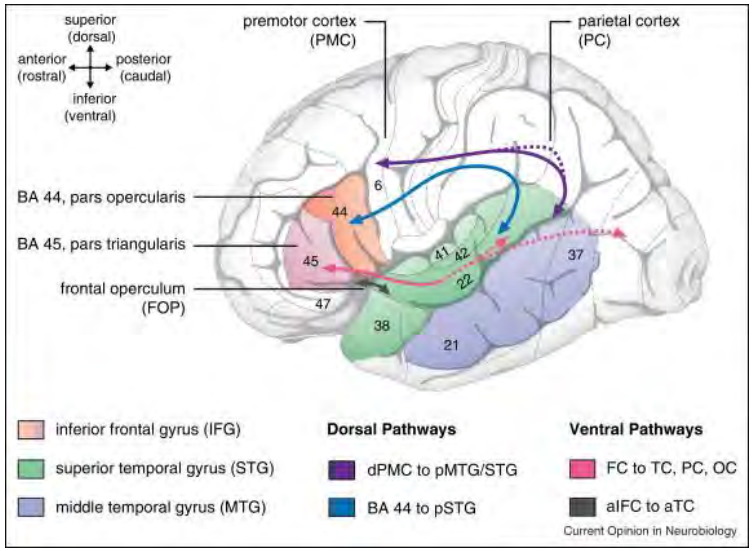


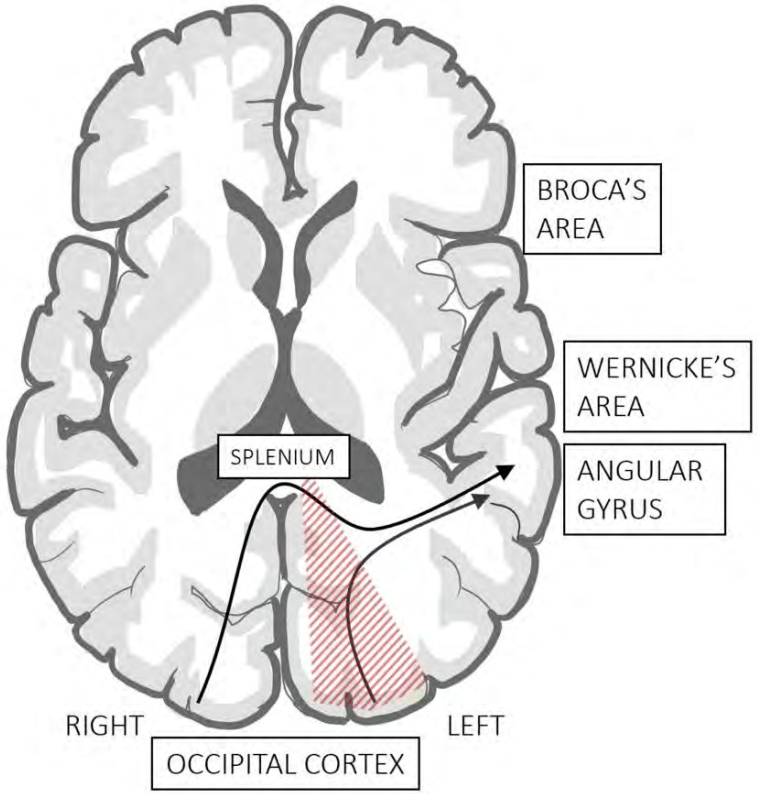


CASE EXAMPLE: ALEXIA WITHOUT AGRAPHIA

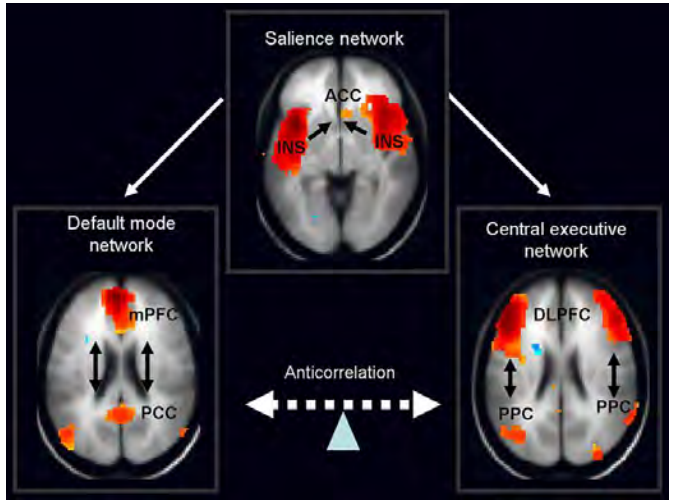


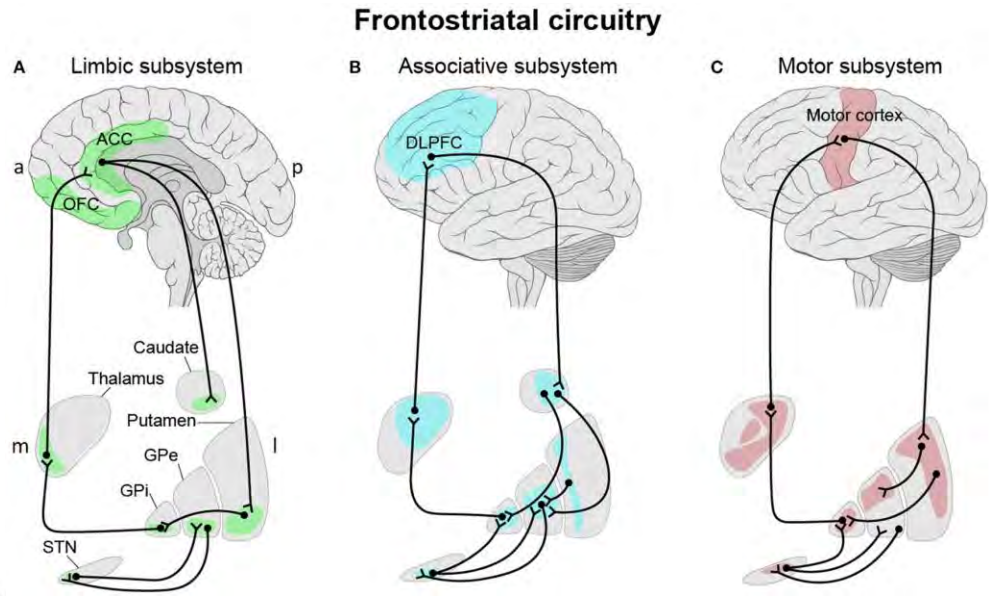


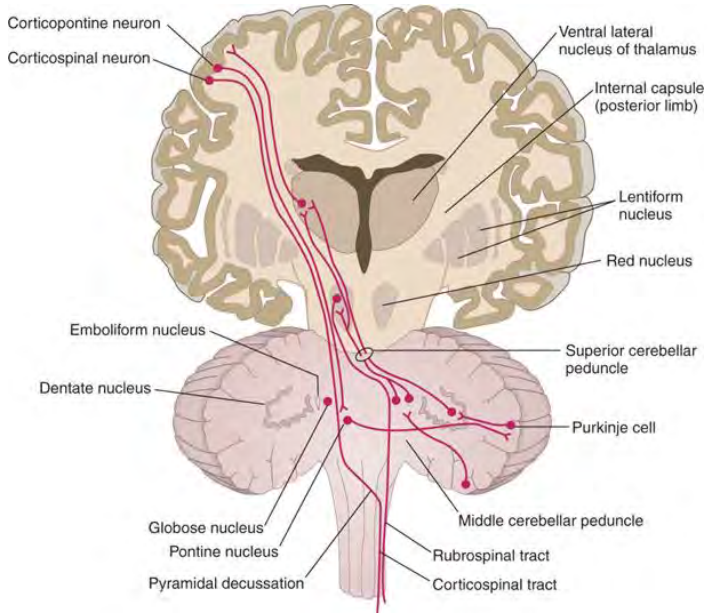




CASE EXAMPLE: EXECUTIVE DYSFUNCTION







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AN OUTLINE OF AN APPROACH

- Establish the nature of the cognitive/behavioral syndrome
- Localize the syndrome
- **Establish the time course**

- A localized syndrome + time course yields a differential diagnosis

- Ancillary testing can probe this differential (does MRI show atrophy pattern in regions which you have localized to?)

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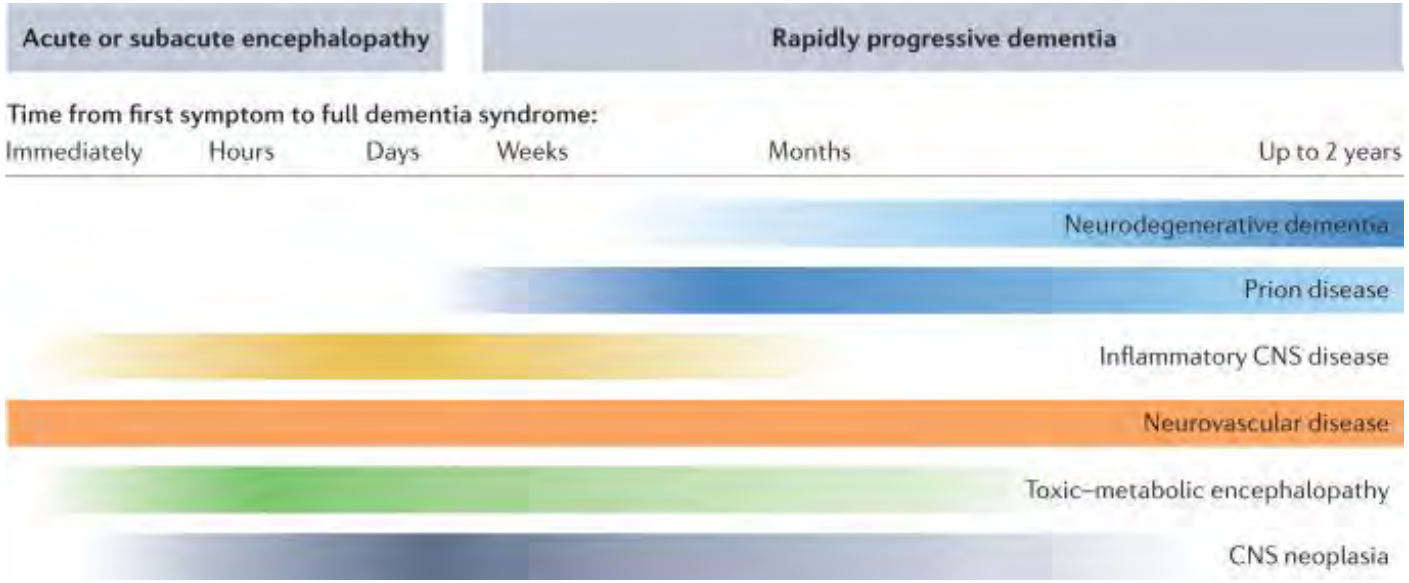
TIME COURSE



- Acute/Subacute (weeks to months to dementia)
  - Delirium
  - Rapidly progressive dementia
    - Prion, autoimmune/inflammatory, infectious, neoplastic, toxic/metabolic
    - Neurodegenerative diseases

- Insidious
  - Neurodegenerative
    - AD, LBD, tau, TDP-43, FUS
  - Non-progressive
    - Monophasic injury like stroke
    - Developmental

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TERMS AND DESCRIPTIVE HIERARCHIES

- Mild Cognitive Impairment
  - Objective cognitive impairment, no/minimal functional impairment

- Dementia
  - Mild: objective cognitive impairment + iADL impairment
  - Moderate: objective cognitive impairment + at least 1 ADL impairment
  - Severe: objective cognitive impairment + multiple ADL impairment

- The MoCA score does not, independently, diagnose MCI or dementia. These are terms which describe how cognitive impairment impacts functional level.

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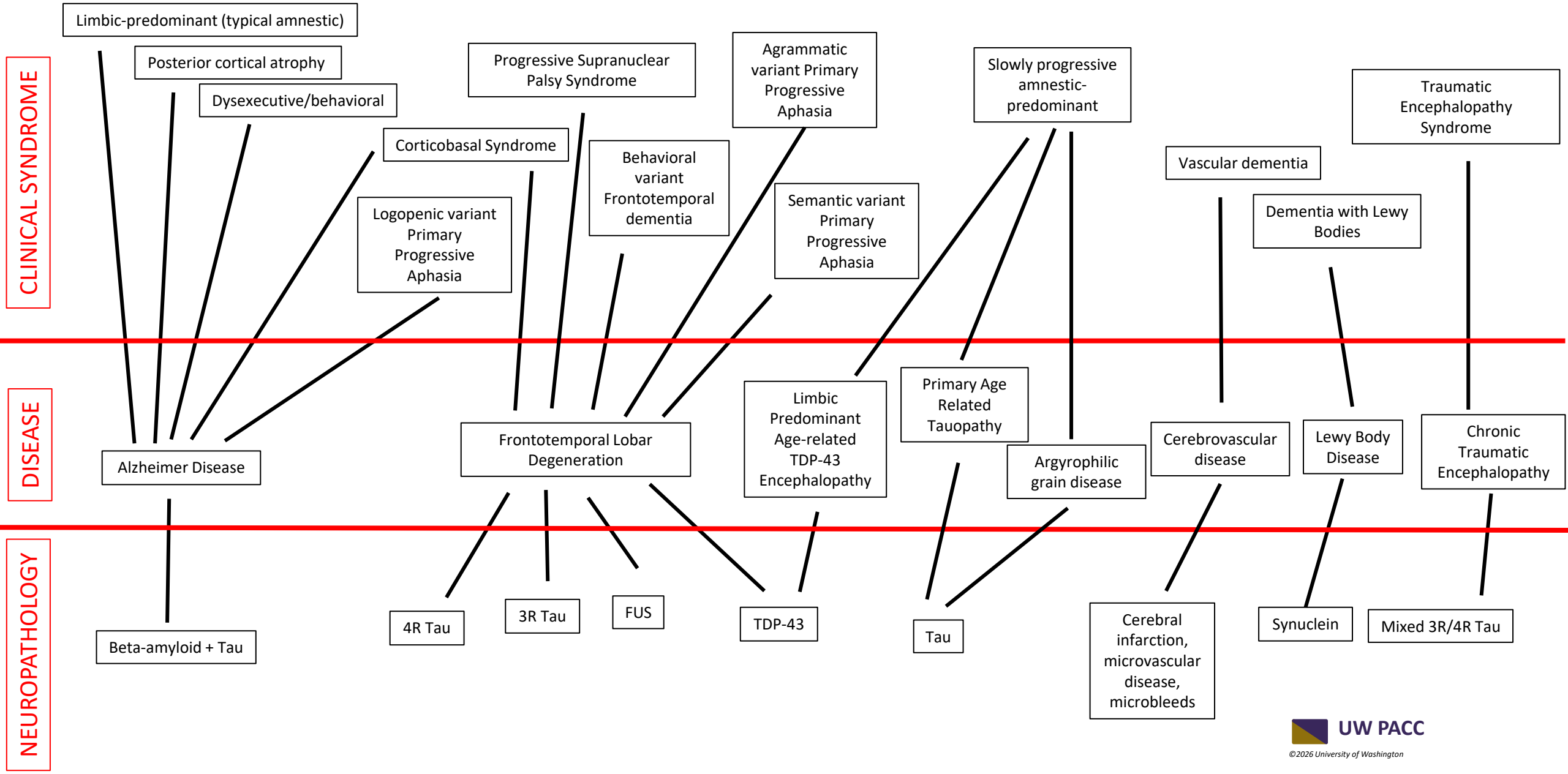

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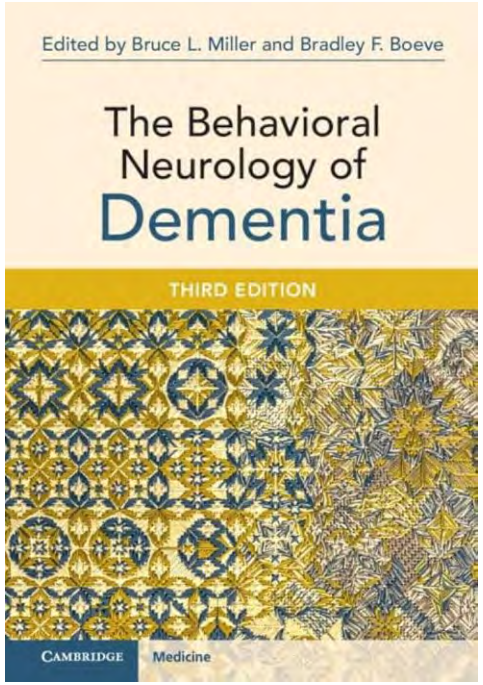
“I HAVE A THINKING PROBLEM”

- Onset
  - Start with the onset of even subtle symptom
  - This symptom implies (via localization) the neurological region where pathology began
    - Memory: hippocampal and DMN networks (AD)
    - Disinhibition: orbitofrontal/striatal networks (FTD)
    - Visual hallucinations: visual association networks (LBD)
- Evolution
  - Progressive? Slow or rapid? Fluctuations?
  - Accumulation of particular symptoms implies spread of pathology to different brain regions
- Cognitive domains
  - Directed questions

Cognitive domain	Corresponding localization	Sample questions
Memory	Mesial temporal lobes Medial thalamus, basal forebrain, and other elements of Papez's circuit	Does he/she recall the details of recent events or upcoming appointments or social engagements? Tend to repeat questions?
Attention/ Concentration	Frontal +/− temporal lobes and subcortical connections	Does he/she struggle to maintain attention or focus?
Executive functions	Frontal +/− temporal lobes and subcortical connections	Does he/she have difficulties planning and reasoning? Managing multiple tasks around the same time? Completing multistep sequential tasks?
Social cognition	Frontal +/− temporal lobes and subcortical connections	Does he/she demonstrate poor judgment? Behave in a socially inappropriate, overly joyful, or markedly sedentary manner? Behave as if he/she does not have empathy for others?
Language	Dominant hemisphere (usually left) frontotemporoparietal	Does he/she struggle to recall the names of individuals or objects? To express his/her thoughts? To understand oral or written information?
Limb praxis	Dominant hemisphere (usually left) parietal or mesial frontal	Is he/she able to use eating utensils or tools correctly? Move the limb in a coordinated manner?
Dressing praxis	Nondominant hemisphere (usually right) parietal	Does he/she have trouble putting clothes on correctly?
Visuospatial functions	Non-dominant hemisphere (usually right) parietal	Does he/she get lost in the home, stores, or while driving?
Vision, reading	Parieto-occipital (ensure no ocular pathology accounts for impaired reading or vision)	Does he/she have trouble reading? Trouble with depth perception? Trouble seeing objects in his/her peripheral fields?
Speed of thought	Frontosubcortical circuits	Does he/she seem to think much slower?



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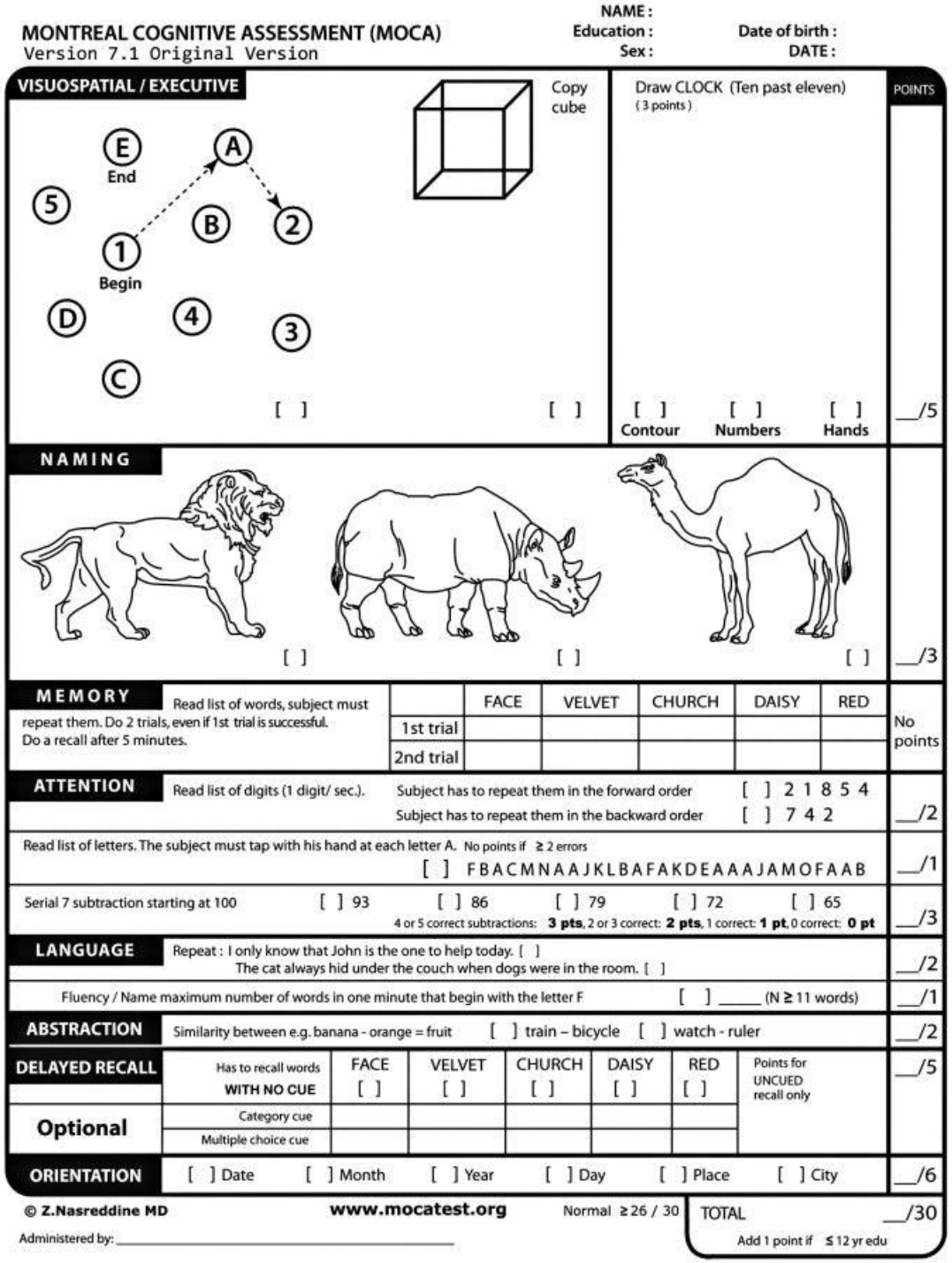
“I HAVE A THINKING PROBLEM”

- Noncognitive domains
  - Neuropsychiatric features (apathy, social disinhibition, hallucinations)
  - Motor phenomenon (tremor, bradykinesia, falls)
  - Autonomic symptoms (constipation, orthostatic hypotension, erectile dysfunction)
  - Sensory issues (decreased smell, hearing, vision, touch)
- Comorbid conditions
- Exposures
  - Head injuries, drugs, alcohol
- Medications
  - Centrally acting medications
  - Ask about sleep meds with anticholinergic properties (Benadryl, doxylamine)
- Family history
  - Dementia (cardinal features)
  - Parkinsonism, motor neuron disease, psychosis



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE

Copy cube

E End
A
5
B
2
1 Begin
D
4
3
C

[ ] [ ]

Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS
/5

NAMING

[ ] [ ] [ ]

/3

MEMORY
Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful.
Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION
Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2
/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B
/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**
/3

LANGUAGE
Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]
/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)
/1

ABSTRACTION
Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler
/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

/5

ORIENTATION
[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City
/6

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL /30
Add 1 point if ≤ 12 yr edu

Administered by: _____

- "This is a thinking test not an intelligence test. Very smart people can do poorly on this. The goal is to assess your relative strengths and weakness and see if there is a pattern. Thus, some of these questions may be very easy and some may be surprisingly challenging, it just depends"
- Executive dysfunction/inattention can show up in a number of ways
  - Poor trails testing, impulsive connections
  - Poor strategy for figure drawing (look at how they construct the clock to judge if visuospatial issue)
  - Semantic fluency > letter fluency (After seeing how my F-words they can recite then ask them to name animals in 1 minute)
  - For delayed recall do the category cue and MC cue and calculate the MIS. This can help determine if the memory loss is more encoding/consolation versus attention/retrieval based
- If the cognitive syndrome cannot be determined, then neuropsych testing may be useful

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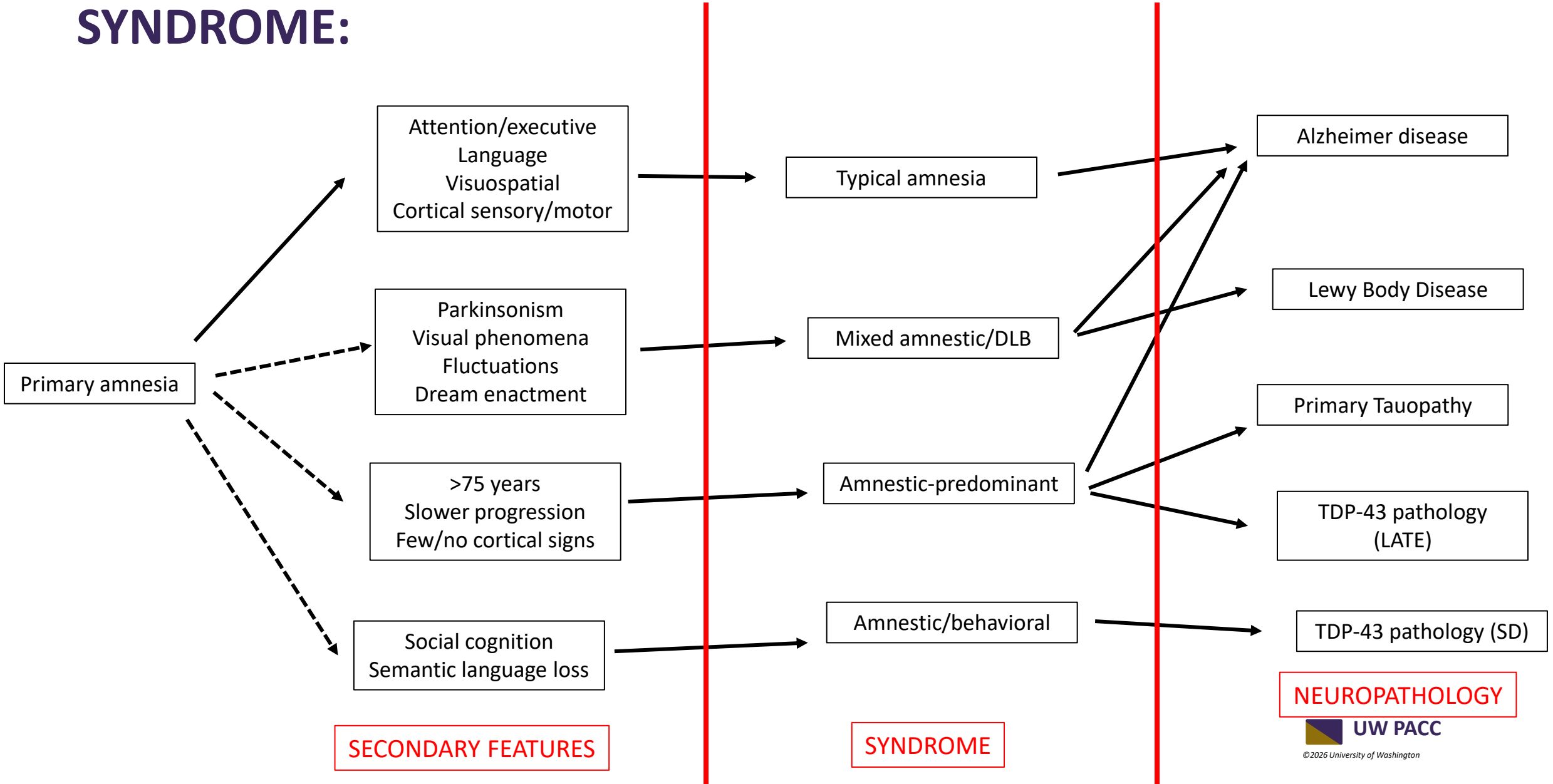
*This is simplified

WITH AN UNDERSTANDING OF FIRST/MOST PROMINENT SYNDROME:



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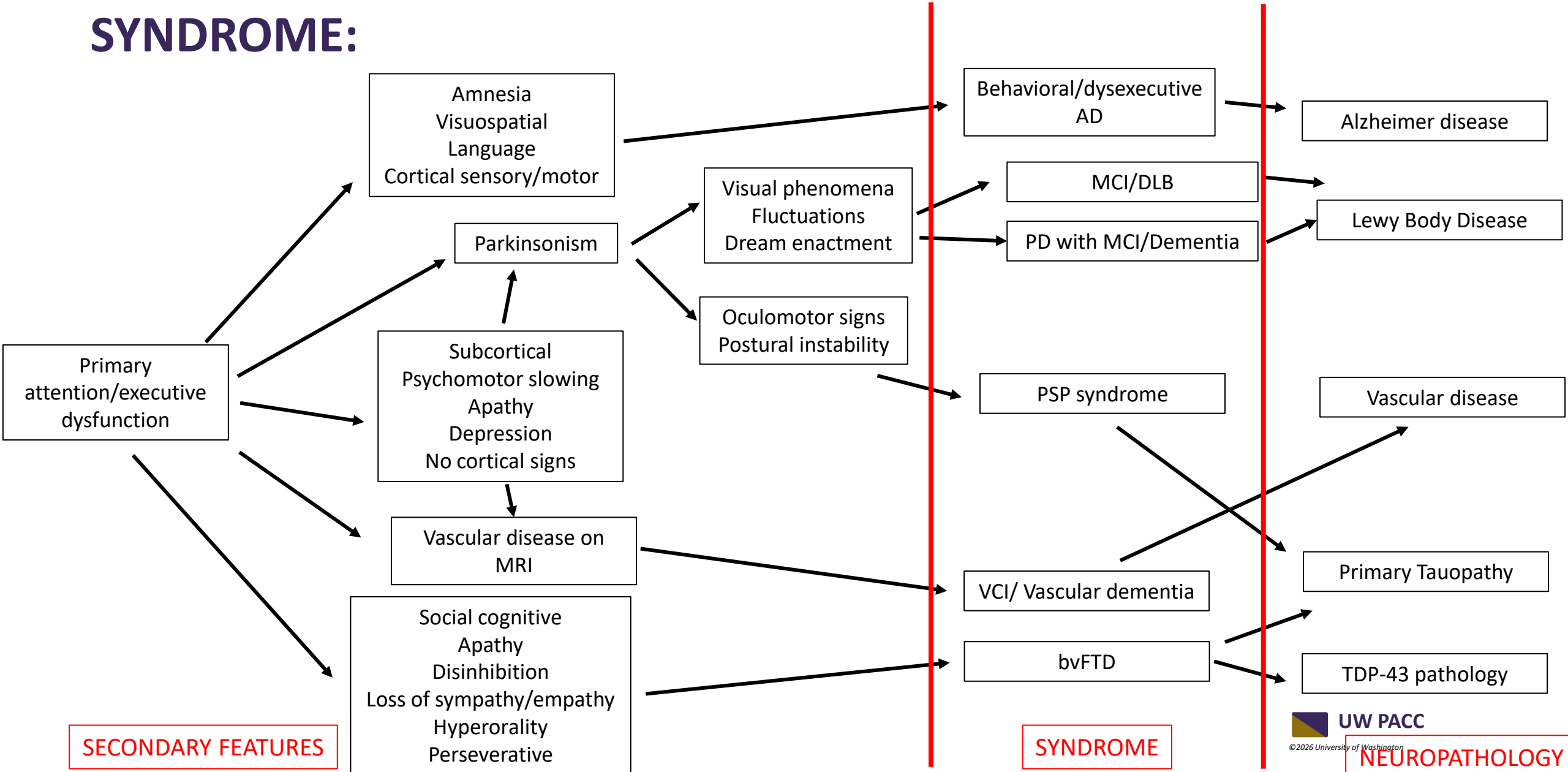

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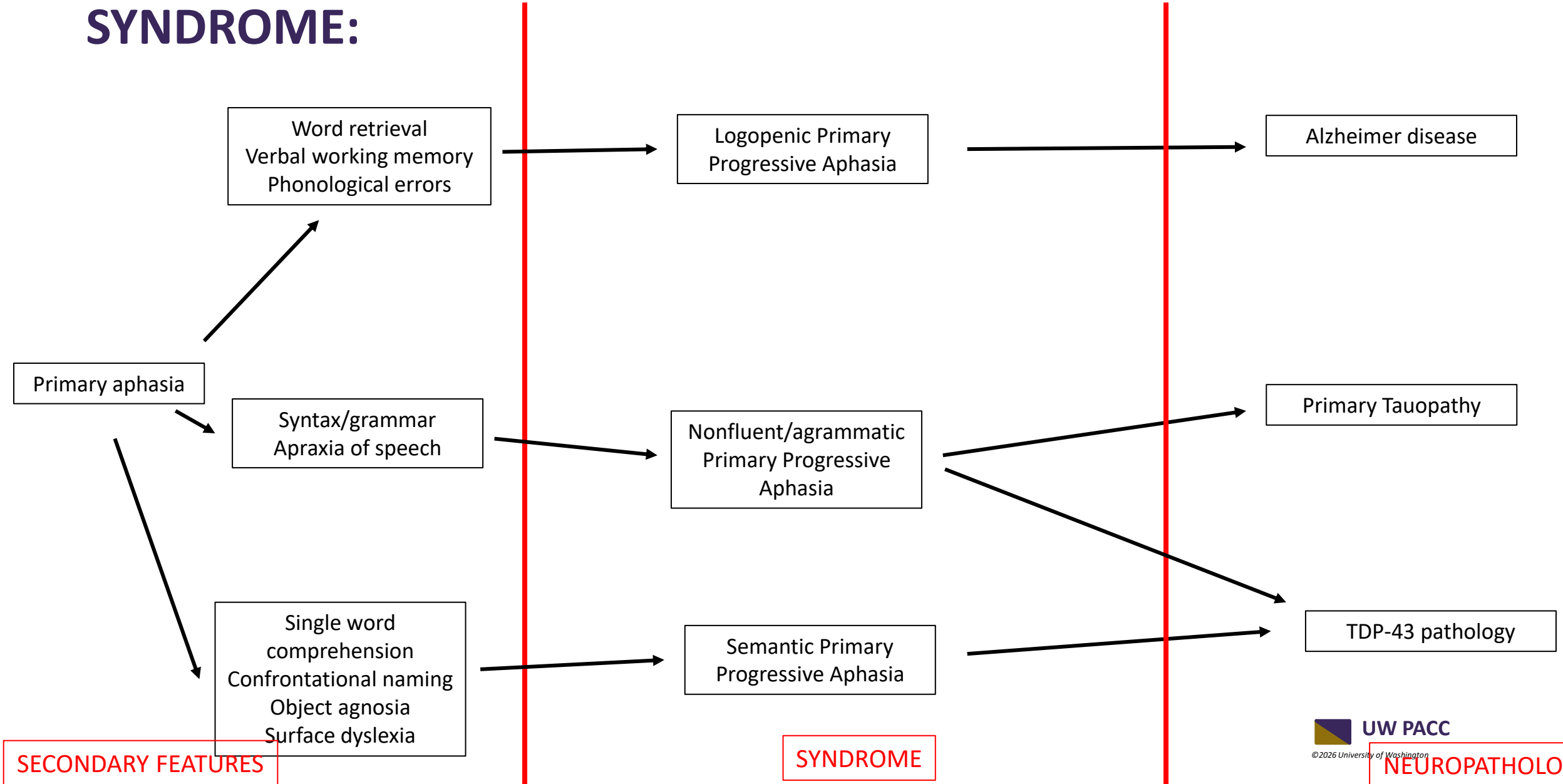

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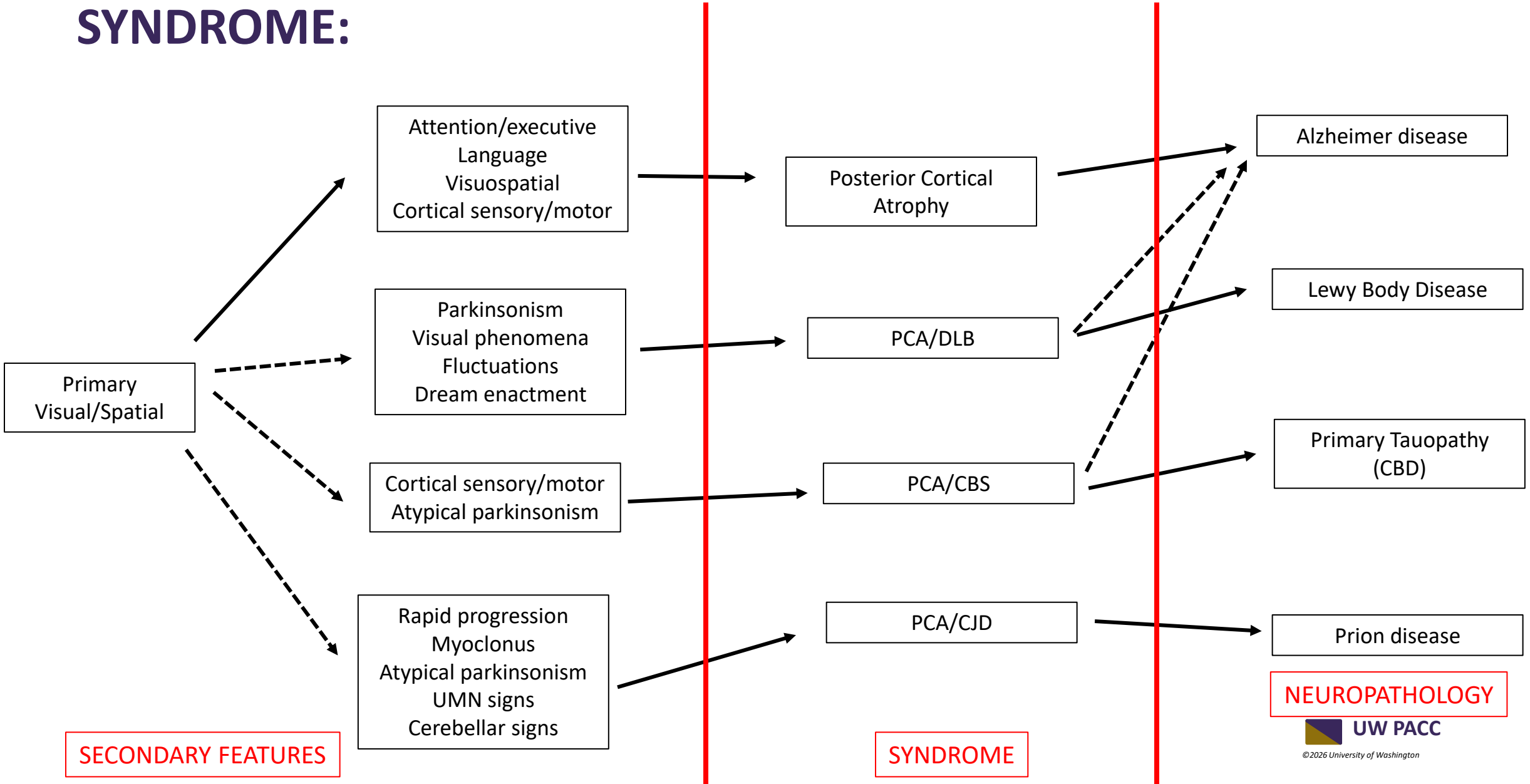

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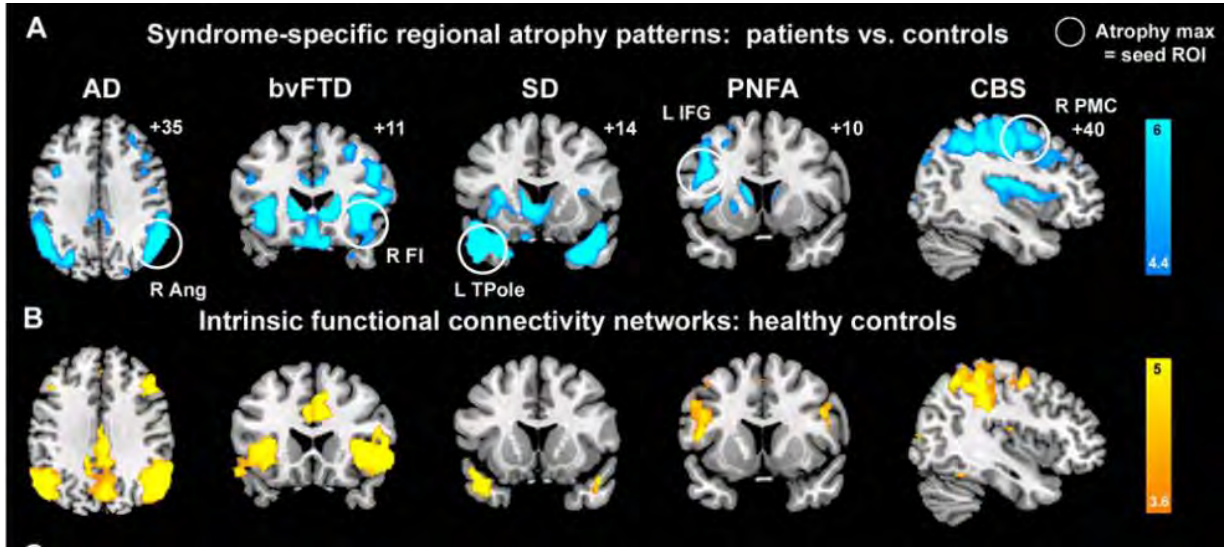
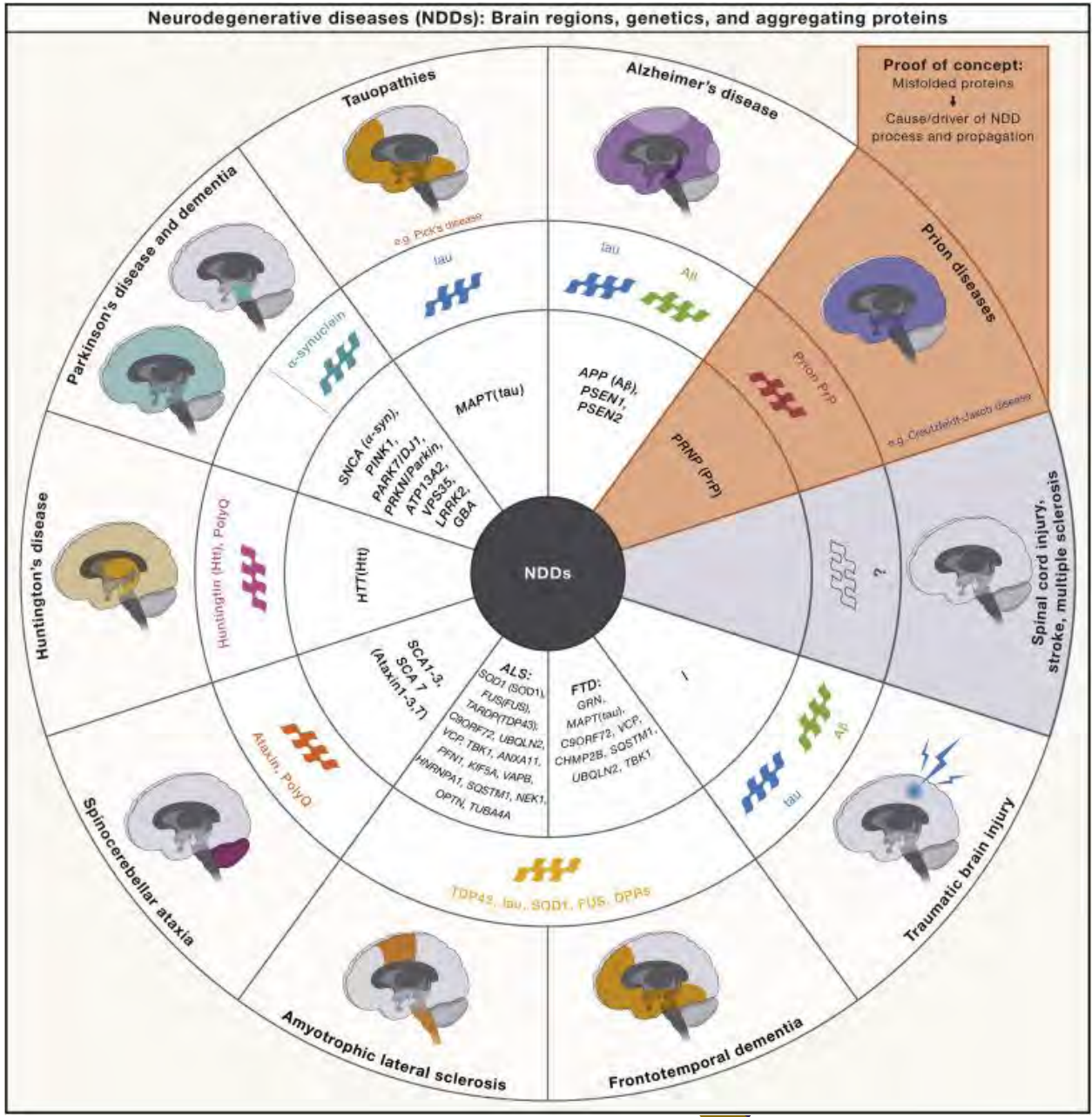
NETWORK SPREAD

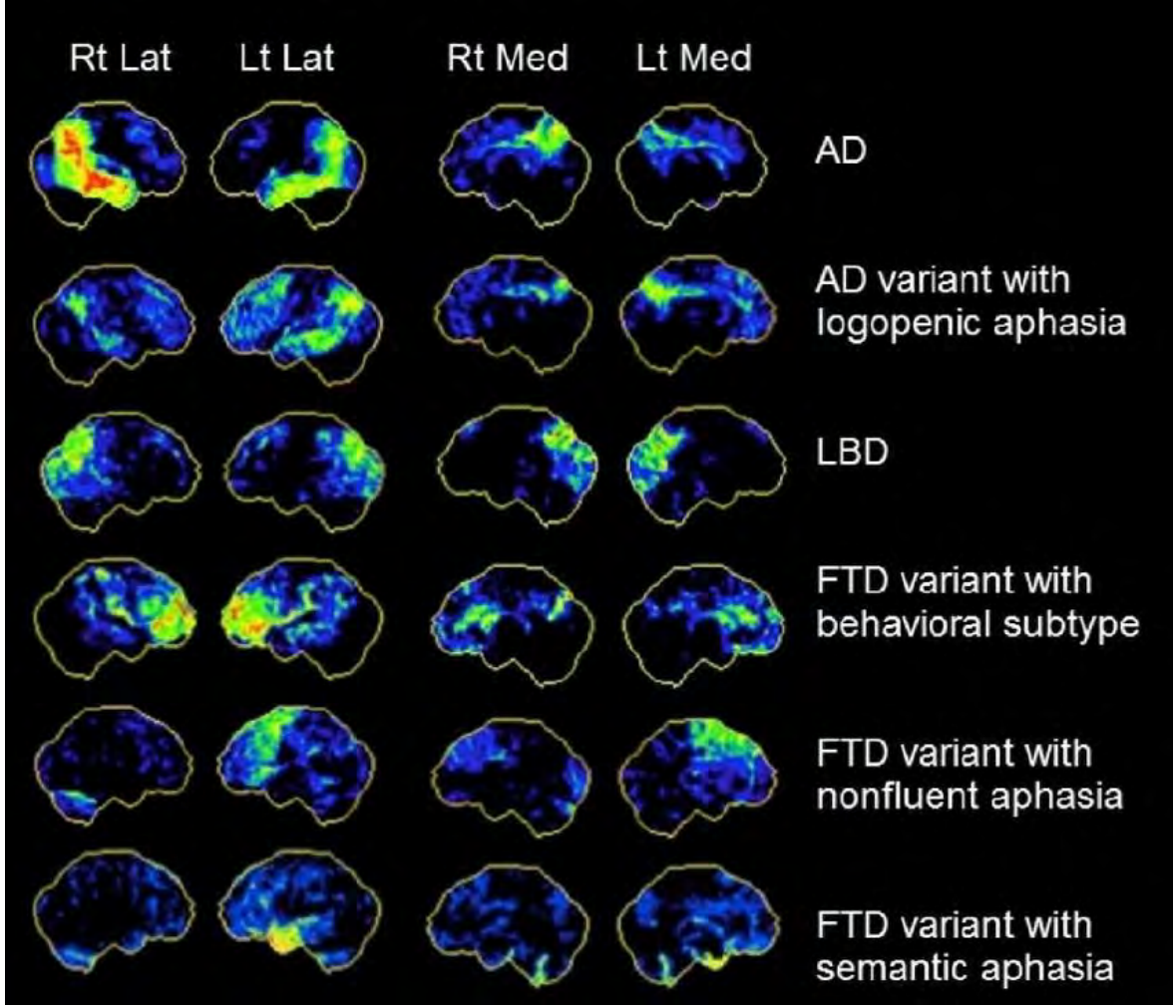




Wilson et al. Hallmarks of neurodegenerative diseases. 2023.

ANCILLARY TESTING

- MRI
  - Atrophy pattern, microvascular disease, microbleeds, old injuries
- FDG-PET scan
  - Helpful if the syndrome is hard to define or if you have a syndrome but no clear corresponding atrophy pattern on MRI
- EEG
  - Seizures?
  - Delirium?
  - Periodic sharp wave complexes (prion disease)
- CSF
  - AD biomarker
  - Synuclein biomarker
  - Prion biomarker
  - Inflammatory markers
  - Malignancy



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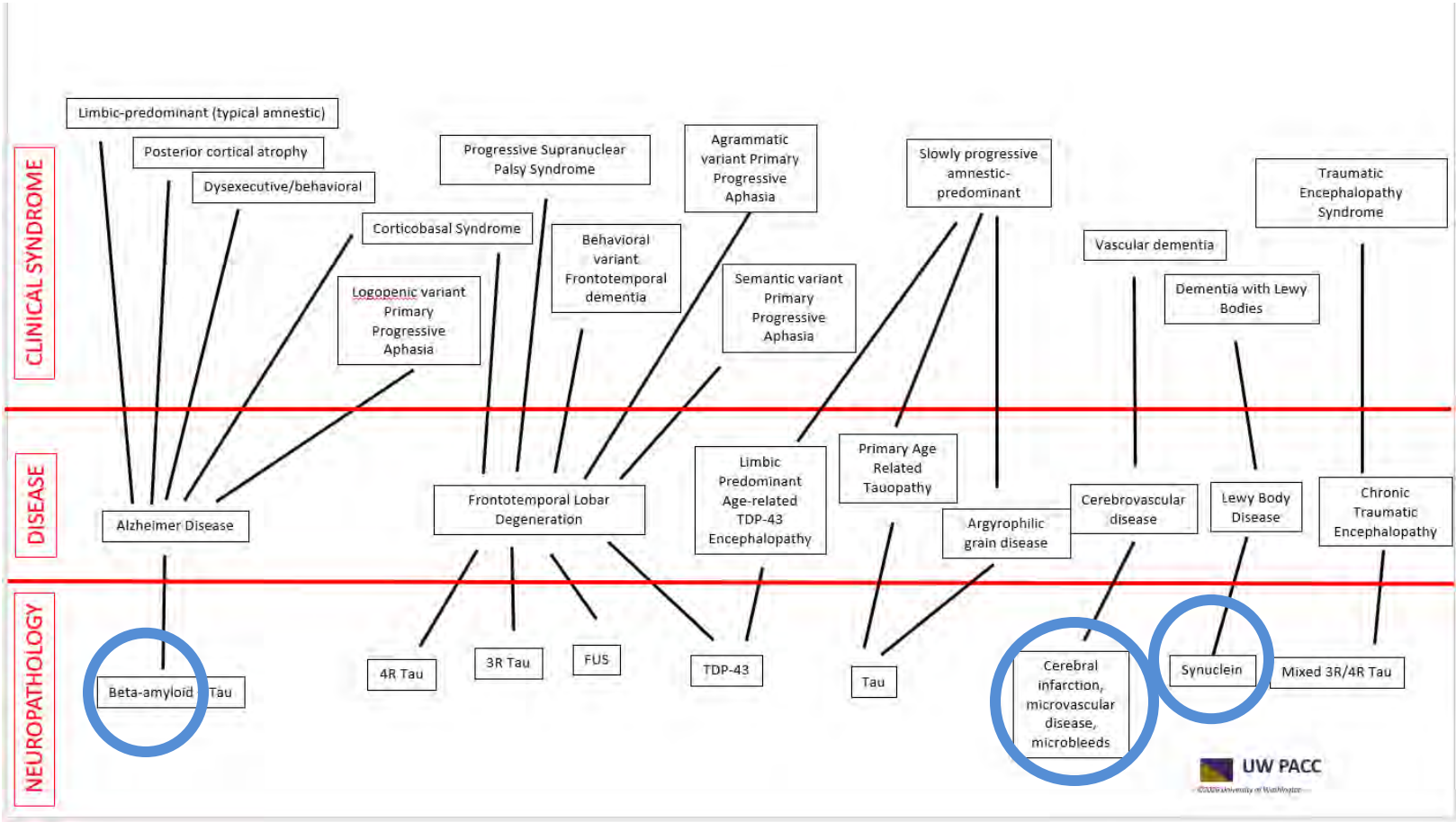
THE BIOMARKER ERA

- Amyloid biomarkers
  - Amyloid PET
    - "Gold standard"
    - Centiloid value for quantification
  - Plasma phosphorylated tau 217
    - 3 tiers
    - Effected by CKD, anemia, obesity, acute infection
  - CSF testing
    - Can check other things simultaneously (e.g. synuclein)



Why check AD biomarker?

- **Amyloid does not correlate directly with cognition. Only check it if there is a syndrome compatible with AD.**
- Diagnostic clarification
  - Symptom attribution
  - Prognosis
- Anti-amyloid therapy
  - Requires candidacy work-up
  - Not a cure
  - Modest slowing in progression

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DON’T FORGET

- Chronic pain, migraines
- Depression, anxiety, PTSD
- Insomnia, fragmented sleep, circadian rhythm disorder, parasomnia, sleep apnea
- Centrally acting medications (ask about OTC sleeping pills, THC)
- Low social/cognitive stimulating environment
- Hearing loss, vision loss

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SUMMARY

- An approach to neurocognitive disorders involves:
  - Establish a first symptom
  - Note the time course and trajectory of symptom accumulation/change
  - Use exam and cognitive testing to localize
  - Clinical history + localized syndrome = Differential diagnosis
  - Consider how entities on the differential may explain the various cognitive/behavioral symptoms
    - If the differential diagnosis includes treatable conditions (medications, poor sleep, sleep apnea, mood disorder, etc.) then address them
    - Symptom attribution is often inferential in this manner
  - Use ancillary testing to corroborate/challenge the remaining hypotheses on the differential
    - All tests require a posed question

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REFRENCES

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