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Non-AD Dementias & Lifestyle Behaviors for Risk Reduction/Prevention

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Talk Outline

I. **Introduction:** Dementia epidemiology, Overview of Clinical evaluations

II. **Case-Based Review:** Non-AD Cases; "Pearls" of care

III. **Modifiable Risk Factors: Dementia Risk Reduction**

IV. **Questions!**

Behavioral Neurology:

- **Neurodegenerative dementias:** Alzheimer disease, vascular dementia, Frontotemporal lobar degeneration (FTLD) including bvFTD, Progressive Supranuclear Palsy (PSP) and corticobasal degeneration (CBD), atypical Parkinsonian dementias like Dementia with Lewy Bodies (DLB), disease and Multiple System Atrophy (MSA), adult-onset leukoencephalopathies, prion diseases, chronic traumatic encephalopathy

- **Cognitive/behavioral disorders from neurologic problems not due to degenerative disease** (Brain tumor, multiple sclerosis, traumatic brain injury, epilepsy, cerebral palsy, NPH)

- **Cognitive/behavioral disorders due to a medical problem(s)** (One or more of: polypharmacy, sleep disorder, chronic pain disorder, autoimmune encephalopathy, anxiety/depression, systemic illnesses [SLE, Sjogren disease], post-chemotherapy cognitive impairment, post-sepsis recovery, hypothyroidism)

Neuropsychiatry and Geriatric Psychiatry:

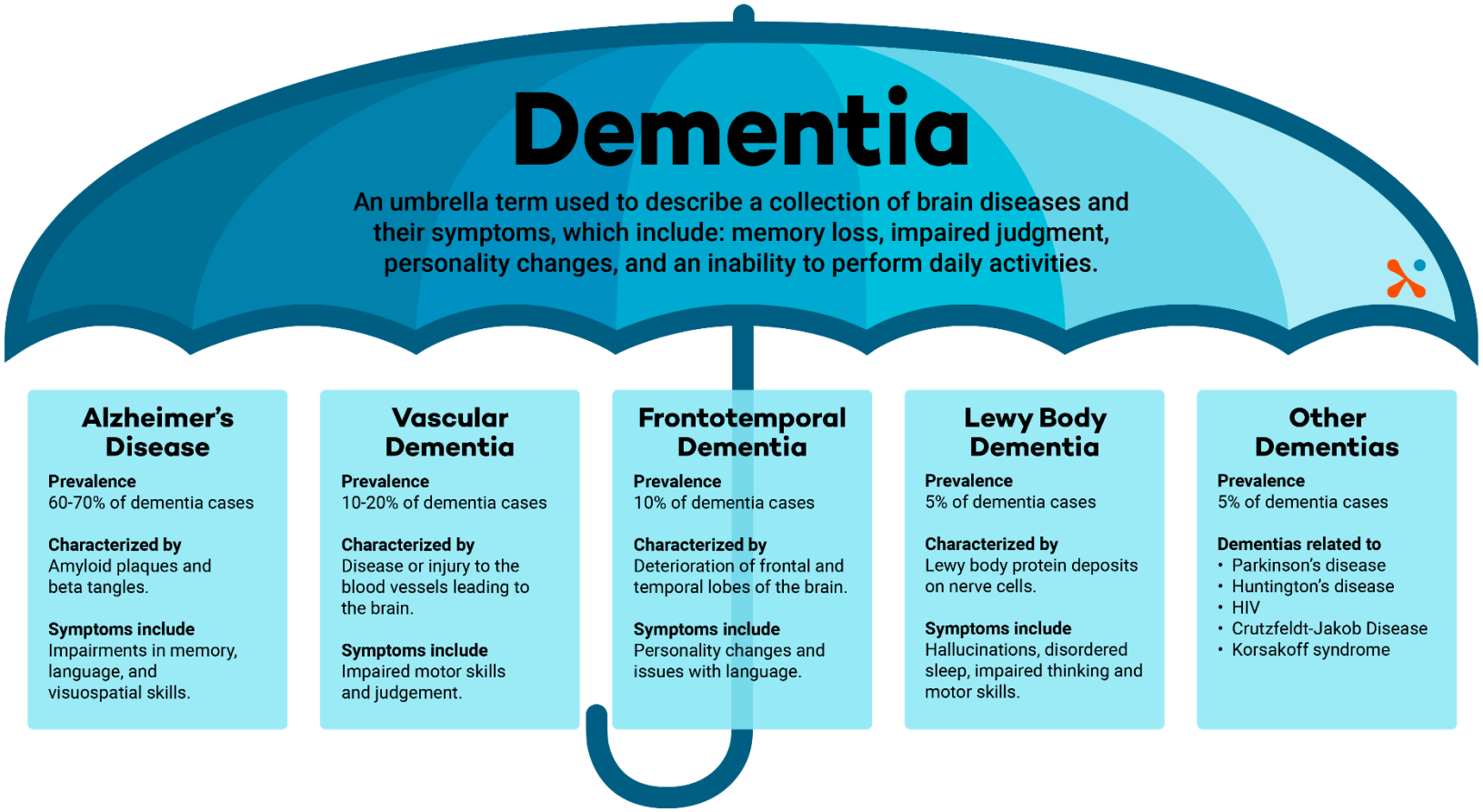
- **Psychiatric disorders/syndromes, with dementia or other neurologic diagnosis** (Depression/anxiety in Multiple Sclerosis, Parkinson disease, traumatic brain injury, epilepsy)

- **Functional neurological symptom or disorder** (Conversion d/o, non-epileptic convulsive disorder)

- **Psychiatric disorders in the elderly** (Depression, Chronic bipolar disorder, anxiety disorders)

Table 1.
Etiology of dementia syndromes

Non-neurodegenerative (previously "reversible")	Neurodegenerative (previously "irreversible")
Vitamin deficiency (B12, thiamine-B1, folic acid)	Alzheimer disease
Normal pressure hydrocephalus	Diffuse Lewy body disease
Metabolic causes (hypothyroidism, chronic uremia, malnutrition)	Frontotemporal dementia (Pick's disease, progressive aphasias)
Chronic/subacute subdural hematomas	Vascular dementia (multi-infarct dementia, large strokes, CADASIL)
Infectious causes (neurosyphilis, AIDS-related dementia complex)	Dementia of PD
Depression, BPD (sometimes called "Pseudo-dementia")	Atypical parkinsonian disorders (multiple system atrophy, PSP, CBD)
Neoplastic/paraneoplastic causes (NMDA-receptor and CRMP-5 antibody encephalopathy, brain tumor)	Non-parkinsonian movement disorders (Huntington's disease, Wilson's disease, DRPLA)
Autoimmune causes (Hashimoto encephalopathy, voltage-gated potassium channel	Hypoxic or ischemic encephalopathy
Toxic exposure (lead, arsenic, chronic stimulant uses)	Alcoholic dementia
Vasculitides (primary vasculitis of the CNS, Behçet's disease, systemic lupus erythematosus-related)	Chronic traumatic encephalopathy ("dementia pugilistica)
	Prion disease (CJD, fatal familial insomnia)
	Dementia related to multiple sclerosis
	Motor neuron disease (amyotrophic lateral sclerosis, progressive lateral sclerosis)



Dementia Epidemiology

- ~7 million people with Alzheimer disease and related dementias (ADRDs) in the U.S., ~55 million globally (60% in LMIC)
- 15-20% of adults 65 and older suffer from mild cognitive impairment (risk factor/stage prior to dementia)
- Black Americans 2x higher risk than Whites; Hispanic Americans 1.5x higher
- Delaying the onset of dementia by 5 years could reduce the prevalence by 50%
- ADRDs will cost the United States an estimated ~$321 billion in 2022 and up to ~$1.1 trillion by 2050

Dementia: Clinical Evaluation

- **Three types** of information used to assess dementia:

1) **Cognitive/Behavioral Abilities:**

- Detailed clinical interview
- Global cognitive screens (MMSE, MoCA, ACE-R)
- Cognitive Domain-specific tests (e.g. Luria 3-step hand sequences, Trail Making test, Frontal Assessment Battery; Cancellation test); neuropsychiatric scales (NPI-Q, GDS), neuropsychological evaluation

2) **Functional status:** (Daily functioning)

- Detailed clinical interview; informant interview
- Functional scales (Lawton-Brody IADL scale, FAQ)

3) **Biological markers:** Neuroimaging (MRI > CT, FDG-PET, Amyloid PET), CSF assays, EEG

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Daily Functioning: Lawton-Brody IADL scale

A. Ability to Use Telephone

1. Operates telephone on own initiative; looks up and dials numbers 1
2. Dials a few well-known numbers 1
3. Answers telephone, but does not dial 1
4. Does not use telephone at all 0

B. Shopping

1. Takes care of all shopping needs independently 1
2. Shops independently for small purchases 0
3. Needs to be accompanied on any shopping trip 0
4. Completely unable to shop 0

C. Food Preparation

1. Plans, prepares, and serves adequate meals independently 1
2. Prepares adequate meals if supplied with ingredients 0
3. Heats and serves prepared meals or prepares meals but does not maintain adequate diet 0
4. Needs to have meals prepared and served 0

D. Housekeeping

1. Maintains house alone with occasion assistance (heavy work) 1
2. Performs light daily tasks such as dishwashing, bed making 1
3. Performs light daily tasks, but cannot maintain acceptable level of cleanliness 1
4. Needs help with all home maintenance tasks 1
5. Does not participate in any housekeeping tasks 0

E. Laundry

1. Does personal laundry completely 1
2. Launders small items, rinses socks, stockings, etc 1
3. All laundry must be done by others 0

F. Mode of Transportation

1. Travels independently on public transportation or drives own car 1
2. Arranges own travel via taxi, but does not otherwise use public transportation 1
3. Travels on public transportation when assisted or accompanied by another 1
4. Travel limited to taxi or automobile with assistance of another 0
5. Does not travel at all 0

G. Responsibility for Own Medications

1. Is responsible for taking medication in correct dosages at correct time 1
2. Takes responsibility if medication is prepared in advance in separate dosages 0
3. Is not capable of dispensing own medication 0

H. Ability to Handle Finances

1. Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income 1
2. Manages day-to-day purchases, but needs help with banking, major purchases, etc 1
3. Incapable of handling money 0

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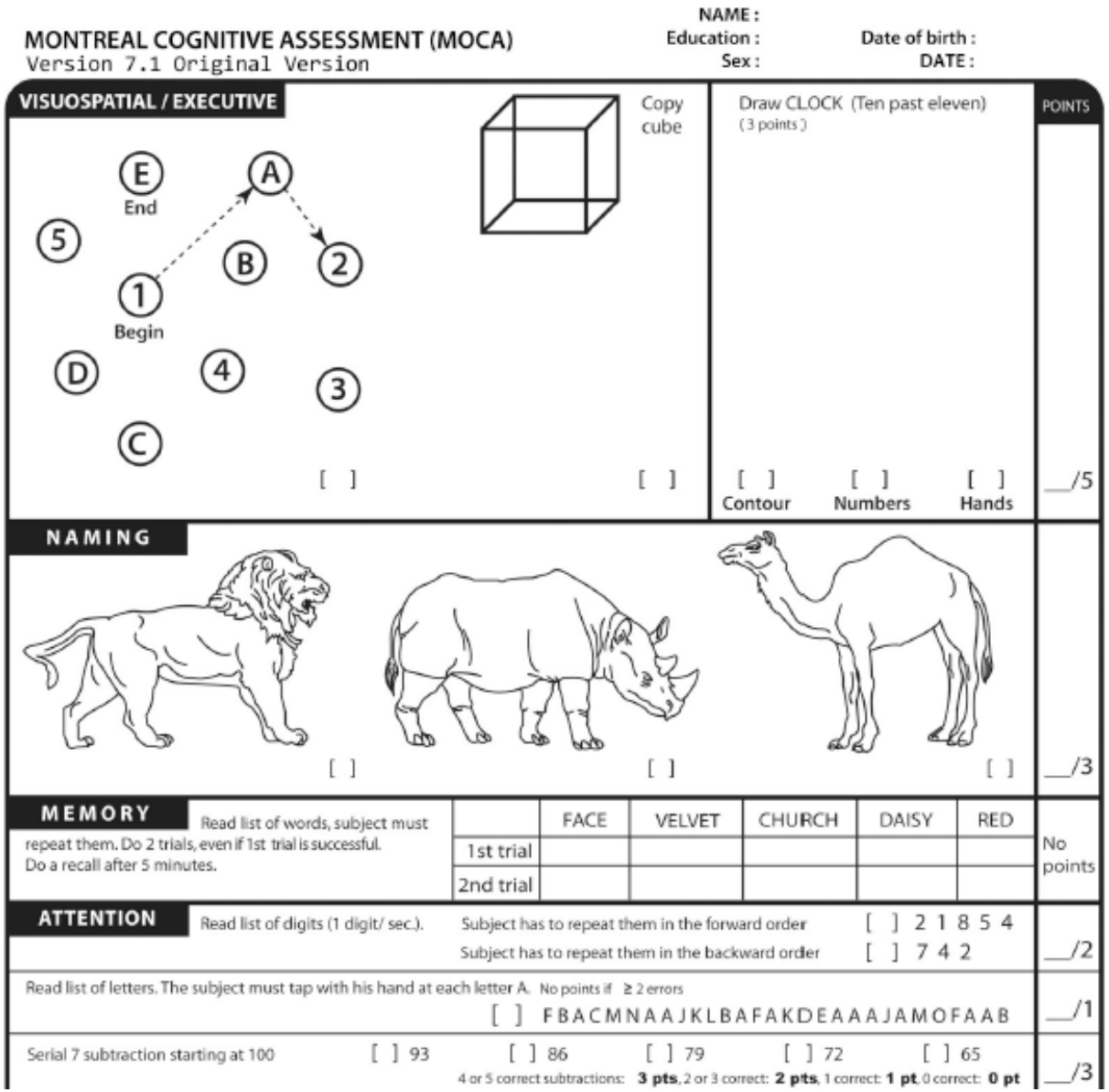
Montreal Cognitive Assessment

mocatest.org



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

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

VISUOSPATIAL / EXECUTIVE

Copy cube

Draw CLOCK (Ten past eleven)
(3 points)

POINTS

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

[ ] [ ]

[ ] Contour [ ] Numbers [ ] Hands

__/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

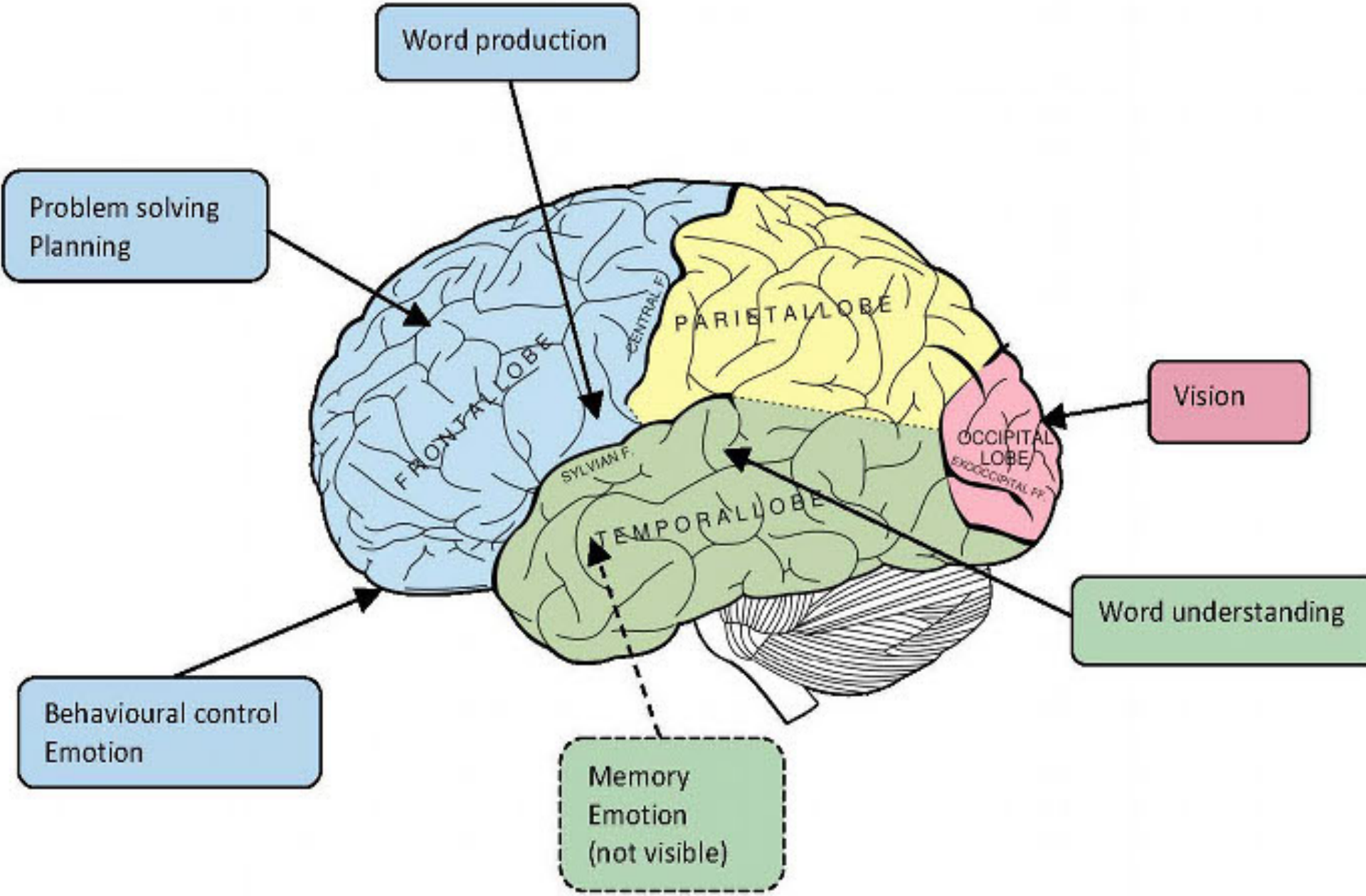
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/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



Case #1- "Daughter's graduation"

68 year-old right-handed M, with changes in behavior, personality, and cognition over the last 11 months.

History of Present Illness:
-He has always been introverted, kept to himself; but **friends have noted he has become more "disengaged" in conversation.** His wife thinks he has become less "polite"; she thinks he actively listens less to conversations.

-He has needed some minor help in managing his medications; **Patient denies he is any different from 1 year ago.**

-He told his wife that he "doesn't understand why" he has to go to his daughter's high school graduation.

-Has become recently obsessed with time. They go to pick up mail at a local P.O. Box, and he must be there exactly at 10:00 am.

-He has had difficulty "pacing" himself through meals; he seems unable to control his speed through food courses and seems to ignore satiety clues.

Case #1- "Daughter's graduation"

PMH:
Sudden fainting episode (with arrythmia), 2005
s/p Appendectomy
Benign colonic polyps

Social/Family History:
Retired restaurant owner. Has 16 grades of education. He is a non-smoker. He drinks 2-3 glasses of wine per week. Family history only of late-life Alzheimer's disease in maternal grandmother.

Neurologic exam:
Mental state: He was awake, alert. He was generally attentive; **did not always maintain direct eye contact.** He grinned with inappropriate affect at points. **He seemed restless at times; stood once and looked out the window. He displayed some mild word-search problems in conversation.** He made one minor speech error in conversation. No evidence of spatial neglect.

Case #1- "Daughter's graduation"

Neurobehavioral status testing:

MoCA : 23/30.
Deductions: 1 point for cube copy (poor organization), 1 point for naming, 1 point from vigilant attention (CPT), 1 point for verbal fluency generation (only 1 S word), 1 point for similarities/abstraction, **1 point for delayed recall.**

NAB-Judgment:
1) Why should you wash your hands before eating? "To get the germs off." *(Did not address spread of germs from hands to food/mouth)*

2) Why are certain foods marked with an expiration date? "You don't want to buy them after." *(Did not address potential for food spoilage, potential for sickness)*

Case #1- "Daughter's graduation"

Differential Diagnosis:

Alzheimer's disease

Adult-onset leukodystrophy (e.g. MLD)

Primary cerebral vasculitis

Prion disease (e.g. CJD)

Behavioral variant fronto-temporal dementia (FTD)

Frontal lobe tumor

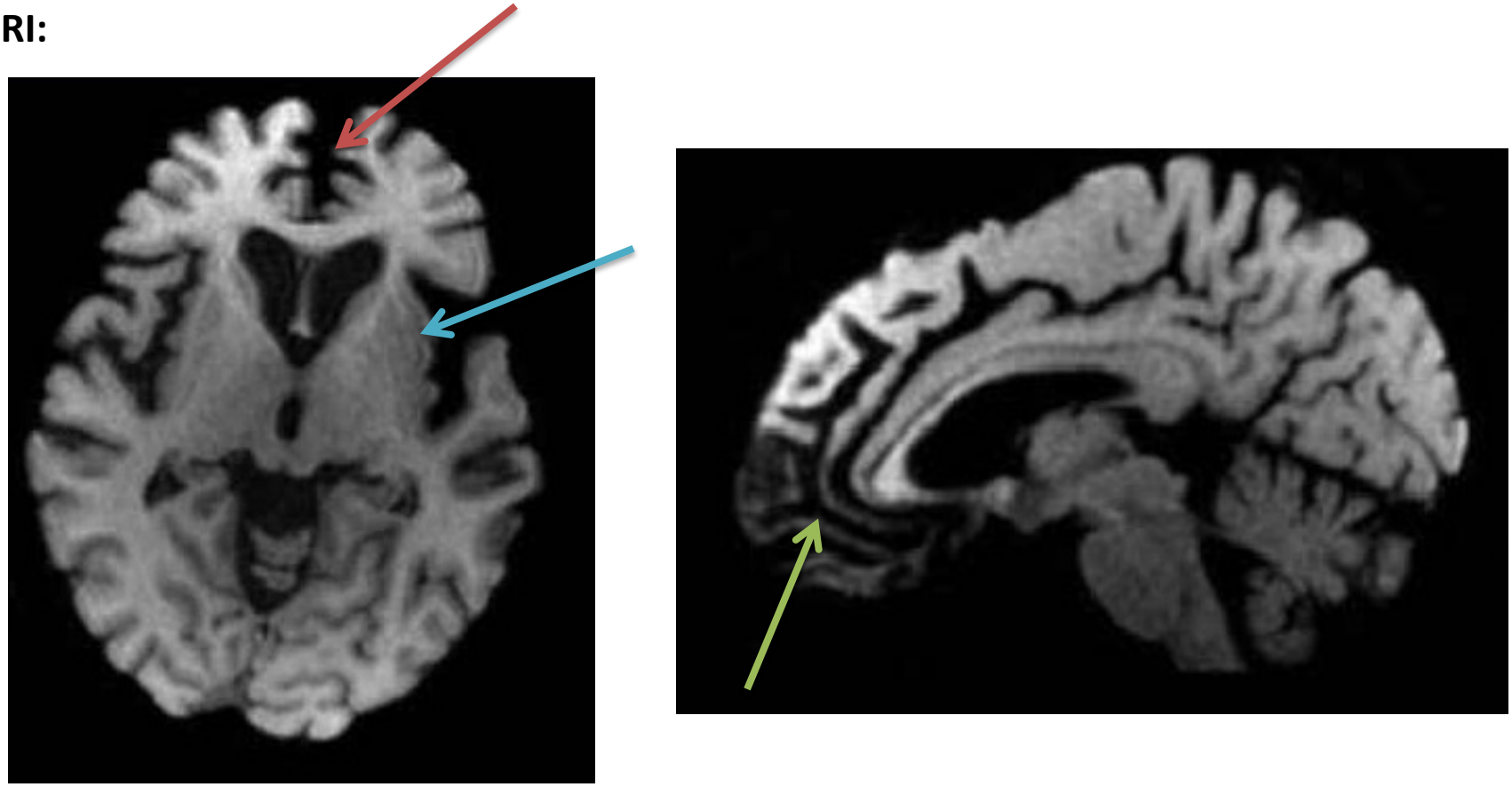
Chronic arsenic toxicity

Case #1- "Daughter's graduation"

Labs:

Serum arsenic: Un-detected. Serum mercury: 5 (normal range 09-ngml). TSH: 2.43 IU/ml. Serum Lyme IGG/IGM: Negative. RPR: non-reactive. LDL cholesterol: 78.

MRI:



Case #1- "Daughter's graduation"

Differential Diagnosis:

Alzheimer Disease

Adult-onset leukodystrophy (like MLD)

Primary cerebral vasculitis

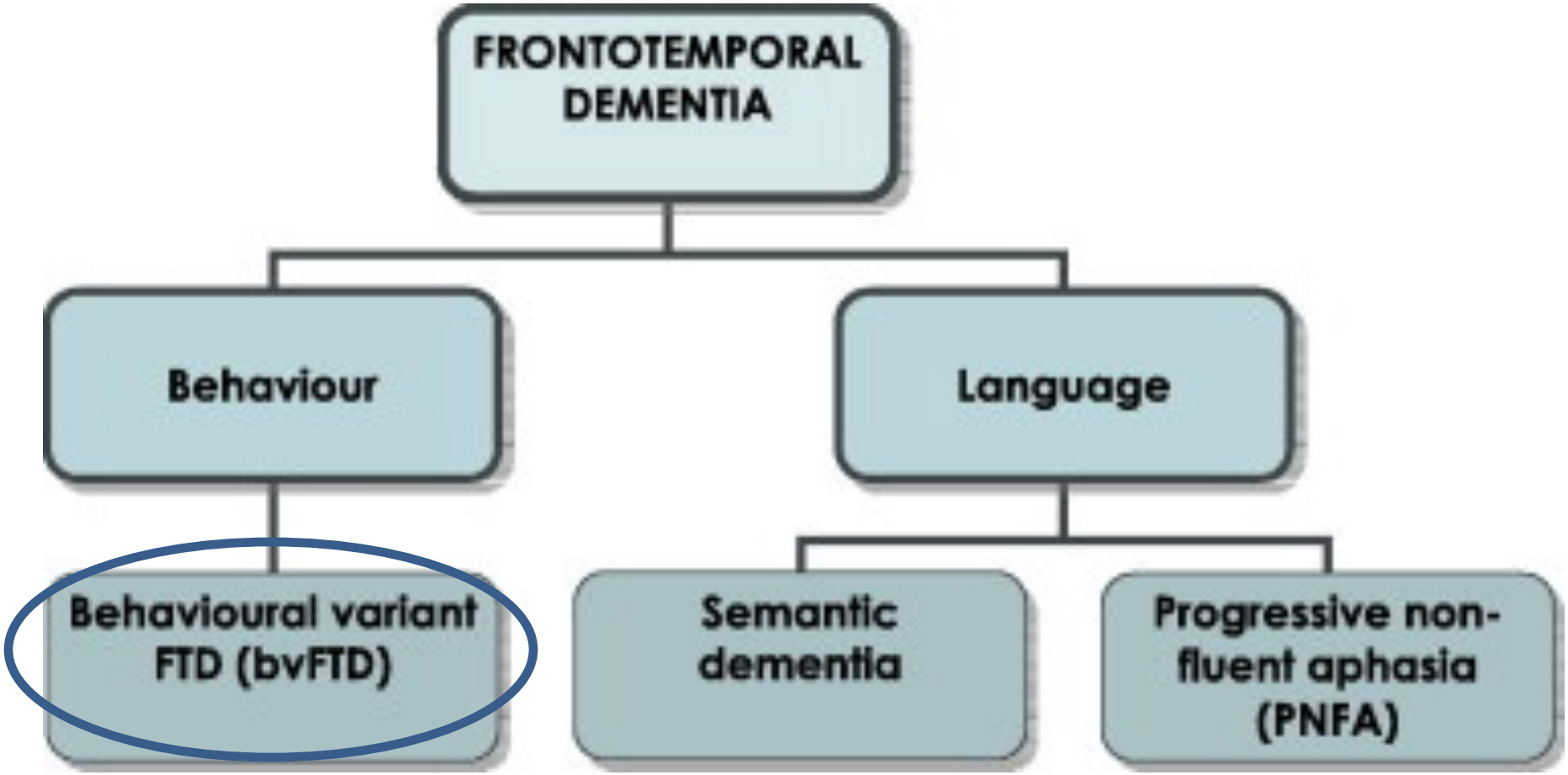
Prion disease (e.g. CJD)

Behavioral variant -fronto-temporal dementia (bvFTD)

Frontal lobe tumor

Chronic arsenic toxicity

Basic Clinical Subtypes of FTD



International Consensus Criteria for bvFTD

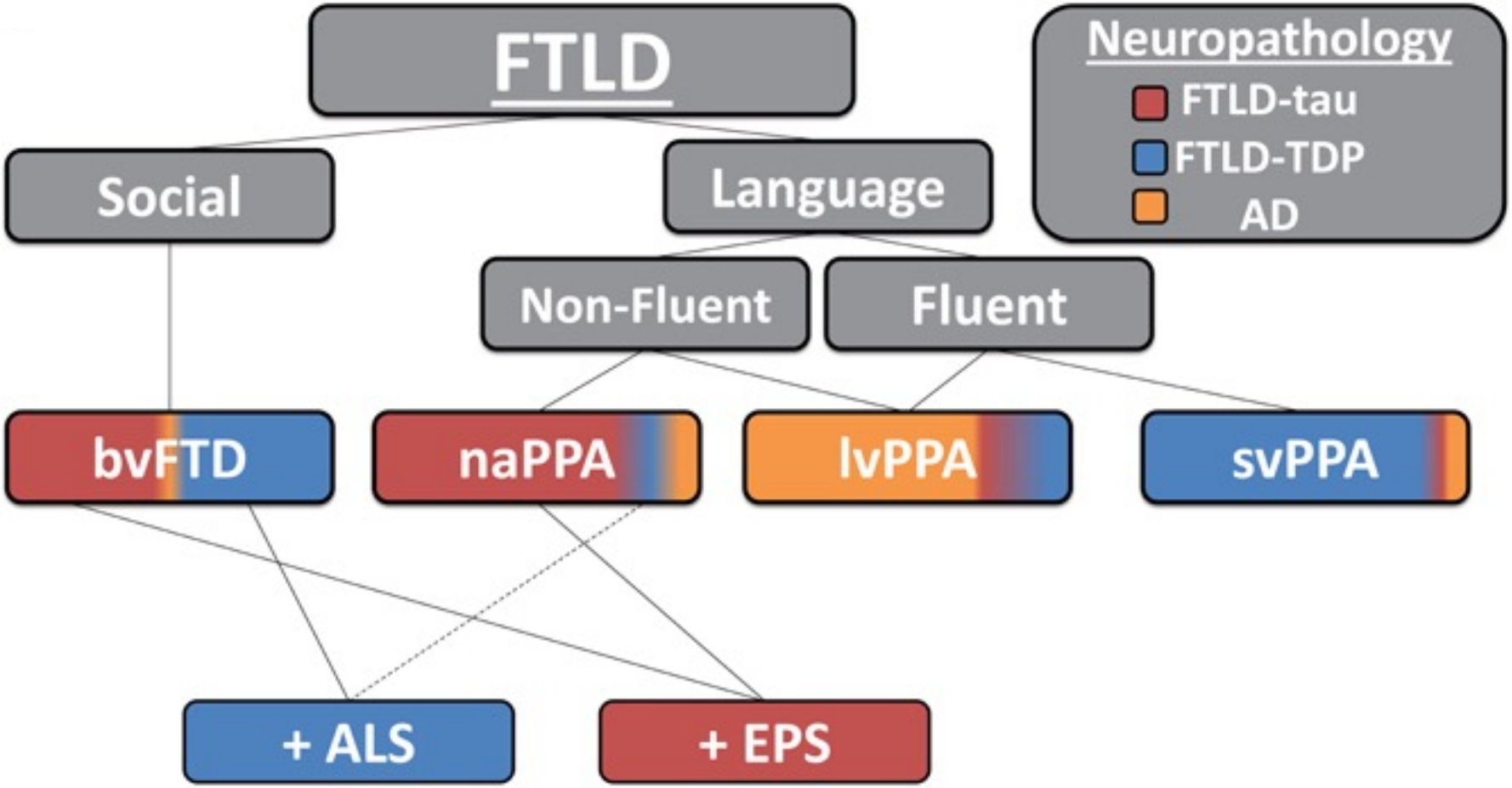
Three of the following must be present for bvFTD:

A. Early behavioral disinhibition
B. Early apathy or inertia
C. Early loss of sympathy or empathy
D. Early perseverative, stereotyped or compulsive/ritualistic behaviour
E. Hyperorality and dietary changes
F. Neuropsychological profile: executive/generation deficits with relative sparing of memory and visuospatial functions [all of the following symptoms (F.1–F.3) must be present]:

F.1. Deficits in executive tasks
F.2. Relative sparing of episodic memory (everyday events)
F.3. Relative sparing of visuospatial skills (navigating;

Rascovsky K et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain. 2011 Sep, 134(pt9): 2456-77.

Symptoms/pathology Correlations in FTLD



D.J. Irwin, M. Grossman, et al. Front. Aging Neurosci., 21 February 2013

Case #1- "Daughter's graduation"

Clinical Pearls and Confounds in Case #3

1) **Disease course from symptom onset until severe impairment or death is often 6-10 years from symptom onset; it may be more like 8-12 for AD.**

2) The leading edge of early signs or symptoms are often **behavior/personality or** language, and ultimately to meet clinical criteria. **Poor insight and emotional indifference** are characteristic.

3) MRI often has **frontal- or temporal-predominant** atrophy. Areas affected are inferior frontal gyri; fronto-insular cortex; anterior temporal lobes

4) **There are some active clinical trials (including tau-protein aggregation inhibitors, tau-antibody for PSP, microtubule stabilizers), but no current disease-modifying therapies.**

Case #1- "A little off"

71 year-old right-handed F, homemaker, with 2 years of subtle forgetfulness, task execution difficulty, and self-report of "increased stress".

History of Present Illness:
-Family members **first observed about 2 years ago that she would forget she has heard a story but may recall given reminders.**

-In subsequent months, **she and others noticed increasing difficulty executing plans with friends; there was frequent miscommunication around logistics.**

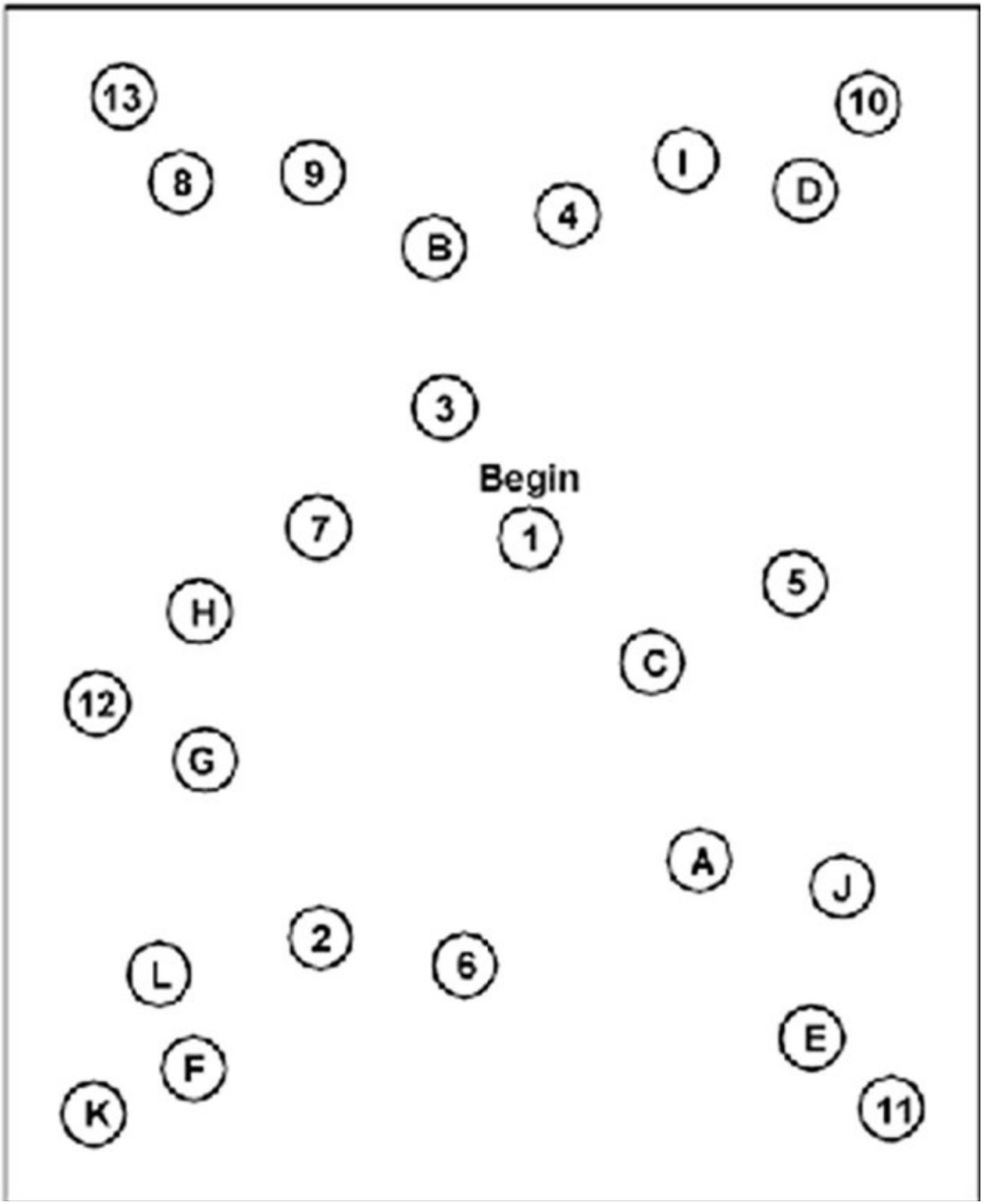
-She has also been careless performing multiple tasks while cooking; *in 2 episodes* in the prior 2 months she either unable to complete a recipe and forgetting to turn an electric pot off (feeling "overwhelmed")

Case #2- "A little off"

PMH:
Osteoarthritis, diffuse
Hyperlipidemia
Raynaud's phenomenon
Hypertension

Social/Family History:
She lives alone, is widowed, and has several adult children in the area. She drinks 3-4 glasses of wine per week. She had functioned independently up to 2-3 months ago, but has just started to lose autonomy in managing her appointments, bills.

Neurologic exam:
Normal elemental neurologic exam.
CERAD (10-word list memory test): Learning trials: 4, 7, 6 = 17/30. Spontaneous recall 5/10. Recognition: 10/10, 1 FP. **TMT-B (set-shifting, working memory): ~3:00 minutes**. BNT (semantic retrieval): 50/60, +8 PC.


13
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Case #2- "A little off"

Differential Diagnosis:

Depression or adjustment disorder

Metabolic encephalopathy

Vascular cognitive impairment (VCI)

MCI due to Alzheimer disease (AD)

Hypothyroidism

Neuropsychiatric Inventory-Questionnaire (NPI-Q) for Informants

Delusions Does the patient believe that others are stealing from him or her, or planning to harm him or her in some way?

Yes No Severity: 1 2 3 Distress: 0 1 2 3 4 5

Hallucinations Does the patient act as if he or she hears voices? Does he or she talk to people who are not there?

Yes No Severity: 1 2 3 Distress: 0 1 2 3 4 5

Agitation or aggression Is the patient stubborn and resistive to help from others?

Yes No Severity: 1 2 3 Distress: 0 1 2 3 4 5

Depression or dysphoria Does the patient act as if he or she is sad or in low spirits? Does he or she cry?

Yes No Severity: 1 2 3 Distress: 0 1 2 3 4 5

Anxiety Does the patient become upset when separated from you? Does he or she have any other signs of nervousness, such as shortness of breath, sighing, being unable to relax, or feeling excessively tense?

Yes No Severity: 1 2 3 Distress: 0 1 2 3 4 5

Elation or euphoria Does the patient appear to feel too good or act excessively happy?

Yes No Severity: 1 2 3 Distress: 0 1 2 3 4 5

Neuropsychiatric Inventory-Questionnaire (NPI-Q) for Informants

Apathy or indifference — Does the patient seem less interested in his or her usual activities and in the activities and plans of others?

Yes **No** Severity: 1 2 3 Distress: 0 1 2 3 4 5

Disinhibition — Does the patient seem to act impulsively? For example, does the patient talk to strangers as if he or she knows them, or does the patient say things that may hurt people's feelings?

Yes **No** Severity: 1 2 3 Distress: 0 1 2 3 4 5

Irritability or lability — Is the patient impatient and cranky? Does he or she have difficulty coping with delays or waiting for planned activities?

Yes **No** Severity: 1 2 3 Distress: 0 1 2 3 4 5

Motor disturbance — Does the patient engage in repetitive activities, such as pacing around the house, handling buttons, wrapping string, or doing other things repeatedly?

Yes **No** Severity: 1 2 3 Distress: 0 1 2 3 4 5

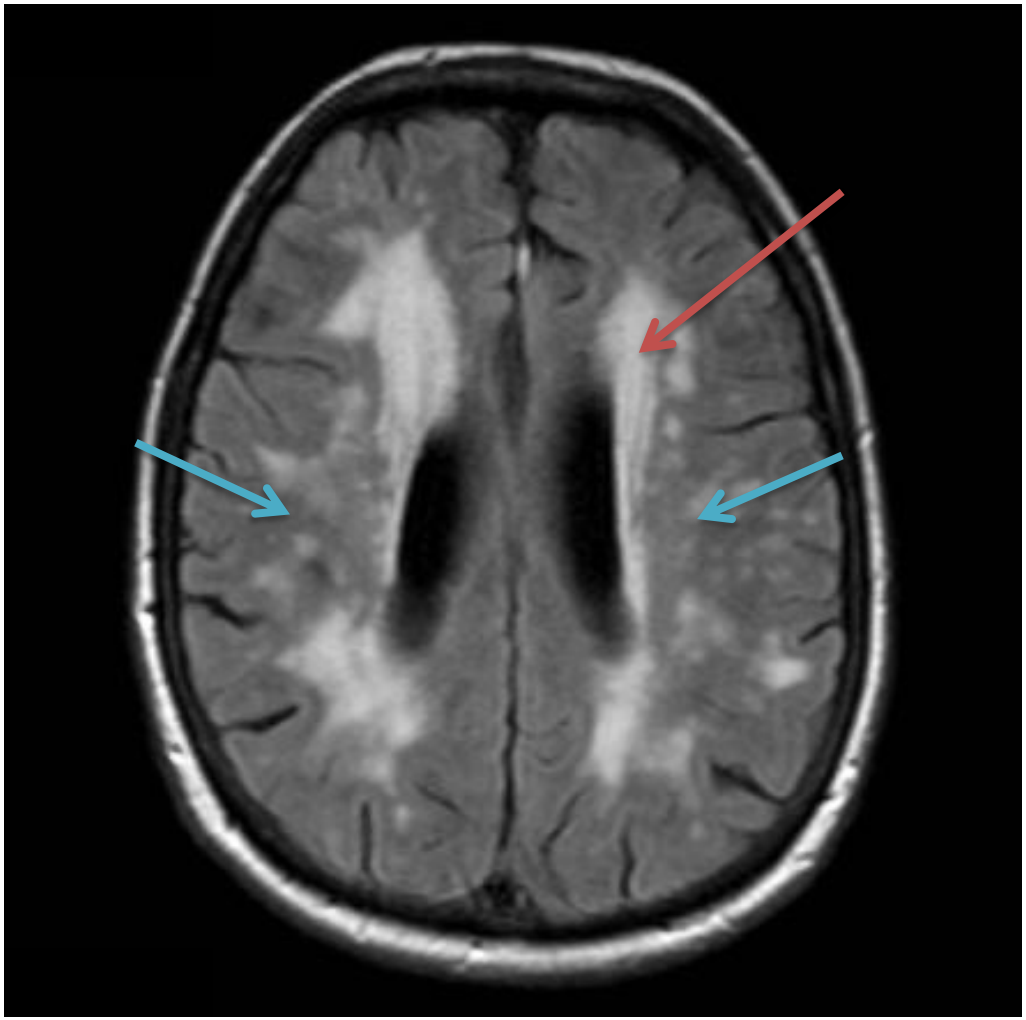
Nighttime behaviors — Does the patient awaken you during the night, rise too early in the morning, or take excessive naps during the day?

Yes No Severity: **1** 2 3 Distress: 0 **1** 2 3 4 5

Appetite and eating — Has the patient lost or gained weight, or had a change in the food he or she likes?

Yes **No** Severity: 1 2 3 Distress: 0 1 2 3 4 5

Case #2- "A little off"



Red arrow: Confluent periventricular microvascular disease

Blue arrows: Some more extensive, bilateral deep white matter microvascular disease

Case #2- "A little off"

Differential Diagnosis:

Depression or adjustment disorder

Metabolic encephalopathy

Vascular cognitive impairment (VCI)

MCI due to Alzheimer disease (AD)

Hypothyroidism

Case #2- "A little off"

Clinical Pearls and Confounds in Case #4:

1) Vascular cognitive impairment (VCI) is a term that encompasses: classical **sub-cortical ischemic vascular dementia** (SIVD), **AD with cerebrovascular disease** (mixed-type), and **MCI due to cerebrovascular disease**

2) Step-wise decline can happen with strategic strokes, but in reality **most** SIVD can have a **slowly progressive onset, sometimes mimicking AD**

3) Growing evidence that VCI has synergistic or causative effects with emergence of AD pathology; **up to 2/3 of patient with VCI develop some AD pathology.**

4) **Frontal-mediated/executive dysfunction, attention, and verbal fluency are often worse** in "pure" VCI than in: AD *or* AD with vascular disease

Jin, Hachinski et al. Alzheimers Dement 2006;2:171-178

Table 4 Summary Guidance Based on Vascular Cognitive Impairment Prevention Studies

Blood pressure control
- Lowering blood pressure, starting at age 55 and probably earlier, decreases the risk of all-cause dementia in later life.
- No single antihypertensive seems favorable over another.
- The longer the duration of treatment, the stronger the preventive effect.

Diet
- Adhering to a Mediterranean-style diet may reduce the risk of VCI in the elderly.

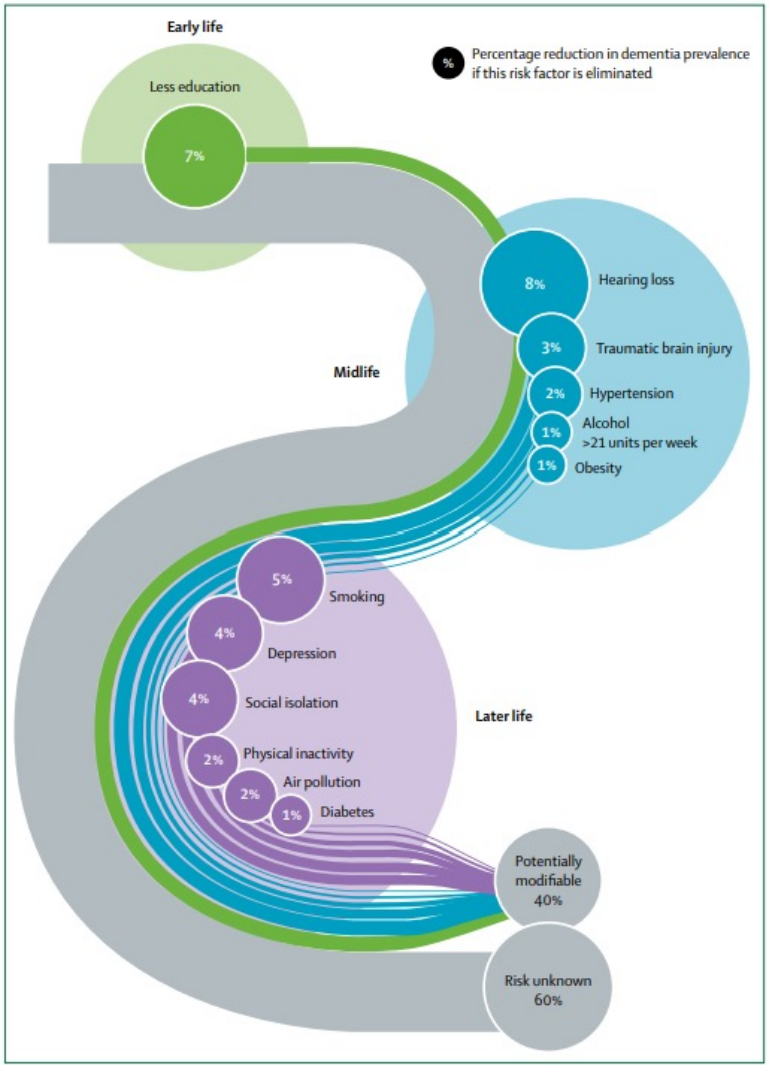
Aerobic exercise
- Aerobic exercise in the elderly clearly reduces rates of all-cause, incident dementia.
- Aerobic exercise also minimizes the cognitive decline attributed to normal aging.

Lipid control
- Treatment with statins for hyperlipidemia does not reduce cognitive decline in the elderly.

Antiplatelet use
- Antiplatelet therapy (aspirin, dipyridamole) over many years does not reliably reduce risk of VCI in the elderly.

Table from: Gale et al. *Cognitive disorders other than Alzheimer disease*. Scientific American Neurology; 2016.

Modifiable Risk Factors, Dementia Risk Reduction

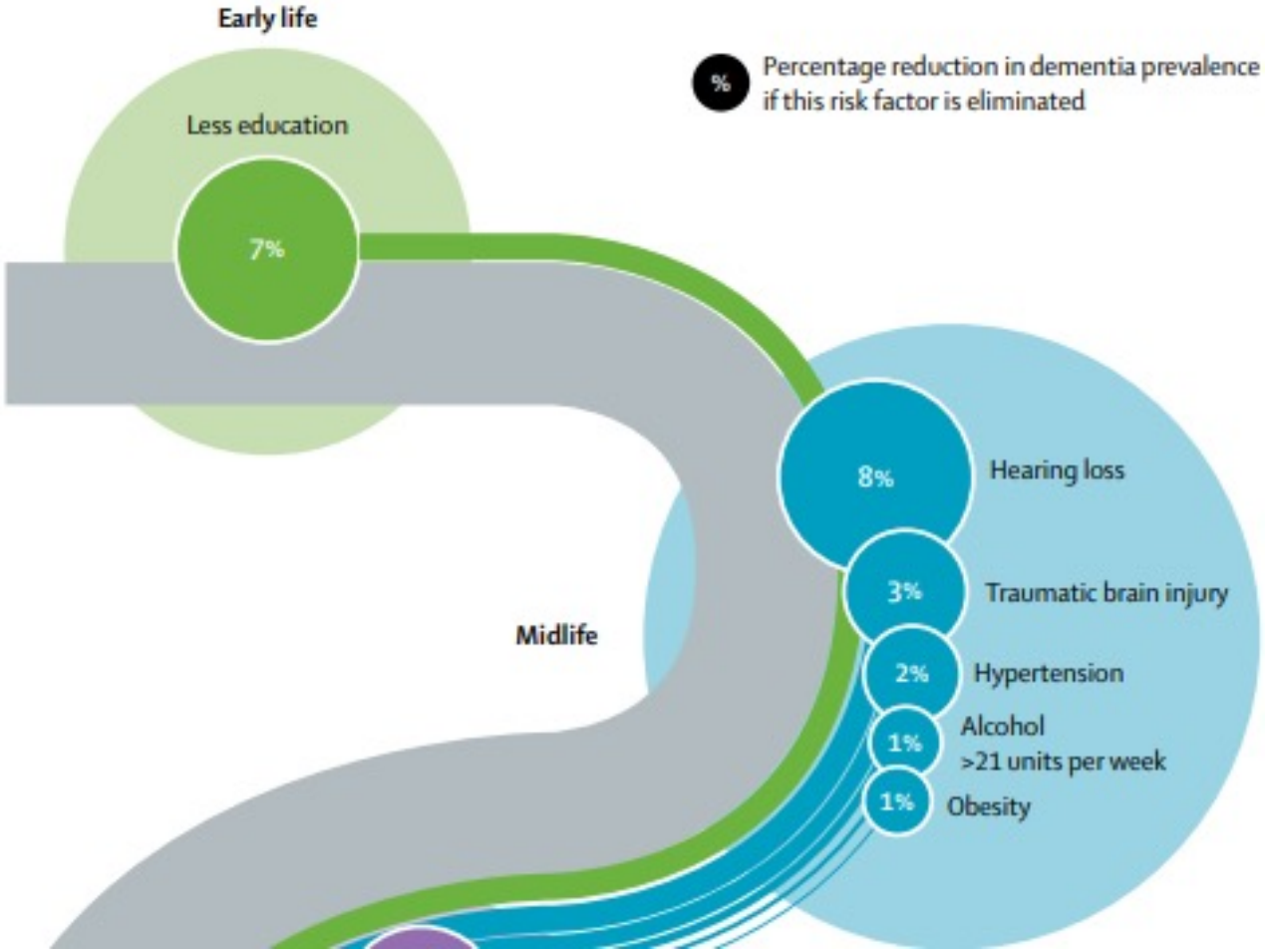


Risk Factors for Dementia

~40% are potentially modifiable

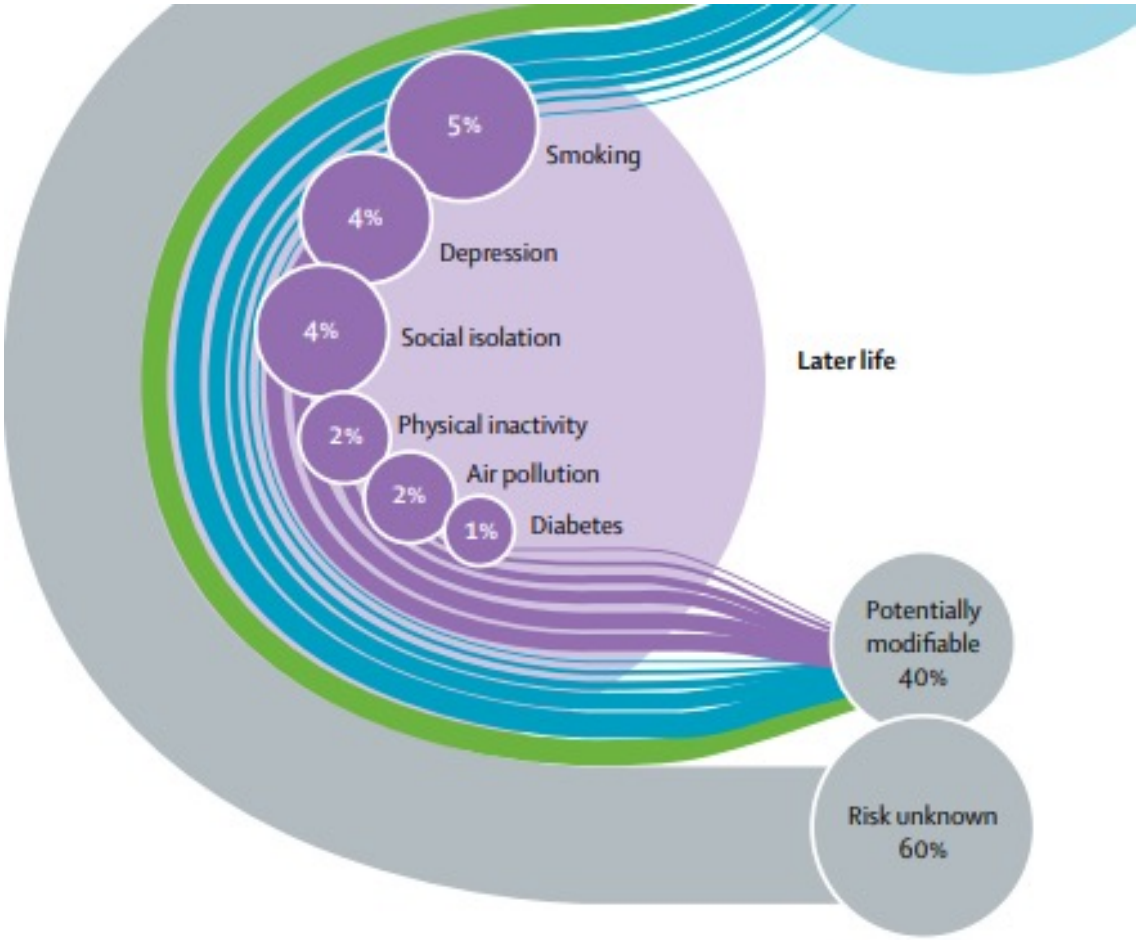
Lancet Commissions
Livingston, et al, 2020

Modifiable Risk Factors, Dementia Risk Reduction



Lancet Commissions
Livingston, et al, 2020

Modifiable Risk Factors, Dementia Risk Reduction



Lancet Commissions
Livingston, et al, 2020

Non-AD Dementias & Lifestyle Behaviors for Risk Reduction/Prevention

Thank you!

Questions….