Alzheimer's disease and Dementia (Vascular, Lewy Body, and Frontal Temporal Lobe)

Clinical presentation
Exam
Diagnosis
Treatment
Prognosis
Neuroimaging

Tom Ala, MD

January 8, 2021

SIU

Educational Objectives

- Understand how the new A/T/N research schema impacts the diagnosis of Alzheimer's disease.
- Review the latest criteria for diagnosing dementia with Lewy bodies.
- Remember the criteria for diagnosing frontotemporal dementia.
- Appreciate the difficulty in diagnosing vascular dementia.
- Review treatment options

SIU

Basic dementia definition

- Impairment of memory and at least one other cognitive domain
- Impairment of social or occupational functioning
- Delirium has been ruled out.
- Depression has been ruled out.

DSM-IV

SIU

Basic dementia definition

- Impairment of memory and at least one other cognitive domain
- Impairment of social or occupational functioning
- Delirium has been ruled out.
- Depression has been ruled out.
- An acquired condition

Basic dementia definition

- Impairment of memory and at least one other cognitive domain
- Impairment of social or occupational functioning
- Delirium has been ruled out.
- Depression has been ruled out.
- An acquired condition
- Irreversible

Dementia in a younger person

- Trauma
- Drug overdose
- Strokes
- Cardiac or respiratory arrest
- Multiple sclerosis
- Many others
- Degenerative

Dementia in the elderly

- Alzheimer's disease 60-75%
- Dementia with Lewy bodies 10-25%
- Vascular dementia ~10%
- Frontotemporal dementia ~10%
- Others ~5%

SIU

Dementia in the elderly

- AD (Alzheimer's disease) 60-75%
- DLB (Dementia with Lewy bodies) 10-25%
- VAD (Vascular dementia) ~10%
- FTD (Frontotemporal dementia) ~10%
- Others ~5%

Dementia in the elderly

- AD (Alzheimer's disease) 60-75%
- DLB (Dementia with Lewy bodies) 10-25%
- VAD (Vascular dementia) ~10%
- FTD (Frontotemporal dementia) ~10%
- Others ~5%

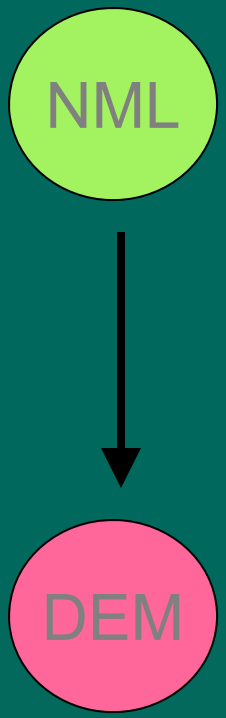
The degenerative dementias cause losses in all the cognitive domains.

- Memory
- Executive ability
- Visuospatial organization
- Language
- Personality
- Attention
- (Psychomotor speed)

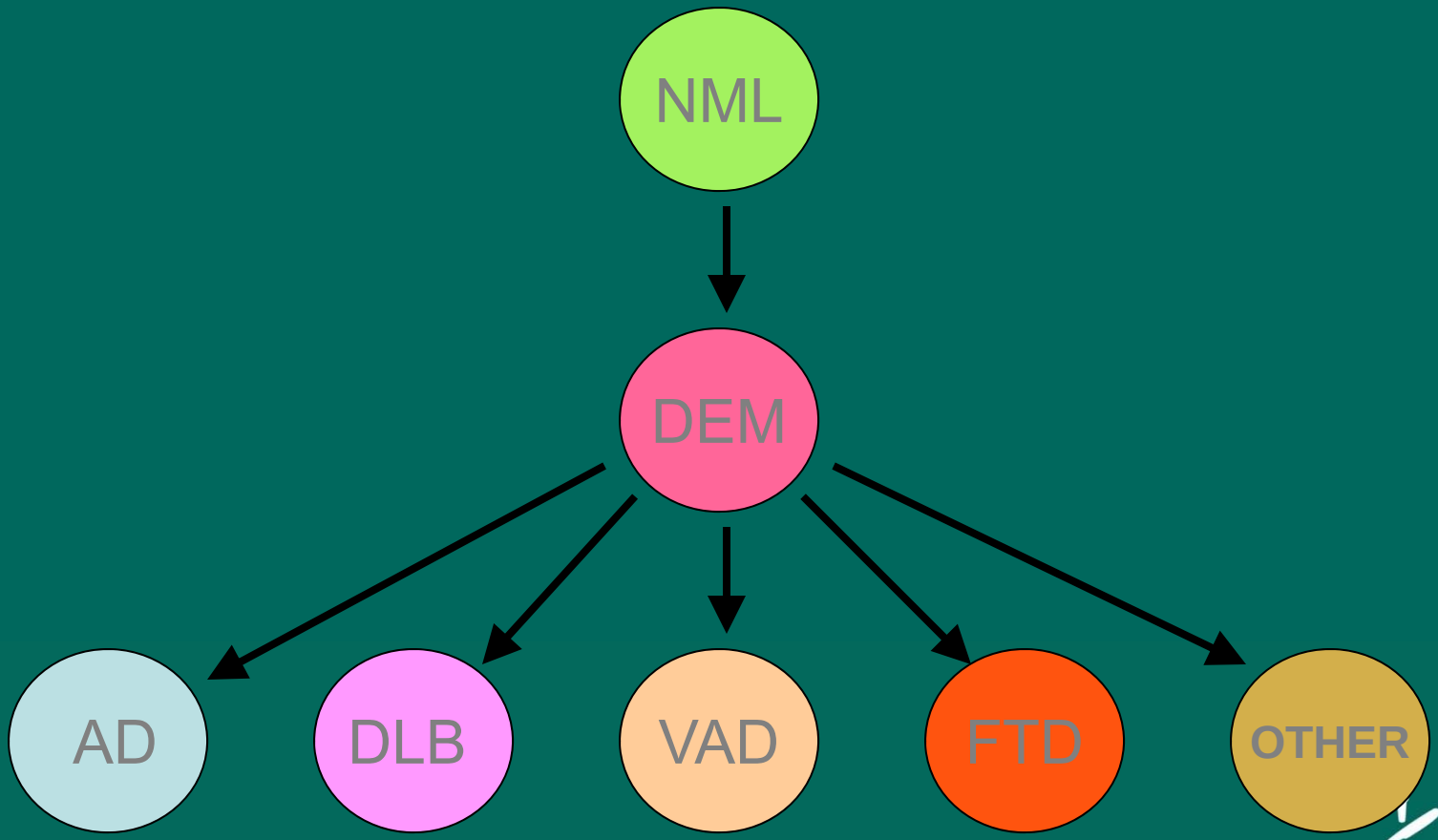
Late dementia

- Unable to care for self
- Behavioral problems
- Disordered sleep
- Incontinence
- Delusions
- Agitation
- Hallucinations
- Etc.

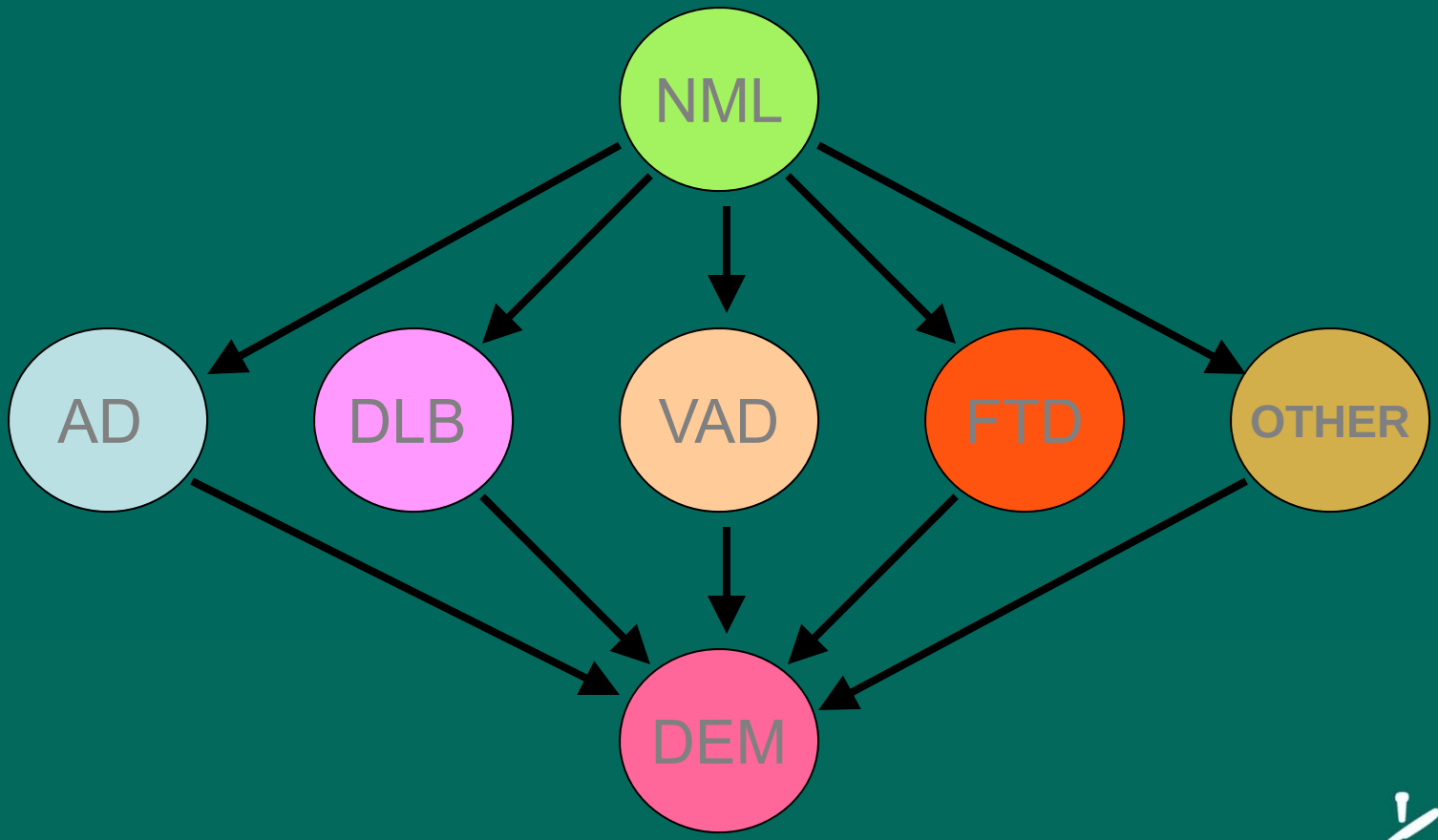
A common dilemma



A common dilemma



The final common pathway



Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of (1) history-taking from the patient and a knowledgeable informant and (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing. Neuropsychological testing should be performed when the routine history and bedside mental status examination cannot provide a confident diagnosis.
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information—symptoms include: repetitive questions or conversations, misplacing personal belongings, forgetting events or appointments, getting lost on a familiar route.
  - Impaired reasoning and handling of complex tasks, poor judgment—symptoms include: poor understanding of safety risks, inability to manage finances, poor decision-making ability, inability to plan complex or sequential activities.
  - Impaired visuospatial abilities—symptoms include: inability to recognize faces or common objects or to find objects in direct view despite good acuity, inability to operate simple implements, or orient clothing to the body.
  - Impaired language functions (speaking, reading, writing)—symptoms include: difficulty thinking of common words while speaking, hesitations; speech, spelling, and writing errors.
  - Changes in personality, behavior, or comportment—symptoms include: uncharacteristic mood fluctuations such as agitation, impaired motivation, initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive or obsessive behaviors, socially unacceptable behaviors.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing.
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing.
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing.
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing.
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a "bedside" mental status examination or neuropsychological testing.
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing..
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

The degenerative dementias cause losses in all the cognitive domains.

- Memory
- Executive ability
- Visuospatial organization
- Language
- Personality
- Attention
- (Psychomotor speed)

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing..
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing..
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing..
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing..
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Criteria for all-cause dementia

- Interfere with the ability to function at work or at usual activities; and
- Represent a decline from previous levels of functioning and performing; and
- Are not explained by delirium or major psychiatric disorder;
- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking and
  - (2) an objective cognitive assessment, either a “bedside” mental status examination or neuropsychological testing..
- The cognitive or behavioral impairment involves a minimum of two of the following domains:
  - Impaired ability to acquire and remember new information.
  - Impaired reasoning and handling of complex tasks, poor judgment.
  - Impaired visuospatial abilities.
  - Impaired language functions (speaking, reading, writing).
  - Changes in personality, behavior, or comportment.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Basic dementia definition

- Impairment of memory and at least one other cognitive domain
- Impairment of social or occupational functioning
- Delirium has been ruled out.
- Depression has been ruled out.

DSM-IV

SIU

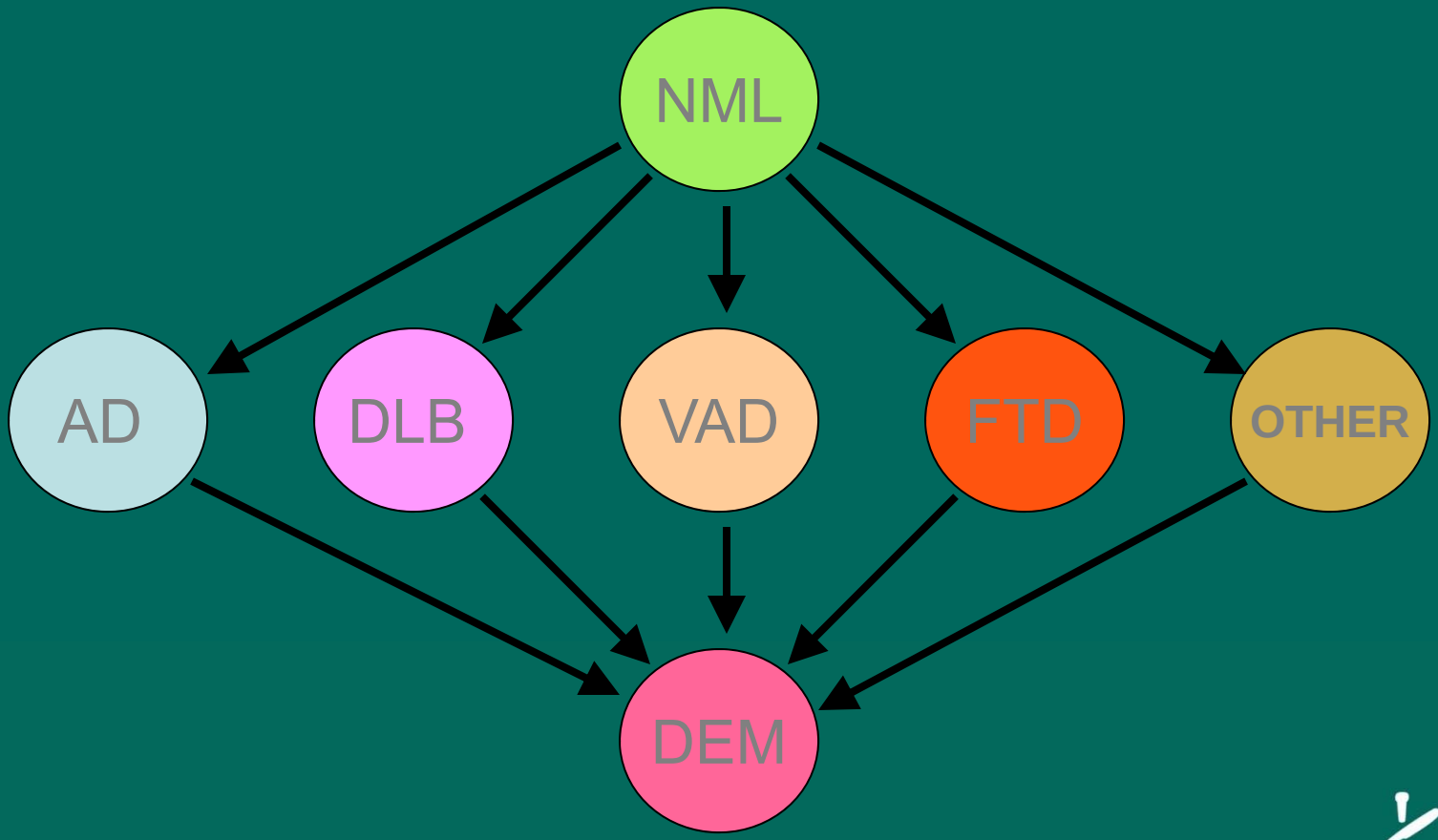
Basic dementia definition

- Impairment of ~~memory and~~ at least two cognitive domains
- Impairment of social or occupational functioning
- Delirium has been ruled out.
- Depression has been ruled out.
- An acquired condition
- Use an objective cognitive test

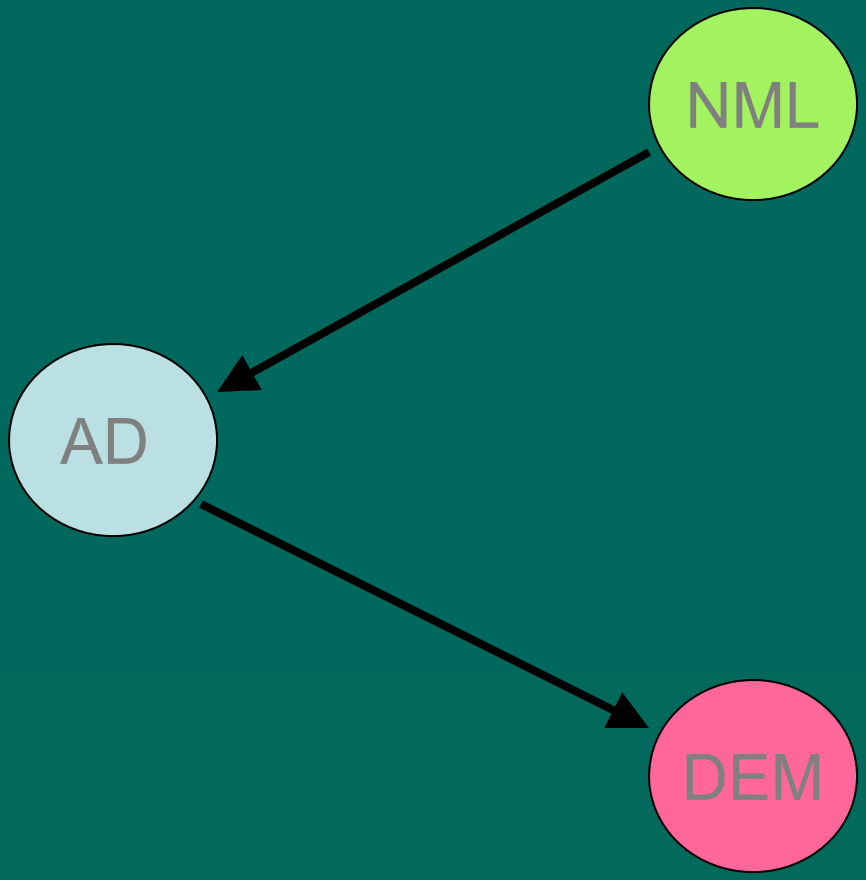
SIU

AD

The final common pathway



Alzheimer's disease



Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset. Symptoms have a gradual onset over months to years, not sudden over hours or days;
  - Clear-cut history of worsening of cognition by report or observation; and
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: It is the most common syndromic presentation of AD dementia. The deficits should include impairment in learning and recall of recently learned information. There should also be evidence of cognitive dysfunction in at least one other cognitive domain, as defined earlier in the text.
    - Nonamnestic presentations:
      - Language presentation: The most prominent deficits are in word-finding, but deficits in other cognitive domains should be present.
      - Visuospatial presentation: The most prominent deficits are in spatial cognition, including object agnosia, impaired face recognition, simultanagnosia, and alexia. Deficits in other cognitive domains should be present.
      - Executive dysfunction: The most prominent deficits are impaired reasoning, judgment, and problem solving. Deficits in other cognitive domains should be present.
  - The diagnosis of probable AD dementia ***should not*** be applied when there is evidence of (a) substantial concomitant cerebrovascular disease, defined by a history of a stroke temporally related to the onset or worsening of cognitive impairment; or the presence of multiple or extensive infarcts or severe white matter hyperintensity burden; or (b) core features of Dementia with Lewy bodies other than dementia itself; or (c) prominent features of behavioral variant frontotemporal dementia; or (d) prominent features of semantic variant primary progressive aphasia or nonfluent/agrammatic variant primary progressive aphasia; or (e) evidence for another concurrent, active neurological disease, or a non-neurological medical comorbidity or use of medication that could have a substantial effect on cognition.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset.
  - Clear-cut history of worsening
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: There should also be evidence of cognitive dysfunction in at least one other cognitive domain
    - Nonamnestic presentations: Deficits in other cognitive domains should be present.
      - Language presentation.
      - Visuospatial presentation.
      - Executive dysfunction.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset.
  - Clear-cut history of worsening
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: There should also be evidence of cognitive dysfunction in at least one other cognitive domain
    - Nonamnestic presentations: Deficits in other cognitive domains should be present.
      - Language presentation.
      - Visuospatial presentation.
      - Executive dysfunction.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset.
  - Clear-cut history of worsening
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: There should also be evidence of cognitive dysfunction in at least one other cognitive domain
    - Nonamnestic presentations: Deficits in other cognitive domains should be present.
      - Language presentation.
      - Visuospatial presentation.
      - Executive dysfunction.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset.
  - Clear-cut history of worsening
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: There should also be evidence of cognitive dysfunction in at least one other cognitive domain
    - Nonamnestic presentations: Deficits in other cognitive domains should be present.
      - Language presentation.
      - Visuospatial presentation.
      - Executive dysfunction.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset.
  - Clear-cut history of worsening
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: There should also be evidence of cognitive dysfunction in at least one other cognitive domain
    - Nonamnestic presentations: Deficits in other cognitive domains should be present.
      - Language presentation.
      - Visuospatial presentation.
      - Executive dysfunction.

McKhann. *Alz & Dem* 2011;7:263.

SIU

The degenerative dementias cause losses in all the cognitive domains.

- Memory
- Executive ability
- Visuospatial organization
- Language
- Personality
- Attention
- (Psychomotor speed)

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset.
  - Clear-cut history of worsening
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: There should also be evidence of cognitive dysfunction in at least one other cognitive domain
    - Nonamnestic presentations: Deficits in other cognitive domains should be present.
      - Language presentation.
      - Visuospatial presentation.
      - Executive dysfunction.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Probable AD dementia: core clinical criteria

Probable AD dementia is diagnosed when the patient

- Meets criteria for dementia described earlier in the text, and in addition, has the following characteristics:
  - Insidious onset. Symptoms have a gradual onset over months to years, not sudden over hours or days;
  - Clear-cut history of worsening of cognition by report or observation; and
  - The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories.
    - Amnestic presentation: It is the most common syndromic presentation of AD dementia. The deficits should include impairment in learning and recall of recently learned information. There should also be evidence of cognitive dysfunction in at least one other cognitive domain, as defined earlier in the text.
    - Nonamnestic presentations:
      - Language presentation: The most prominent deficits are in word-finding, but deficits in other cognitive domains should be present.
      - Visuospatial presentation: The most prominent deficits are in spatial cognition, including object agnosia, impaired face recognition, simultanagnosia, and alexia. Deficits in other cognitive domains should be present.
      - Executive dysfunction: The most prominent deficits are impaired reasoning, judgment, and problem solving. Deficits in other cognitive domains should be present.
  - The diagnosis of probable AD dementia ***should not*** be applied when there is evidence of (a) substantial concomitant cerebrovascular disease, defined by a history of a stroke temporally related to the onset or worsening of cognitive impairment; or the presence of multiple or extensive infarcts or severe white matter hyperintensity burden; or (b) core features of Dementia with Lewy bodies other than dementia itself; or (c) prominent features of behavioral variant frontotemporal dementia; or (d) prominent features of semantic variant primary progressive aphasia or nonfluent/agrammatic variant primary progressive aphasia; or (e) evidence for another concurrent, active neurological disease, or a non-neurological medical comorbidity or use of medication that could have a substantial effect on cognition.

McKhann. *Alz & Dem* 2011;7:263.

SIU

Alzheimer's disease

- Memory impairment
- One or more of the following has been acquired:
  - Aphasia
  - Apraxia
  - Agnosia
  - Disturbance in executive functioning
- (Onset usually > 65)

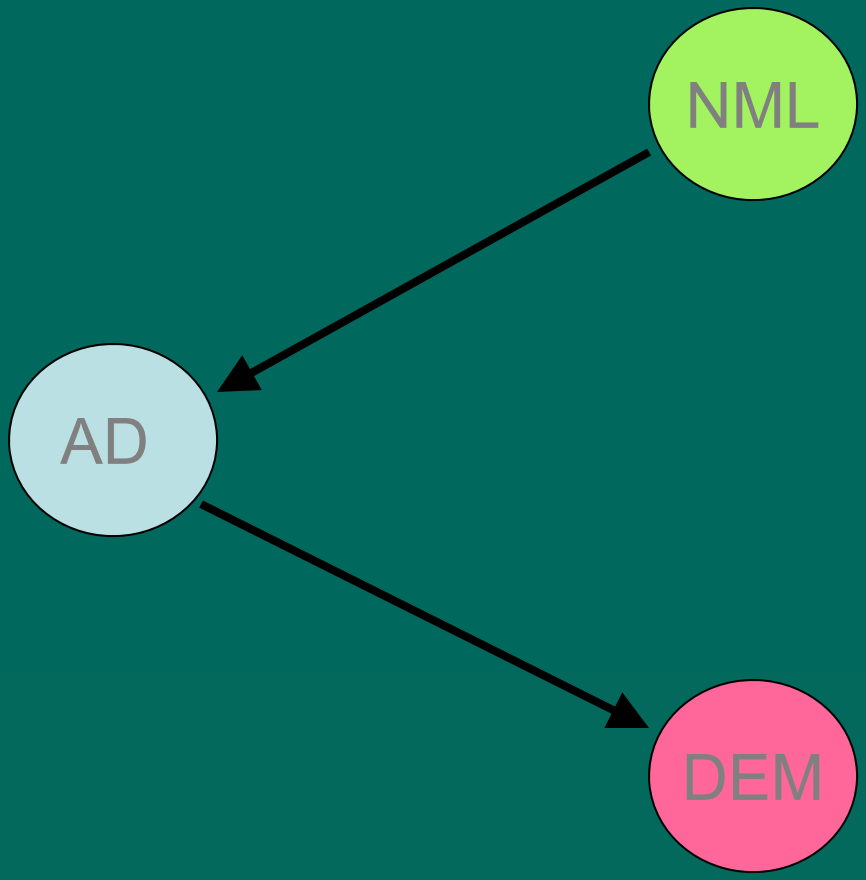
DSM-IV. 1994, p 1420.

SIU

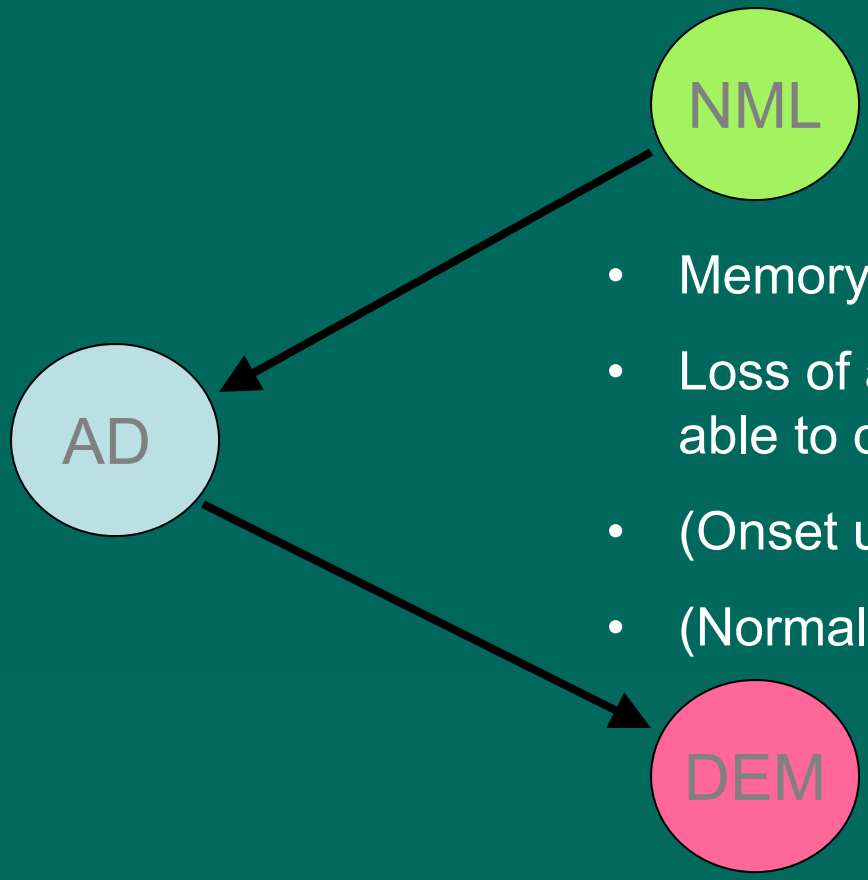
Alzheimer's disease

- Memory impairment
- Loss of ability to do something they were able to do in the past
- (Onset usually > 65)
- (Normal exam in early stages

Alzheimer's disease



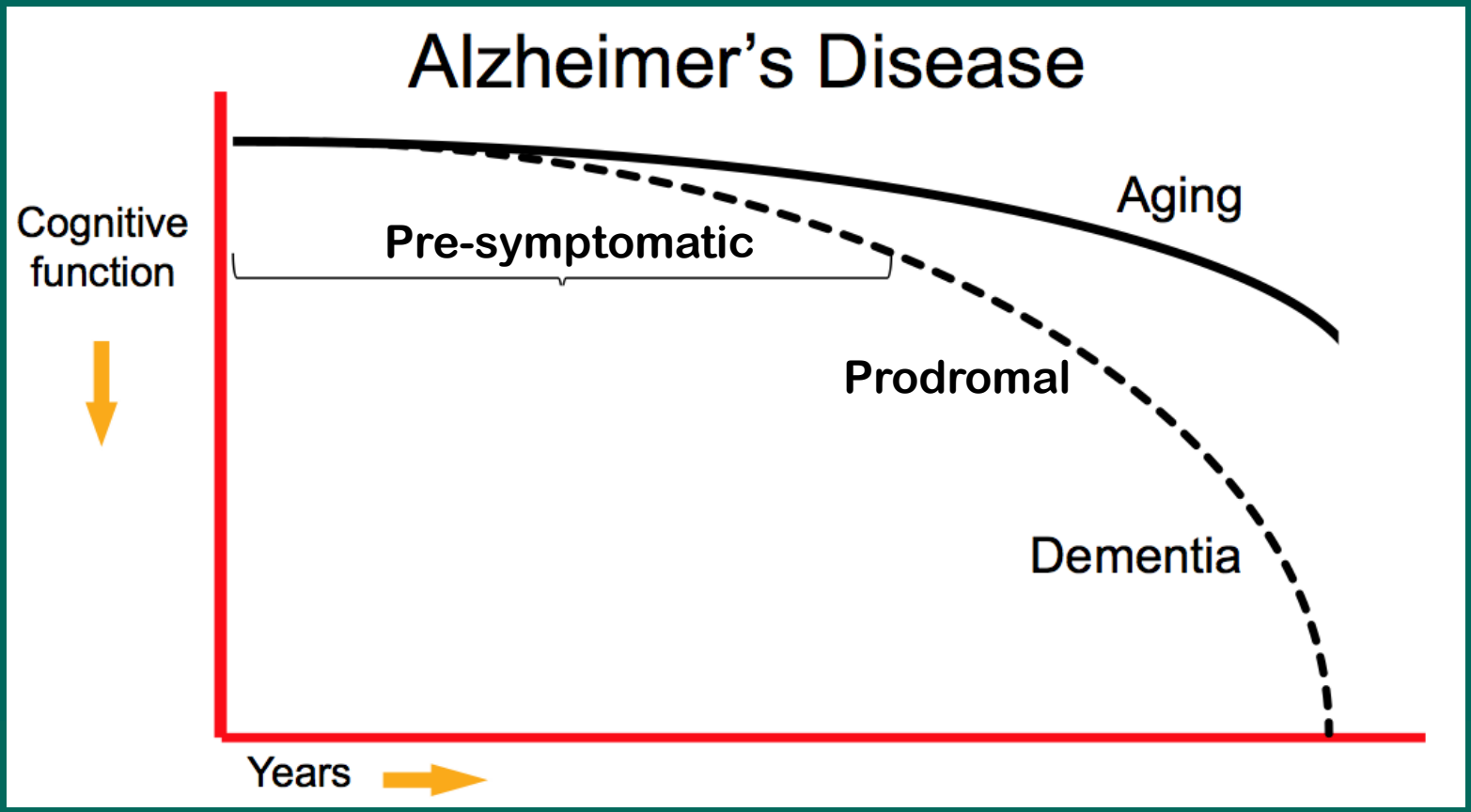
Alzheimer's disease



- Memory impairment
- Loss of ability to do something they were able to do in the past
- (Onset usually > 65)
- (Normal exam in early stages)

SIU

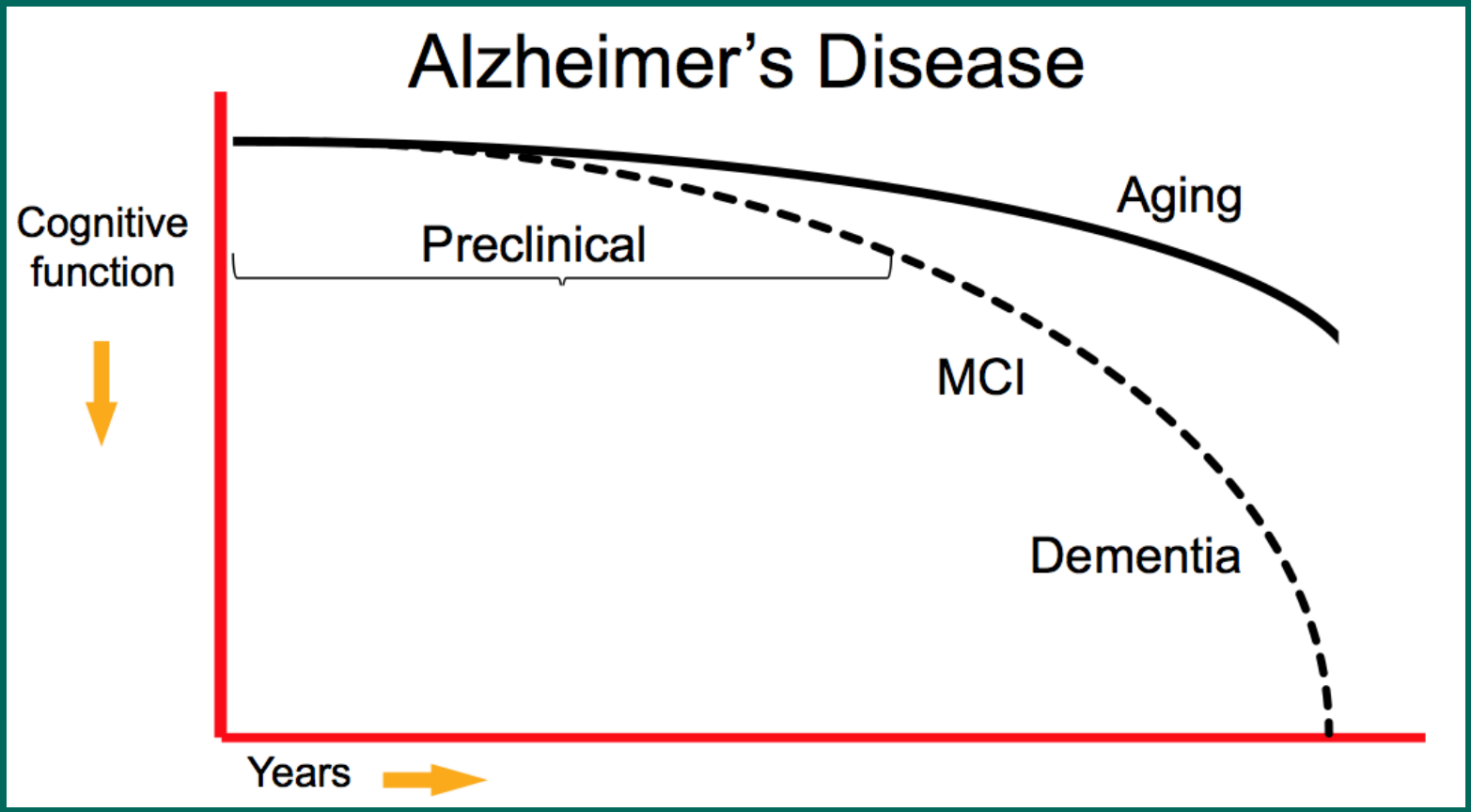
Model of the clinical trajectory of AD



Recommendations to Update Diagnostic Criteria, 2010
http://www.alz.org/research/diagnostic_criteria/

SIU

Model of the clinical trajectory of AD



Recommendations to Update Diagnostic Criteria, 2010
http://www.alz.org/research/diagnostic_criteria/

SIU

The final common pathway

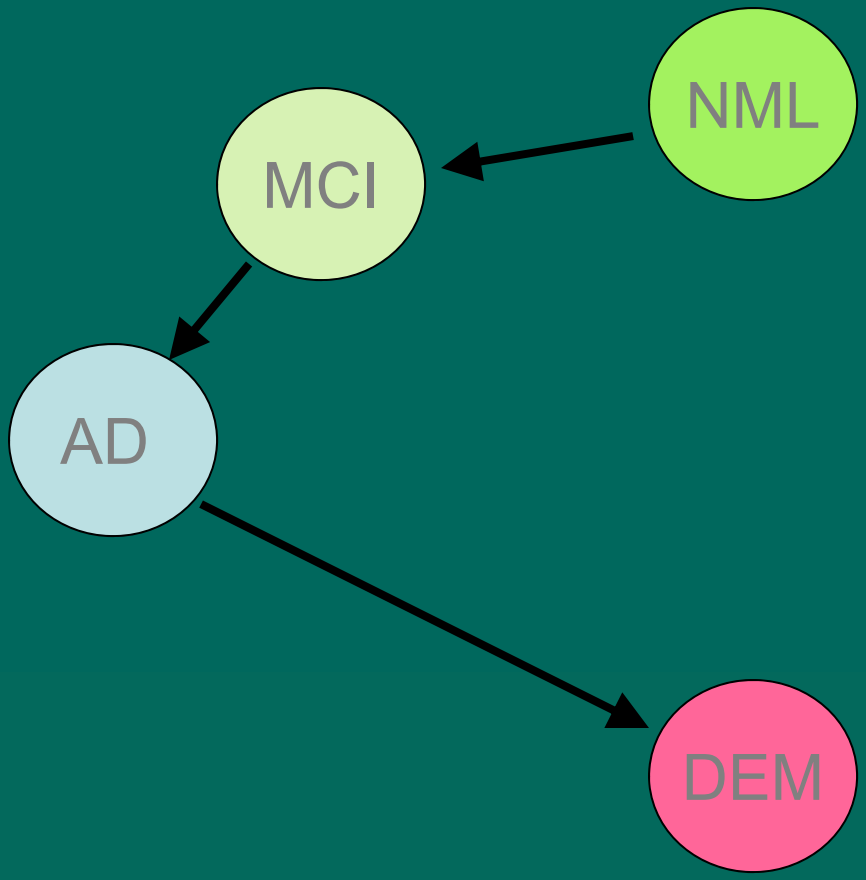


Table 1
Summary of clinical and cognitive evaluation for MCI due to AD

Establish clinical and cognitive criteria

Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time)

Objective evidence of impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains)

Preservation of independence in functional abilities

Not demented

Examine etiology of MCI consistent with AD pathophysiological process

Rule out vascular, traumatic, medical causes of cognitive decline, where possible

Provide evidence of longitudinal decline in cognition, when feasible

Report history consistent with AD genetic factors, where relevant

Albert. *Alz & Dem* 2011;7:270.

SIU

Table 1
Summary of clinical and cognitive evaluation for MCI due to AD

Establish clinical and cognitive criteria

Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time)

Objective evidence of impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains)

Preservation of independence in functional abilities

Not demented

Examine etiology of MCI consistent with AD pathophysiological process

Rule out vascular, traumatic, medical causes of cognitive decline, where possible

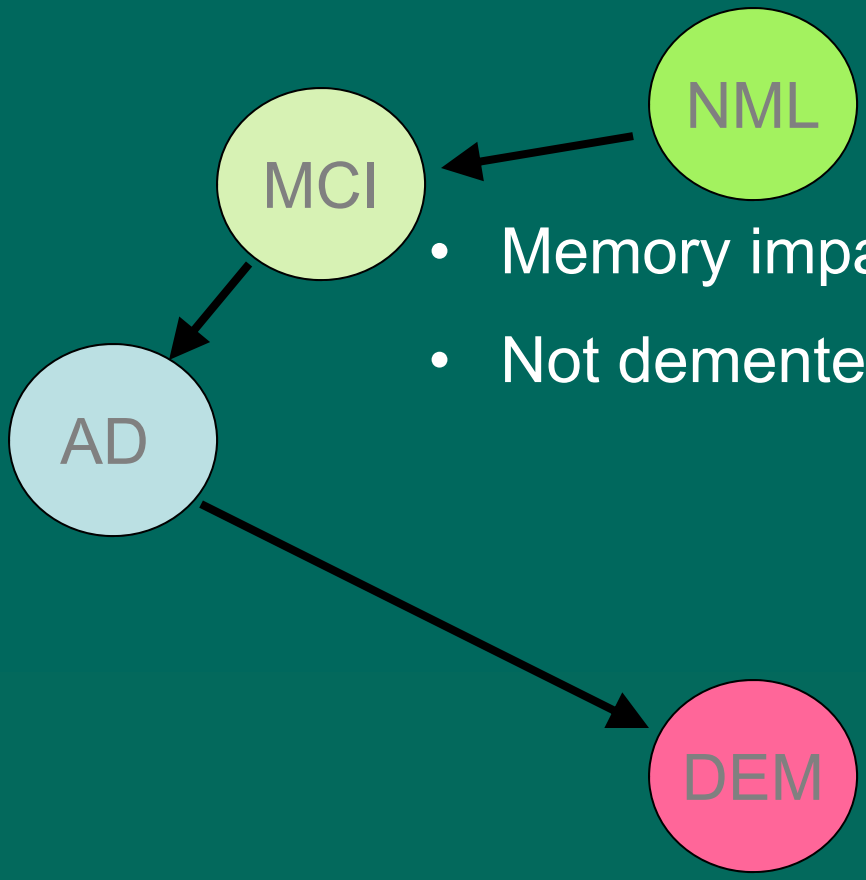
Provide evidence of longitudinal decline in cognition, when feasible

Report history consistent with AD genetic factors, where relevant

Albert. *Alz & Dem* 2011;7:270.

SIU

The final common pathway



- Memory impairment
- Not demented

Table 1
Summary of clinical and cognitive evaluation for MCI due to AD

Establish clinical and cognitive criteria

Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time)

Objective evidence of impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains)

Preservation of independence in functional abilities

Not demented

Examine etiology of MCI consistent with AD pathophysiological process

Rule out vascular, traumatic, medical causes of cognitive decline, where possible

Provide evidence of longitudinal decline in cognition, when feasible

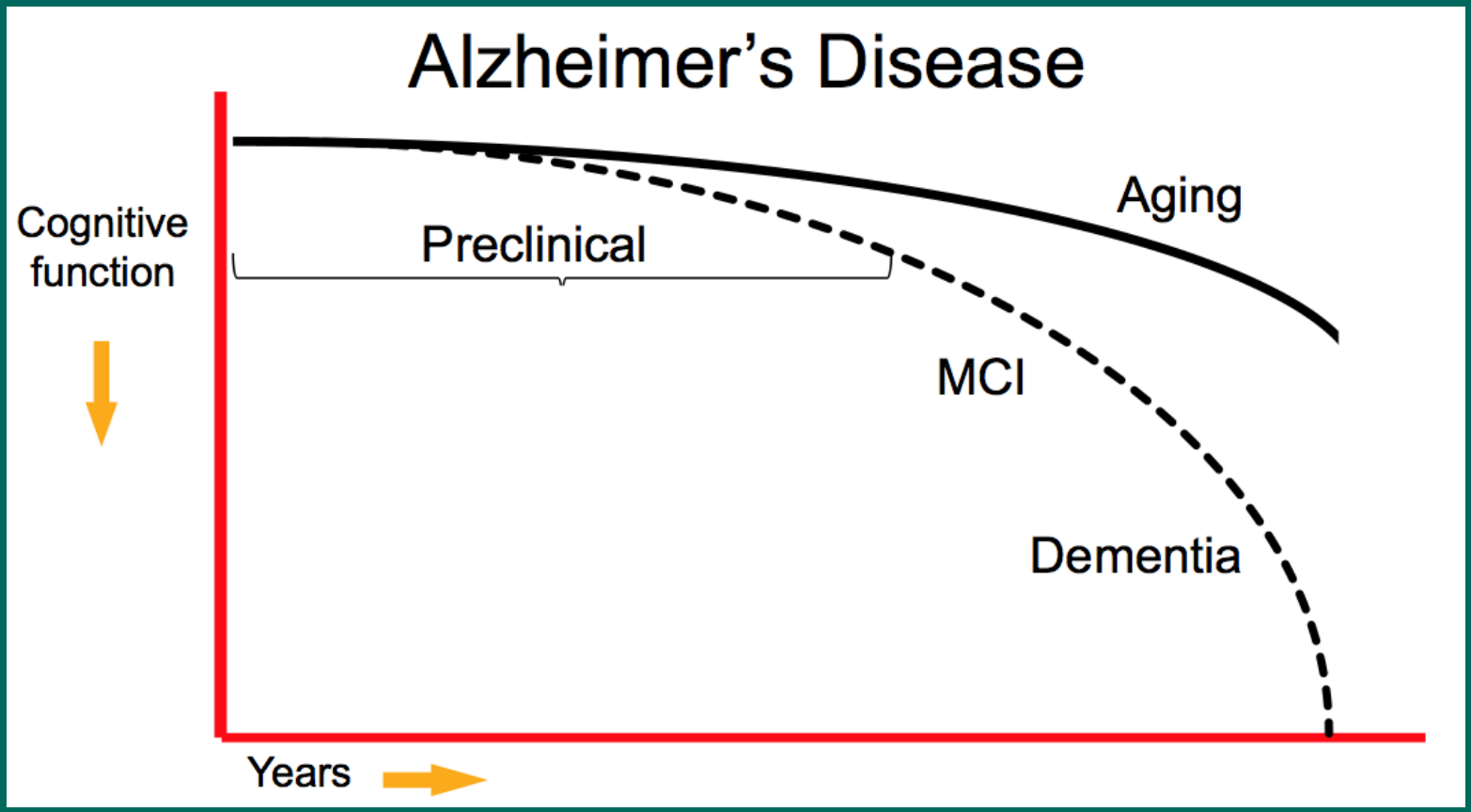
Report history consistent with AD genetic factors, where relevant

Albert. *Alz & Dem* 2011;7:270.

SIU

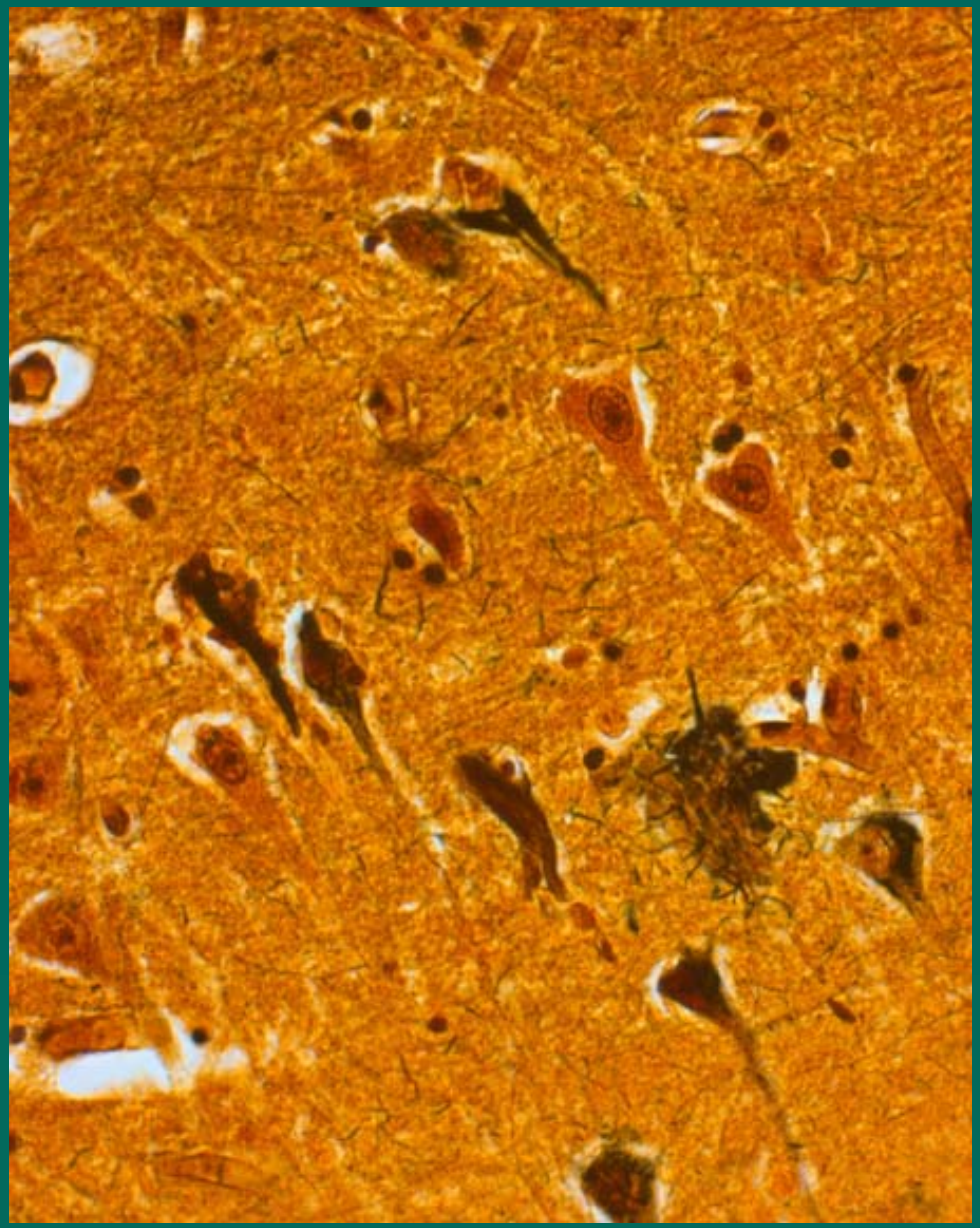
Biomarkers for AD

Model of the clinical trajectory of AD



Recommendations to Update Diagnostic Criteria, 2010
http://www.alz.org/research/diagnostic_criteria/

SIU



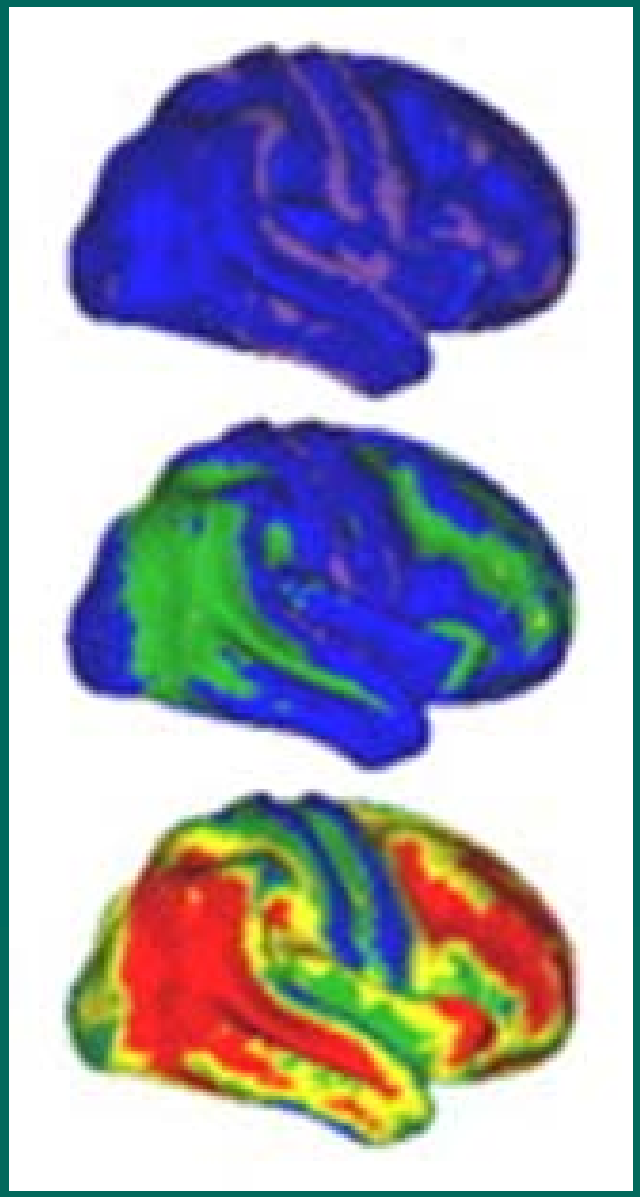
Alzheimer's disease

- Neurofibrillary tangles
- Senile plaques

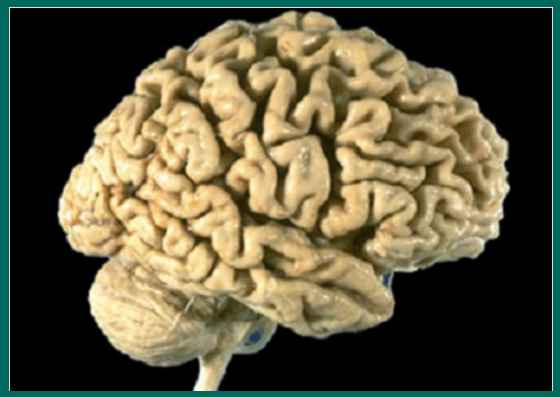
SIU

Biomarkers

- AD
- MCI (prodromal AD)
- Preclinical or pre-symptomatic AD



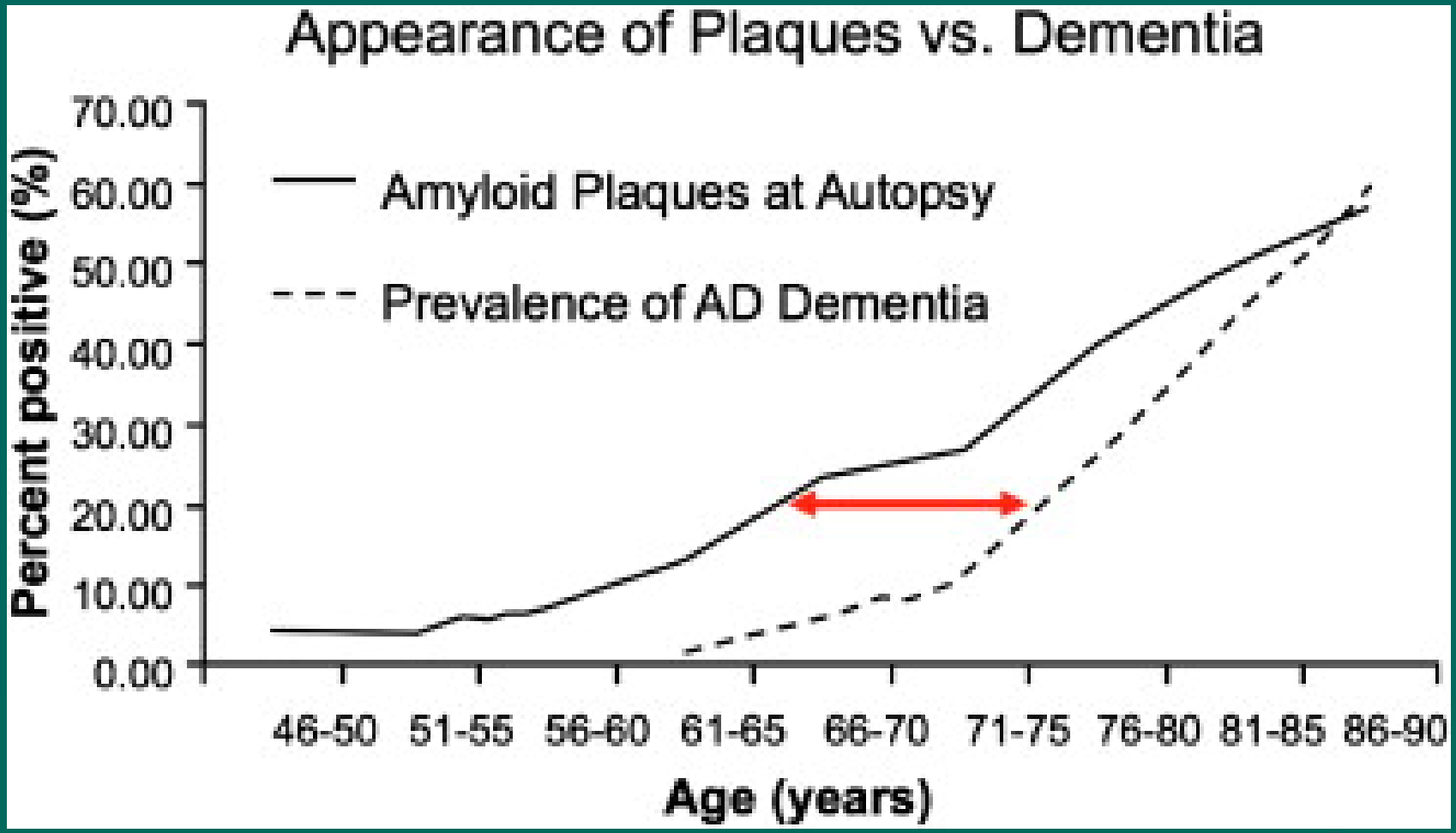
Accumulation of amyloid in Alzheimer's disease



Vlassenko. *Biochimica Biophysica Acta* 2012;1822:370.

SIU

Amyloid precedes dementia by decades



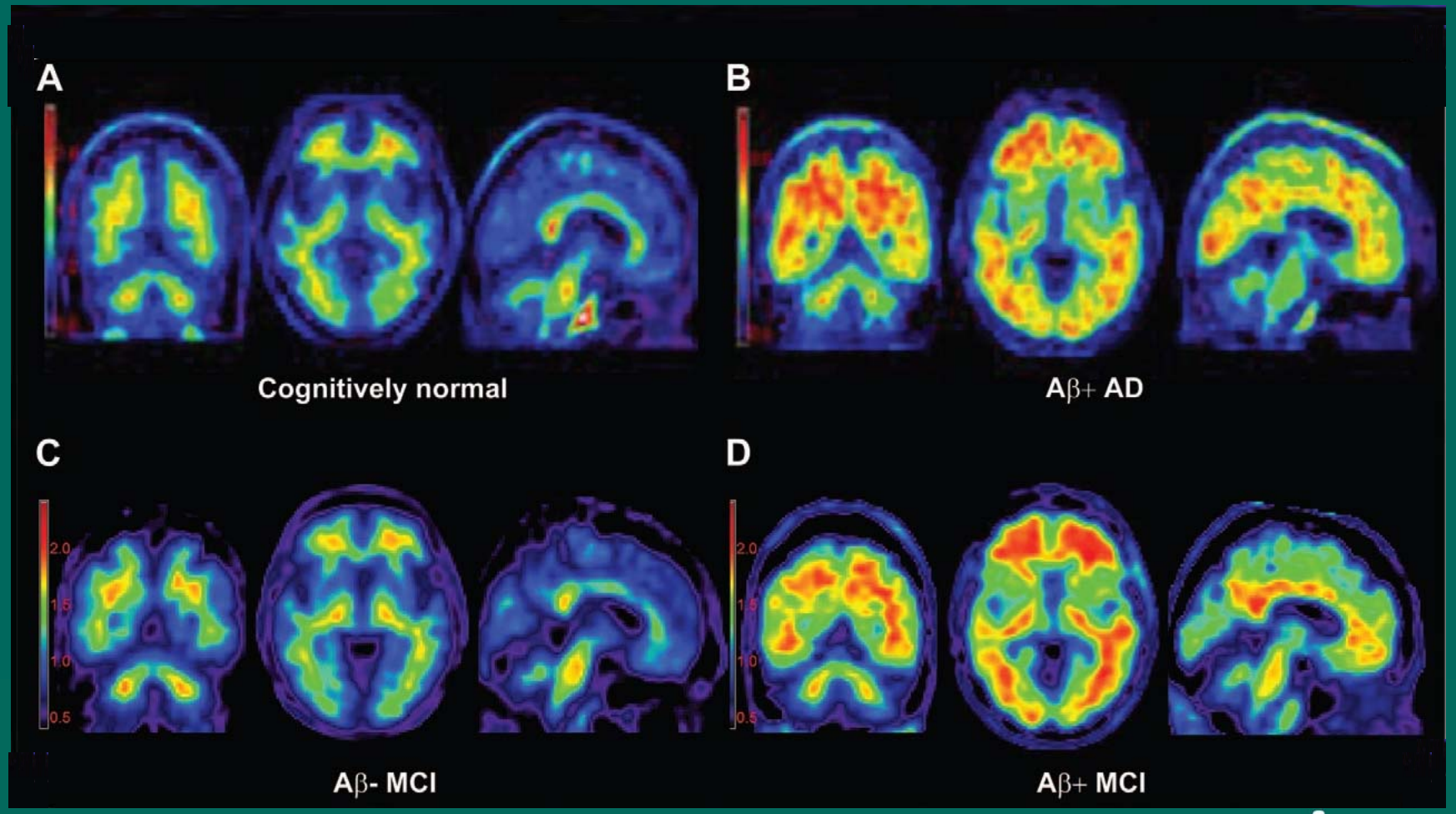
Sperling. *Alz & Dem* 2011;7:280.

SIU

PET scan imaging of amyloid

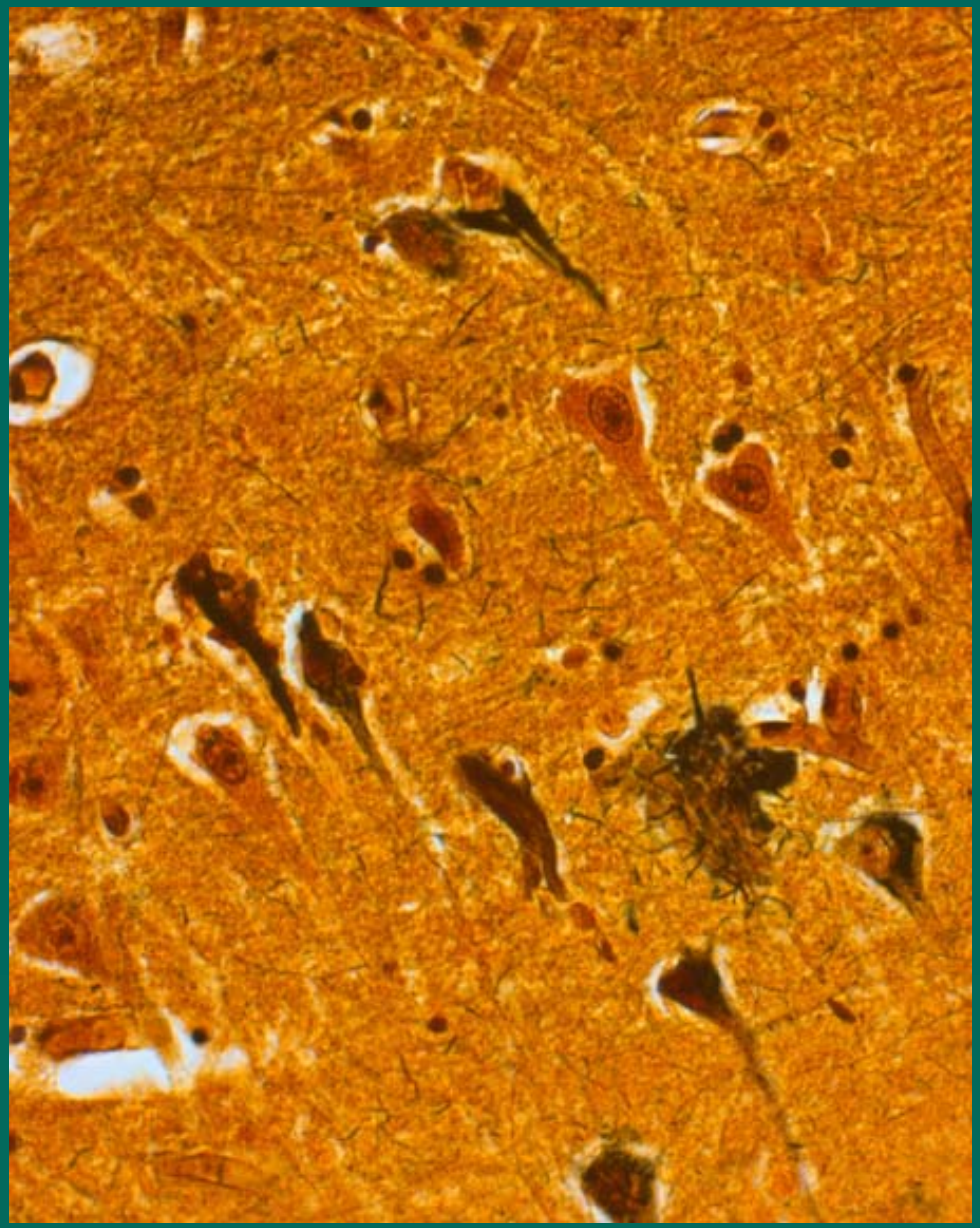
- Three PET scan imaging systems are now FDA-approved for imaging amyloid.
  - flutemetamol (Vizamyl®)
  - florbetapir (Amyvid®)
  - florbetaben (Neuraceq®)
- Confirm the diagnosis of Alzheimer's?
- Use as a biomarker to show treatment response?

Florbetapir (Amyvid®) PET scan



Doraiswamy. *Neurology* 2012;79:1636.

SIU

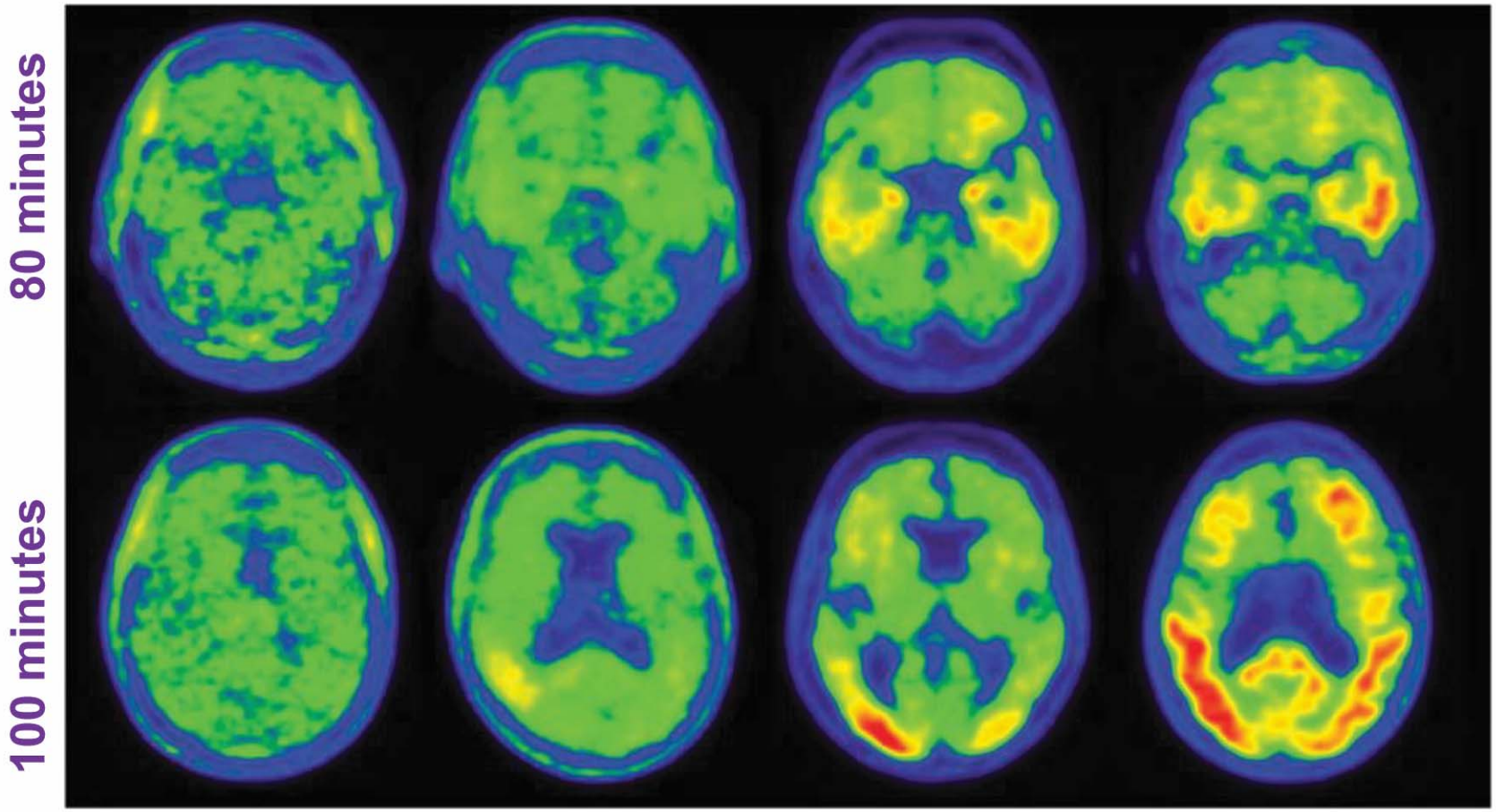


Alzheimer's disease

- Neurofibrillary tangles
- Senile plaques

SIU

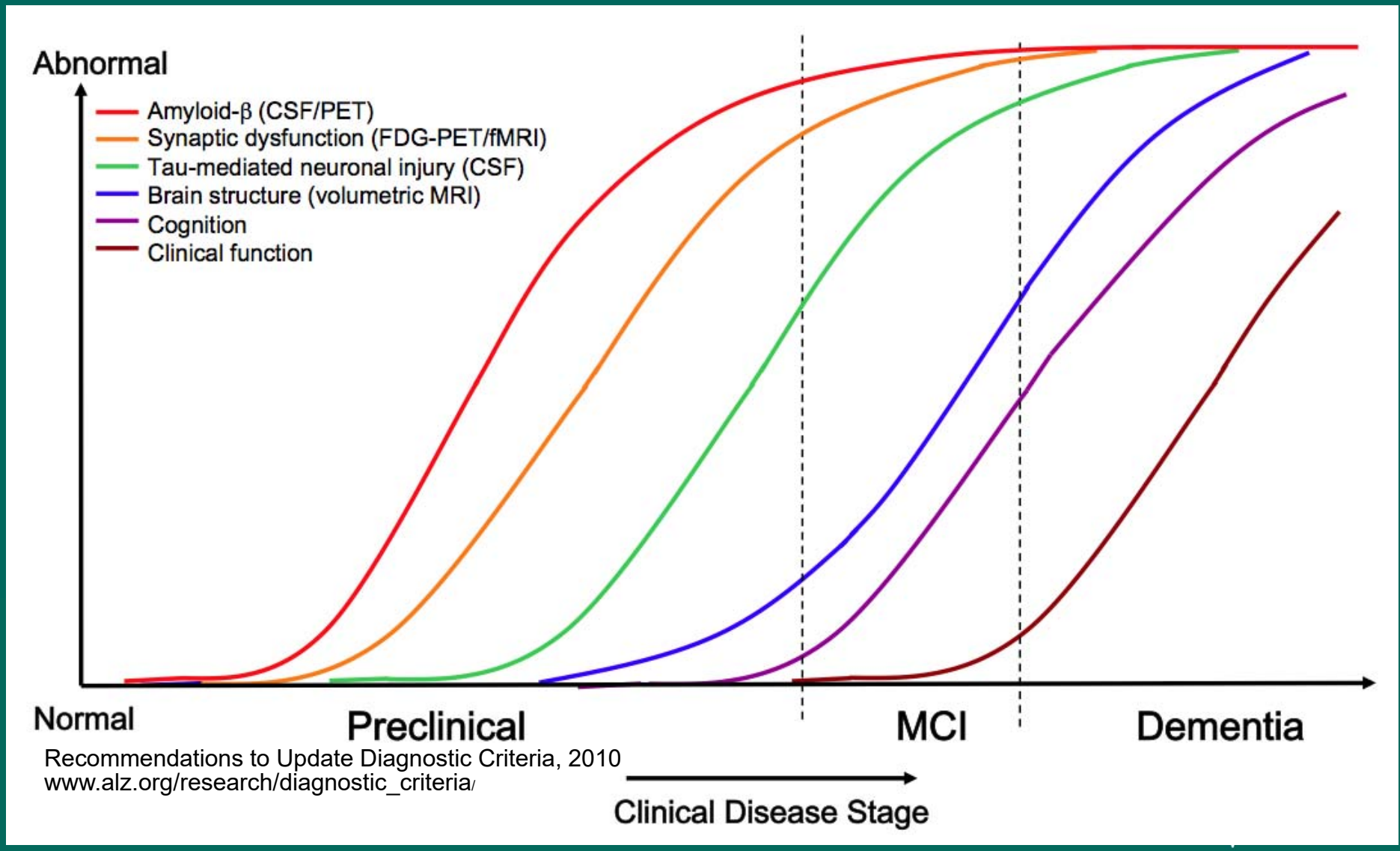
Alzheimer's disease: Tau Imaging



JT Chien et al. *Journal of Alzheimer's Disease* 2013

alzheimer's association®

Hypothetical model of dynamic biomarkers of the AD pathological cascade, expanded in the preclinical phase



Recommendations to Update Diagnostic Criteria, 2010
www.alz.org/research/diagnostic_criteria/

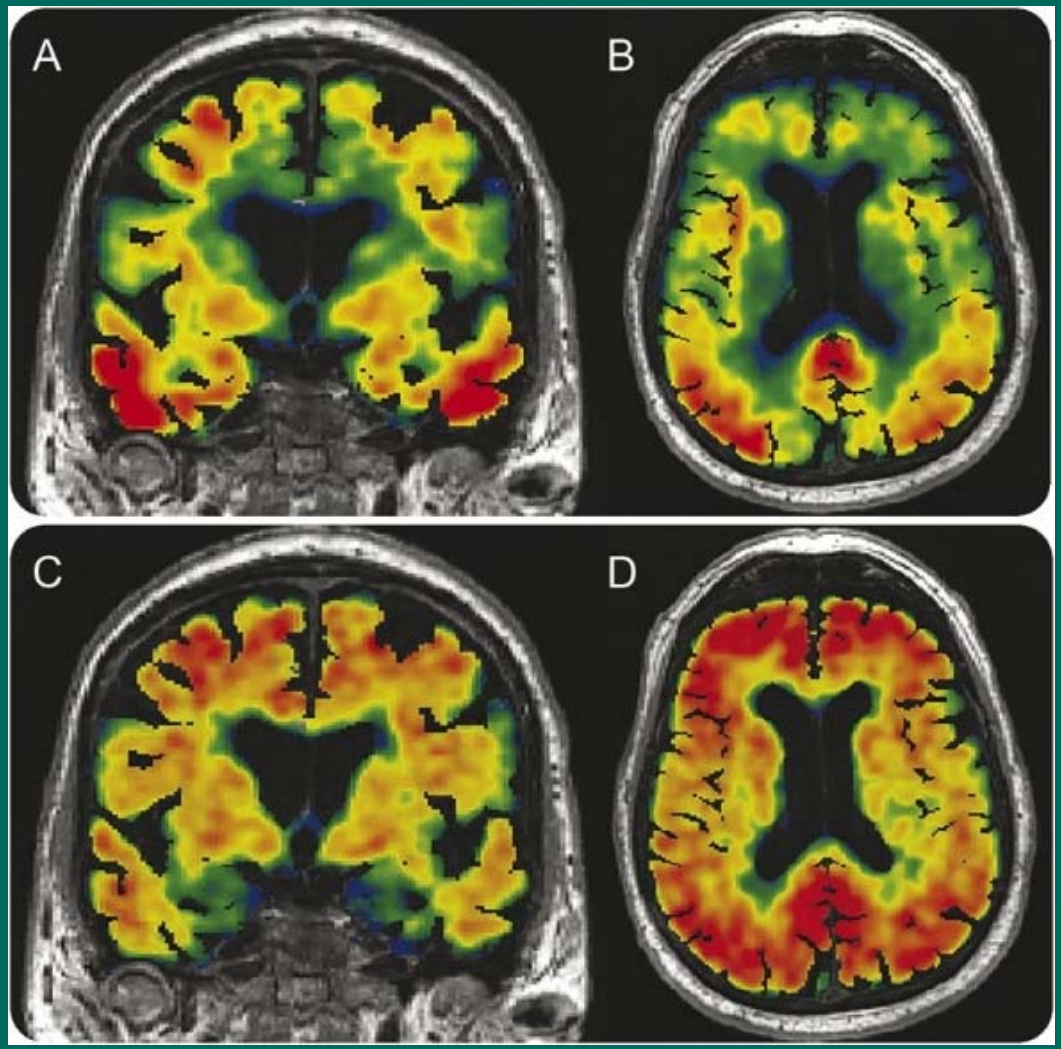
A / T / N

- An unbiased descriptive classification scheme for AD biomarkers
- Amyloid
  - Amyloid PET
  - CSF $A\beta^{42}$
- Tau
  - CSF phospho tau
  - Tau PET
- Neurodegeneration or neuronal injury
  - FDG PET
  - Structural MRI
  - CSF total tau

Jack. *Neurology* 2016;87:539.

SIU

Tau and amyloid PET imaging in AD

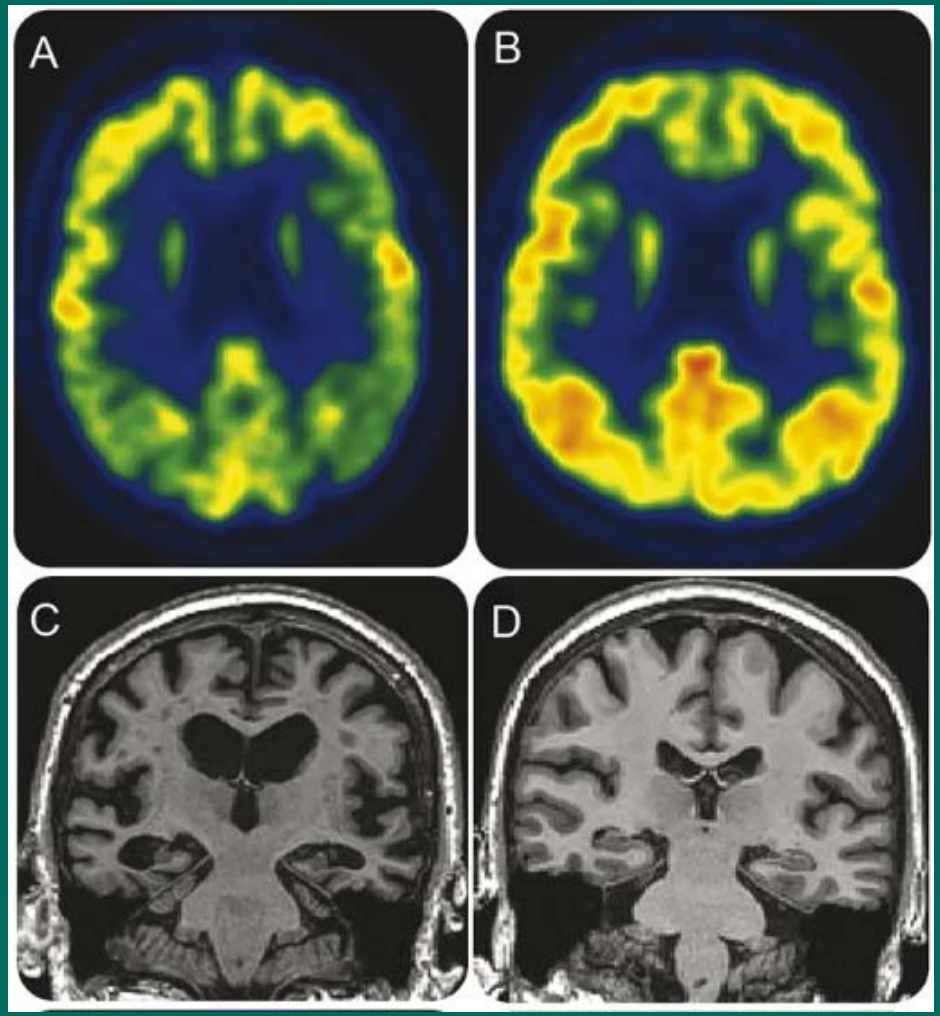


A 79-year-old man with a clinical diagnosis of AD dementia. He is a participant in the Mayo Alzheimer's Disease Research Center study. (A, B) Coronal and axial tau PET images (AV1451) superimposed on MRI. (C, D) Coronal and axial Pittsburgh compound B PET images superimposed on MRI. The tau PET images (top) illustrate extensive tracer uptake in basal lateral temporal, parietal, and frontal isocortex with sparing of sensory motor and primary visual cortices. Off-target binding is seen in the basal ganglia, which is characteristic of this tracer. Although areas of spatial overlap between the tau and amyloid tracers are present, abundant amyloid tracer uptake is seen in the frontal lobes, but not with the tau tracer. Conversely, abundant uptake is seen in the medial temporal lobes with the tau ligand but not with the amyloid ligand. AD = Alzheimer disease.

Jack. *Neurology* 2016;87:539.

SIU

Images of clinically normal individuals and participants with AD



Individuals with AD dementia are clinically diagnosed participants in Mayo Alzheimer's Disease Research Center study while clinically normal individuals are participants in the Mayo Clinic Study of Aging. (A) FDG-PET of 75-year-old man with AD dementia. Hypometabolism in medial parietal and lateral temporal-parietal isocortex with relative preservation of frontal metabolism, which is characteristic of typical (multidomain amnestic) AD. (B) FDG-PET of clinically normal 71-year-old man. Uniform FDG uptake is present throughout the isocortex. (C) MRI of 71-year-old man with AD dementia. Atrophy is present in the medial temporal allocortex and the basal-lateral temporal isocortex, which is characteristic of typical (multidomain amnestic) AD. (D) MRI of clinically normal 71-year-old woman without atrophy.. AD = Alzheimer disease; FDG = [^{18}F]-fluorodeoxyglucose.

Jack. *Neurology* 2016;87:539.

SIU

Table 3 Individuals who meet clinical criteria for probable AD dementia

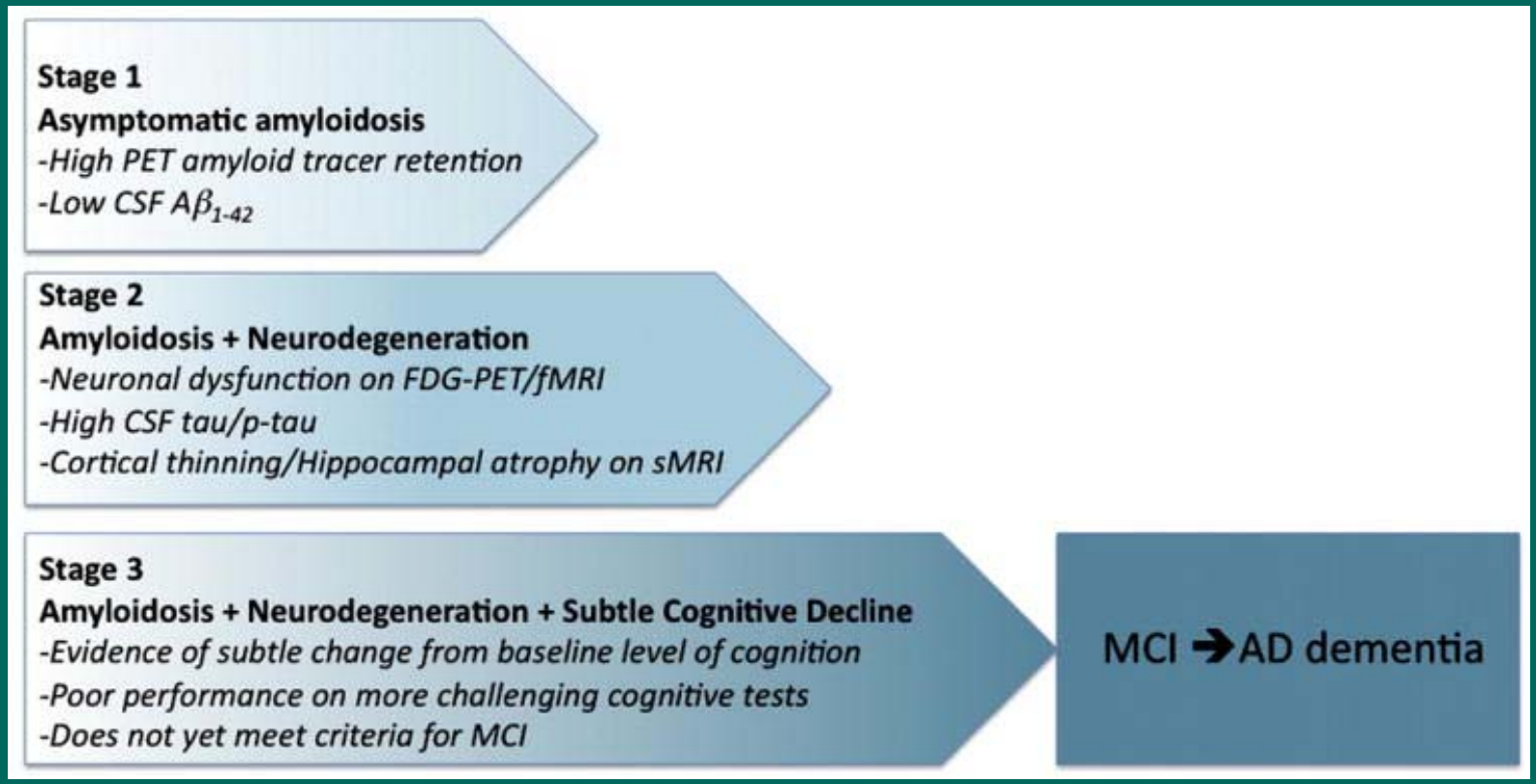
A/T/N score	NIA-AA classification	2014 IWG classification
A−/T−/N−	Dementia, unlikely due to AD	Not defined
A+/T−/N−	Intermediate likelihood; probable AD dementia; based on clinical criteria[a]	Typical AD (if A+ established by amyloid PET)
A+/T+/N−	High likelihood probable AD dementia; based on clinical criteria[a]	Typical AD
A+/T−/N+	High likelihood; probable AD dementia; based on clinical criteria[a]	Typical AD (if A+ established by amyloid PET)
A+/T+/N+	High likelihood AD pathophysiology	Typical AD
A−/T+/N−	Probable AD dementia; based on clinical criteria[a]	Not defined
A−/T−/N+	Intermediate likelihood; probable AD dementia; based on clinical criteria[a]	Not defined
A−/T+/N+	Intermediate likelihood; probable AD dementia; based on clinical criteria[a]	Not defined

Abbreviations: AD = Alzheimer disease; IWG = International Working Group; NIA-AA = National Institute on Aging-Alzheimer's Association.

[a] In the event of conflicting results, biomarkers are regarded as "uninformative" and therefore do not alter the individual's diagnostic classification based on clinical assessment alone.

Jack. *Neurology* 2016;87:539.

SIU



Graphic representation of the proposed staging framework for preclinical AD. Note that some individuals will not progress beyond Stage 1 or Stage 2. Individuals in Stage 3 are postulated to be more likely to progress to MCI and AD dementia.

Sperling. *Alz & Dem* 2011;7:280.

SIU

A / T / N

- A biomarker classification scheme
- Includes all individuals in any population
- Does not specify disease labels (not a diagnostic classification system)
- Descriptive system for categorizing multidomain biomarker findings at the individual person level

Jack. Neurology 2016;87:539.

SIU

Current AD research direction

- Treat Alzheimer's before too much damage is done.

Current AD research direction

- Treat Alzheimer's before too much damage is done.
- Treat Alzheimer's before the patient has symptoms.

Current AD research direction

- Treat Alzheimer's before too much damage is done.
- Treat Alzheimer's before the patient has symptoms.
- How do you identify those patients?

A / T / N system

- State vs stage
- Good discussion
  - Knopman, et al. Perspectives from the Research Roundtable. *Alzheimer's & Dementia* 2018; 563

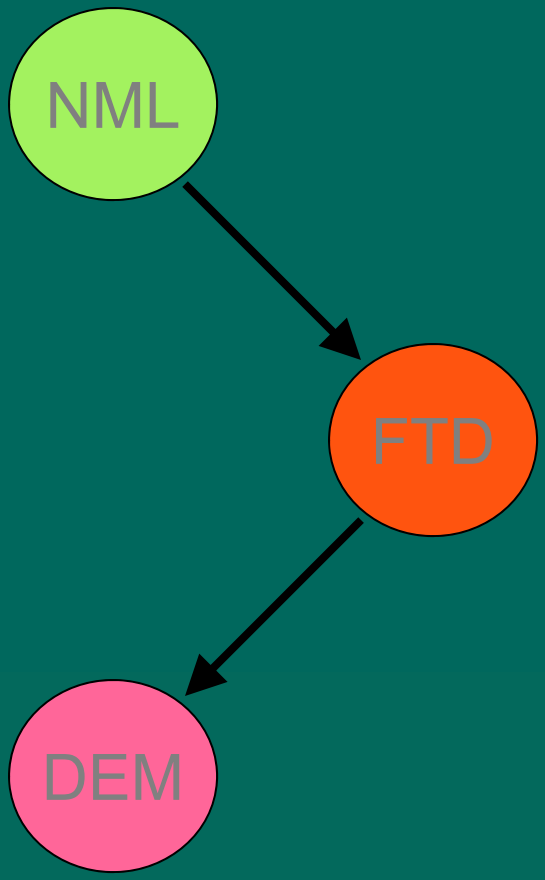
Nota Bene

- At present the ATN system is a research construct.
- At present it is not helpful for the patients we see in clinic with AD.
- At present FDA criteria for AD drug approval require clinical benefit.

SIU

FTD

Frontotemporal dementia



Clinical FTD

- Behavioral variant
- Primary progressive aphasia

International consensus criteria for behavioural variant FTD (FTDC)

I. Neurodegenerative disease
The following symptom must be present to meet criteria for bvFTD
A. Shows progressive deterioration of behaviour and/or cognition by observation or history (as provided by a knowledgeable informant).
II. Possible bvFTD
Three of the following behavioural/cognitive symptoms (A–F) must be present to meet criteria. Ascertainment requires that symptoms be persistent or recurrent, rather than single or rare events.
A. Early* behavioural disinhibition [one of the following symptoms (A.1–A.3) must be present]:
A.1. Socially inappropriate behaviour
A.2. Loss of manners or decorum
A.3. Impulsive, rash or careless actions
B. Early apathy or inertia [one of the following symptoms (B.1–B.2) must be present]:
B.1. Apathy
B.2. Inertia
C. Early loss of sympathy or empathy [one of the following symptoms (C.1–C.2) must be present]:
C.1. Diminished response to other people's needs and feelings
C.2. Diminished social interest, interrelatedness or personal warmth
D. Early perseverative, stereotyped or compulsive/ritualistic behaviour [one of the following symptoms (D.1–D.3) must be present]:
D.1. Simple repetitive movements
D.2. Complex, compulsive or ritualistic behaviours
D.3. Stereotypy of speech
E. Hyperorality and dietary changes [one of the following symptoms (E.1–E.3) must be present]:
E.1. Altered food preferences
E.2. Binge eating, increased consumption of alcohol or cigarettes
E.3. Oral exploration or consumption of inedible objects
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
F.3. Relative sparing of visuospatial skills
III. Probable bvFTD
All of the following symptoms (A–C) must be present to meet criteria.
A. Meets criteria for possible bvFTD
B. Exhibits significant functional decline (by caregiver report or as evidenced by Clinical Dementia Rating Scale or Functional Activities Questionnaire scores)
C. Imaging results consistent with bvFTD [one of the following (C.1–C.2) must be present]:
C.1. Frontal and/or anterior temporal atrophy on MRI or CT
C.2. Frontal and/or anterior temporal hypoperfusion or hypometabolism on PET or SPECT
IV. Behavioural variant FTD with definite FTLD Pathology
Criterion A and either criterion B or C must be present to meet criteria.
A. Meets criteria for possible or probable bvFTD
B. Histopathological evidence of FTLD on biopsy or at post-mortem
C. Presence of a known pathogenic mutation
V. Exclusionary criteria for bvFTD
Criteria A and B must be answered negatively for any bvFTD diagnosis. Criterion C can be positive for possible bvFTD but must be negative for probable bvFTD.
A. Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders
B. Behavioural disturbance is better accounted for by a psychiatric diagnosis
C. Biomarkers strongly indicative of Alzheimer's disease or other neurodegenerative process

Rascovsky. Brain 2011;134:2456.

SIU

International consensus criteria for behavioural variant FTD (FTDC)

I. Neurodegenerative disease
The following symptom must be present to meet criteria for bvFTD
A. Shows progressive deterioration of behaviour and/or cognition by observation or history (as provided by a knowledgeable informant).
II. Possible bvFTD
Three of the following behavioural/cognitive symptoms (A–F) must be present to meet criteria. Ascertainment requires that symptoms be persistent or recurrent, rather than single or rare events.
A. Early* behavioural disinhibition [one of the following symptoms (A.1–A.3) must be present]:
A.1. Socially inappropriate behaviour
A.2. Loss of manners or decorum
A.3. Impulsive, rash or careless actions
B. Early apathy or inertia [one of the following symptoms (B.1–B.2) must be present]:
B.1. Apathy
B.2. Inertia
C. Early loss of sympathy or empathy [one of the following symptoms (C.1–C.2) must be present]:
C.1. Diminished response to other people's needs and feelings
C.2. Diminished social interest, interrelatedness or personal warmth
D. Early perseverative, stereotyped or compulsive/ritualistic behaviour [one of the following symptoms (D.1–D.3) must be present]:
D.1. Simple repetitive movements
D.2. Complex, compulsive or ritualistic behaviours
D.3. Stereotypy of speech
E. Hyperorality and dietary changes [one of the following symptoms (E.1–E.3) must be present]:
E.1. Altered food preferences
E.2. Binge eating, increased consumption of alcohol or cigarettes
E.3. Oral exploration or consumption of inedible objects
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
F.3. Relative sparing of visuospatial skills
III. Probable bvFTD
All of the following symptoms (A–C) must be present to meet criteria.
A. Meets criteria for possible bvFTD
B. Exhibits significant functional decline (by caregiver report or as evidenced by Clinical Dementia Rating Scale or Functional Activities Questionnaire scores)
C. Imaging results consistent with bvFTD [one of the following (C.1–C.2) must be present]:
C.1. Frontal and/or anterior temporal atrophy on MRI or CT
C.2. Frontal and/or anterior temporal hypoperfusion or hypometabolism on PET or SPECT
IV. Behavioural variant FTD with definite FTLD Pathology
Criterion A and either criterion B or C must be present to meet criteria.
A. Meets criteria for possible or probable bvFTD
B. Histopathological evidence of FTLD on biopsy or at post-mortem
C. Presence of a known pathogenic mutation
V. Exclusionary criteria for bvFTD
Criteria A and B must be answered negatively for any bvFTD diagnosis. Criterion C can be positive for possible bvFTD but must be negative for probable bvFTD.
A. Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders
B. Behavioural disturbance is better accounted for by a psychiatric diagnosis
C. Biomarkers strongly indicative of Alzheimer's disease or other neurodegenerative process

Rascovsky. Brain 2011;134:2456.

SIU

International consensus criteria for behavioural variant FTD

I. Neurodegenerative disease

Shows progressive deterioration of behaviour and/or cognition by observation or history

II. Possible bvFTD

III. Probable bvFTD

All of the following symptoms must be present to meet criteria.

- Meets criteria for possible bvFTD
- Exhibits significant functional decline
- Imaging results consistent with bvFTD

Rascovsky. Brain 2011;134:2456.

SIU

International consensus criteria for behavioural variant FTD

II. Possible bvFTD. Three of the following must be present.

A. Early behavioural disinhibition [one of the following must be present]:
- Socially inappropriate behaviour
- Loss of manners or decorum
- Impulsive, rash or careless actions

B. Early apathy or inertia [one of the following must be present]:
- Apathy
- Inertia

C. Early loss of sympathy or empathy [one of the following must be present]:
- Diminished response to other people's needs and feelings
- Diminished social interest, interrelatedness or personal warmth

D. Early perseverative, stereotyped or compulsive/ritualistic behaviour [one of the following must be present]:
- Simple repetitive movements
- Complex, compulsive or ritualistic behaviours
- Stereotypy of speech

E. Hyperorality and dietary changes [one of the following must be present]:
- Altered food preferences
- Binge eating, increased consumption of alcohol or cigarettes
- Oral exploration or consumption of inedible objects

F. Neuropsychological profile: executive/generation deficits with relative sparing of memory and visuospatial functions [all of the following must be present]:
- Deficits in executive tasks
- Relative sparing of episodic memory
- Relative sparing of visuospatial skills

Rascovsky. Brain 2011;134:2456.

SIU

FTD behavioral variant

- I. Progressive deterioration of behavior
- II. Requires three of the following:
  - Early behavioral disinhibition
  - Early apathy or inertia
  - Early loss of sympathy or empathy
  - Early perseverative, stereotyped compulsive/ritualistic behavior
  - Hyperorality and dietary changes
  - Neuropsychological profile: executive deficits with relative sparing of memory and visuospatial functions

First Report of the International bvFTD Criteria Consortium

SIU

International consensus criteria for behavioural variant FTD

I. Neurodegenerative disease

Shows progressive deterioration of behaviour and/or cognition by observation or history

II. Possible bvFTD

III. Probable bvFTD

All of the following symptoms must be present to meet criteria.

- Meets criteria for possible bvFTD
- Exhibits significant functional decline
- Imaging results consistent with bvFTD

Rascovsky. Brain 2011;134:2456.

SIU

Imaging results consistent with bvFTD

One of the following must be present

- Frontal and/or anterior temporal atrophy on MRI or CT
- Frontal and/or anterior temporal hypoperfusion or hypometabolism on PET or SPECT

Clinical FTD

- Behavioral variant
- Primary progressive aphasia

2011 consensus criteria

Inclusion and exclusion criteria for the diagnosis of PPA

- Inclusion: criteria 1–3 must be answered positively
  - 1. Most prominent clinical feature is difficulty with language.
  - 2. These deficits are the principal cause of impaired daily living activities.
  - 3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease.
- Exclusion: criteria 1–4 must be answered negatively
  - 1. Pattern of deficits is better accounted for by other nondegenerative nervous system or medical disorders.
  - 2. Cognitive disturbance is better accounted for by a psychiatric diagnosis.
  - 3. Prominent initial episodic memory, visual memory, and visuoperceptual impairments.
  - 4. Prominent, initial behavioral disturbance.

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Primary Progressive Aphasia

1. Most prominent clinical feature is difficulty with language.

2. These deficits are the principal cause of impaired daily living activities.

3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease.

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Primary Progressive Aphasia

1. Most prominent clinical feature is difficulty with language.

2. These deficits are the principal cause of impaired daily living activities.

3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease.

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Primary Progressive Aphasia

1. Most prominent clinical feature is difficulty with language.

2. These deficits are the principal cause of impaired daily living activities.

3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease.

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Clinical diagnosis of FTD

- Behavioral variant
- Primary progressive aphasia (PPA)
  - Nonfluent / agrammatic variant
  - Semantic variant
  - Logopenic variant

2011 consensus criteria

SIU

Primary progressive aphasia

- Nonfluent / agrammatic variant
- Semantic variant
- Logopenic variant

Primary progressive aphasia

- nonfluent/agrammatic variant (navPPA)
- semantic variant (svPPA)
- logopenic variant (lvPPA)

Clinical diagnosis of navPPA

- At least one of the following core features must be present:
  - Agrammatism in language production
  - Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)
- At least 2 of 3 of the following other features must be present:
  - Impaired comprehension of syntactically complex sentences
  - Spared single-word comprehension
  - Spared object knowledge

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Clinical diagnosis of navPPA

- At least one of the following core features must be present:
  - Agrammatism in language production
  - Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)
- At least 2 of 3 of the following other features must be present:
  - Impaired comprehension of syntactically complex sentences
  - Spared single-word comprehension
  - Spared object knowledge

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

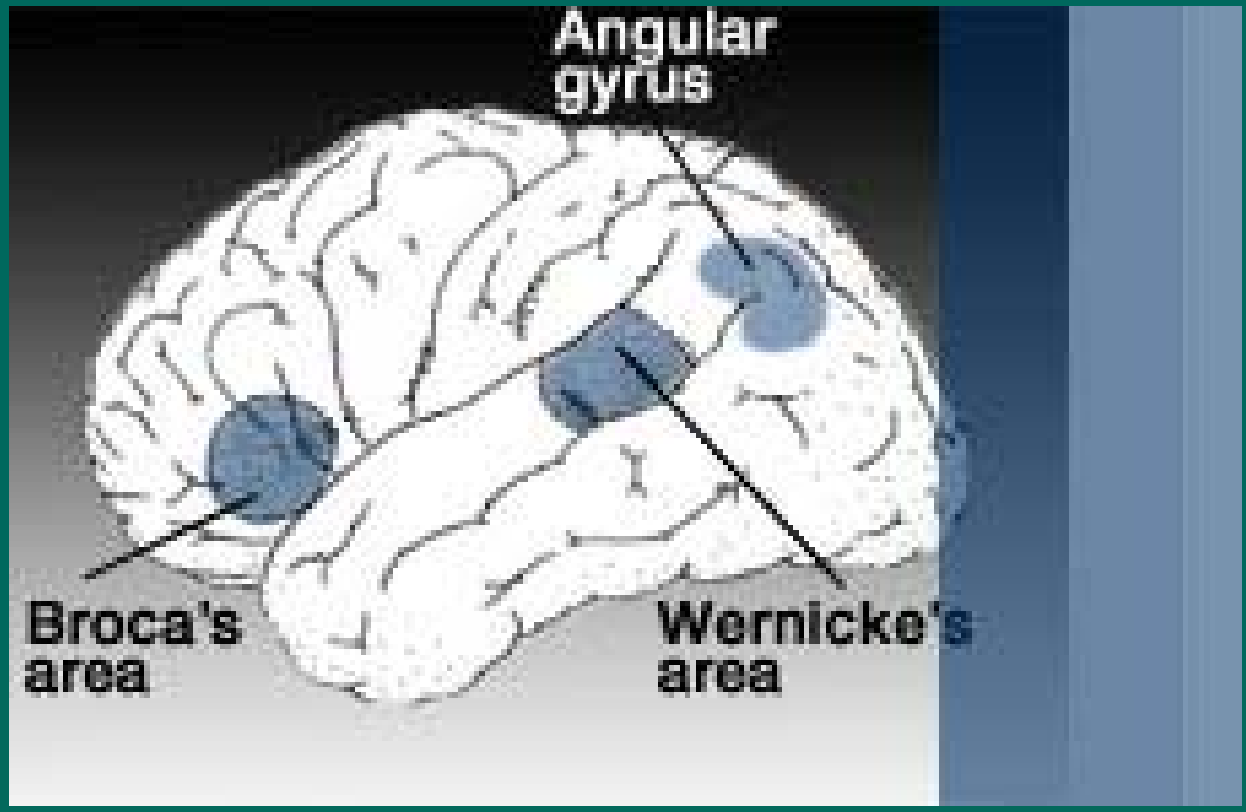
Imaging-supported navPPA diagnosis

- Both of the following criteria must be present:
  - Clinical diagnosis of navPPA
  - Imaging must show one or more of the following:
    - Predominant left posterior fronto-insular atrophy on MRI, or
    - Predominant left posterior fronto-insular hypoperfusion or hypometabolism on SPECT or PET

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Think about it



Clinical diagnosis of svPPA

- Both of the following core features must be present:
  - Impaired confrontation naming
  - Impaired single-word comprehension
- At least 3 of the following other diagnostic features must be present:
  - Impaired object knowledge, particularly for low frequency or low-familiarity items
  - Surface dyslexia or dysgraphia
  - Spared repetition
  - Spared speech production (grammar and motor speech)

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Clinical diagnosis of svPPA

- Both of the following core features must be present:
  - Impaired confrontation naming
  - Impaired single-word comprehension
- At least 3 of the following other diagnostic features must be present:
  - Impaired object knowledge, particularly for low frequency or low-familiarity items
  - Surface dyslexia or dysgraphia
  - Spared repetition
  - Spared speech production (grammar and motor speech)

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

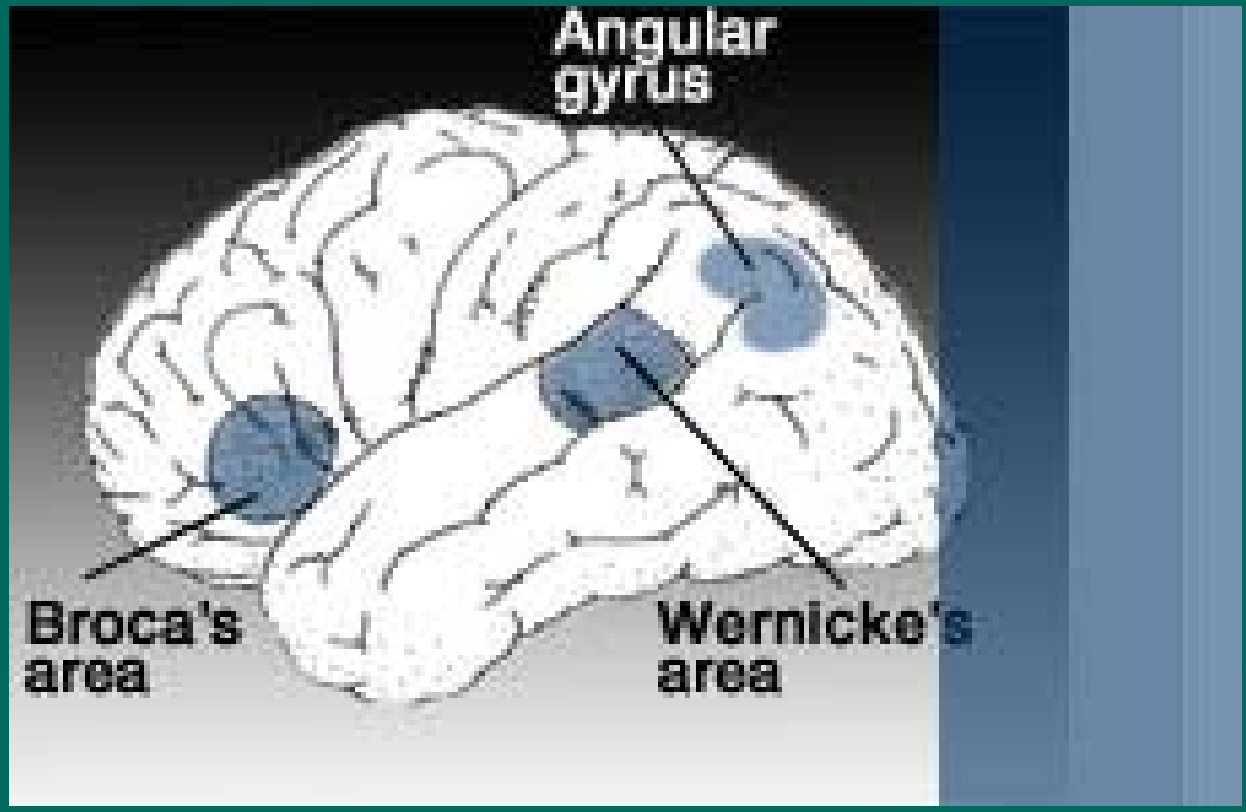
Imaging-supported svPPA diagnosis

- Both of the following criteria must be present:
  - Clinical diagnosis of semantic variant PPA
  - Imaging must show one or more of the following:
    - Predominant anterior temporal lobe atrophy, or
    - Predominant anterior temporal hypoperfusion or hypometabolism on SPECT or PET

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Think about it



Clinical diagnosis of lvPPA

- Both of the following core features must be present:
  - Impaired single-word retrieval in spontaneous speech and naming
  - Impaired repetition of sentences and phrases
- At least 3 of the following other features must be present:
  - Speech (phonologic) errors in spontaneous speech and naming
  - Spared single-word comprehension and object knowledge
  - Spared motor speech
  - Absence of frank agrammatism

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Clinical diagnosis of lvPPA

- Both of the following core features must be present:
  - Impaired single-word retrieval in spontaneous speech and naming
  - Impaired repetition of sentences and phrases
- At least 3 of the following other features must be present:
  - Speech (phonologic) errors in spontaneous speech and naming
  - Spared single-word comprehension and object knowledge
  - Spared motor speech
  - Absence of frank agrammatism

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

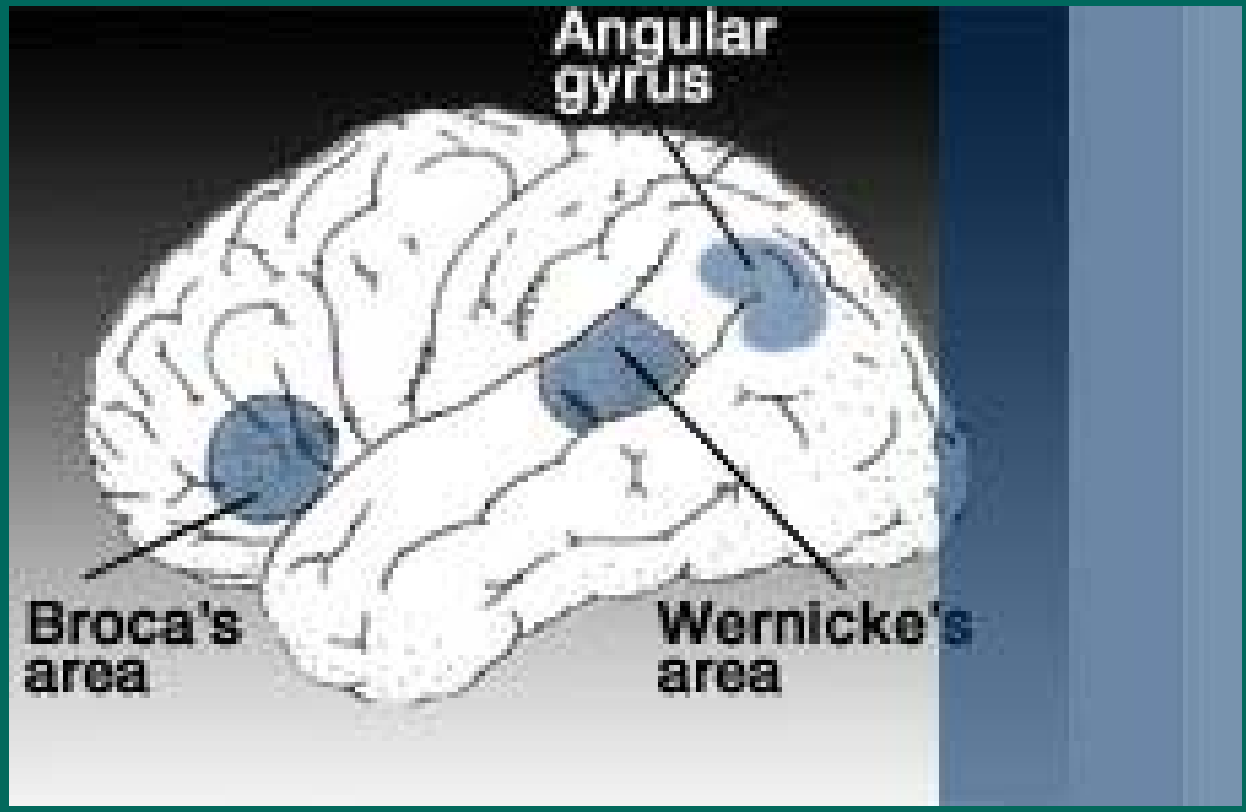
Imaging-supported lvPPA diagnosis

- Both criteria must be present:
  - Clinical diagnosis of lvPPA
  - Imaging must show at least one of the following:
    - Predominant left posterior perisylvian or parietal atrophy on MRI, or
    - Predominant left posterior perisylvian or parietal hypoperfusion or hypometabolism on SPECT or PET

Gorno-Tempini. *Neurology* 2011;76:1006.

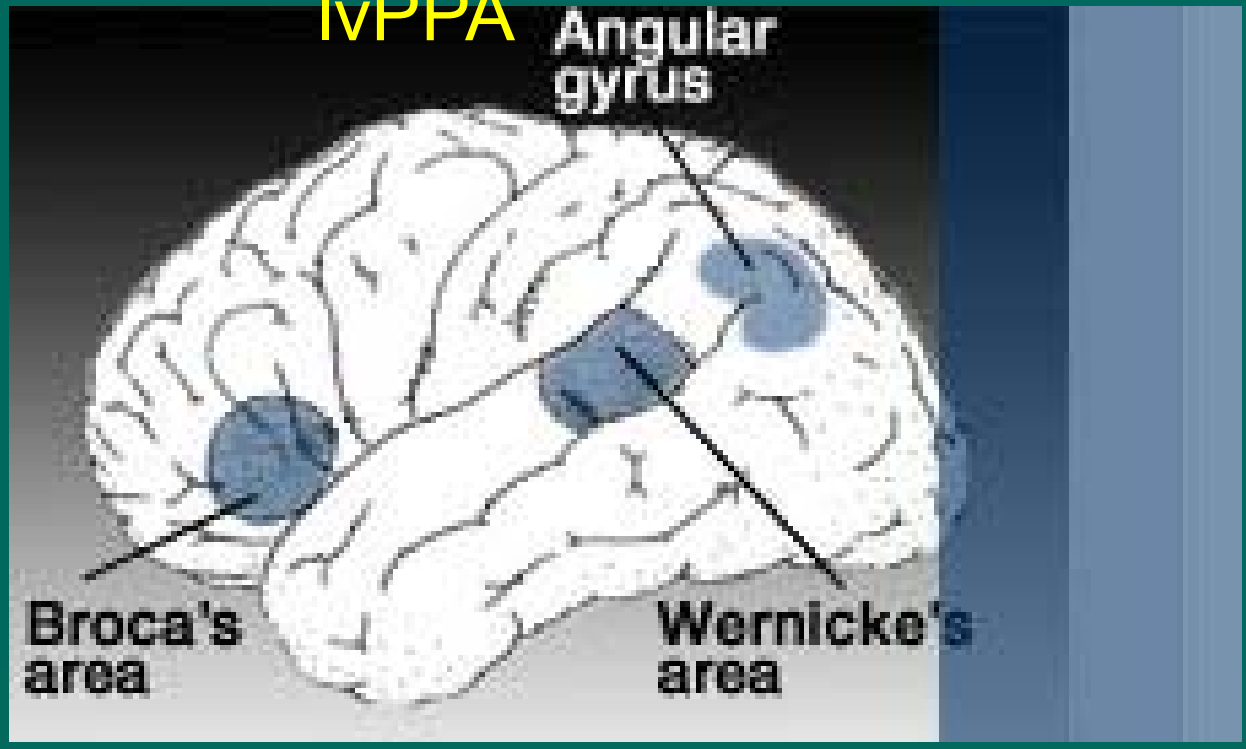
SIU

Think about it



Think about it

lvPPA



navPPA

svPPA

Bedside aphasia screening

- Fluency
- Naming
- Repetition
- Comprehension

Ala's cheat sheet

	Fluency	Naming	Repetition	Comprehension
navPPA	-	+	+	+
svPPA	+	-	+	-
lvPPA	+	-	-	+

SIU

Ala's cheat sheet

	Fluency	Naming	Repetition	Comprehension
Non-fluent PPA	-	+	+	+
Semantic PPA	+	-	+	-
Logopenic PPA	+	-	-	+

SIU

Ala's cheat sheet

	Fluency	Naming	Repetition	Comprehension
Nonfluent	-	+	+	+
Semantic	+	-	+	-
Logopenic	+	-	-	+

PPA observations

- Non-fluent: Effortful, halting speech (apraxia of speech)
  - Usually FTLD-tau (MAPT) (Pick's disease)
- Semantic: Impaired single-word comprehension
  - Usually FTLD-TDP
- Logopenic: Impaired repetition
  - Usually Alzheimer's

SIU

Nonfluent PPA

- At least one of the following core features must be present:
  - Agrammatism in language production
  - Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)
- At least 2 of 3 of the following other features must be present:
  - Impaired comprehension of syntactically complex sentences
  - Spared single-word comprehension
  - Spared object knowledge

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Semantic PPA

- Both of the following core features must be present:
  - Impaired confrontation naming
  - Impaired single-word comprehension
- At least 3 of the following other diagnostic features must be present:
  - Impaired object knowledge, particularly for low frequency or low-familiarity items
  - Surface dyslexia or dysgraphia
  - Spared repetition
  - Spared speech production (grammar and motor speech)

Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

Logopenic PPA

- Both of the following core features must be present:
  - Impaired single-word retrieval in spontaneous speech and naming
  - Impaired repetition of sentences and phrases
- At least 3 of the following other features must be present:
  - Speech (phonologic) errors in spontaneous speech and naming
  - Spared single-word comprehension and object knowledge
  - Spared motor speech
  - Absence of frank agrammatism

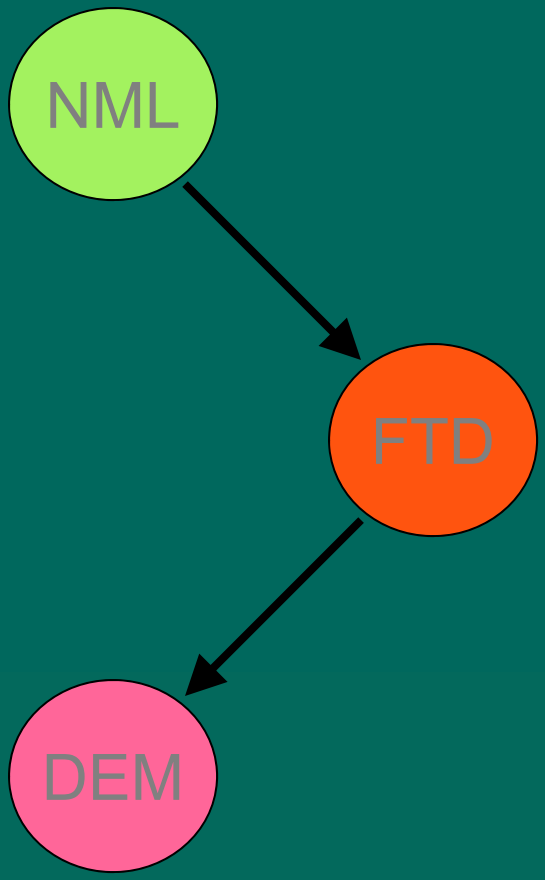
Gorno-Tempini. *Neurology* 2011;76:1006.

SIU

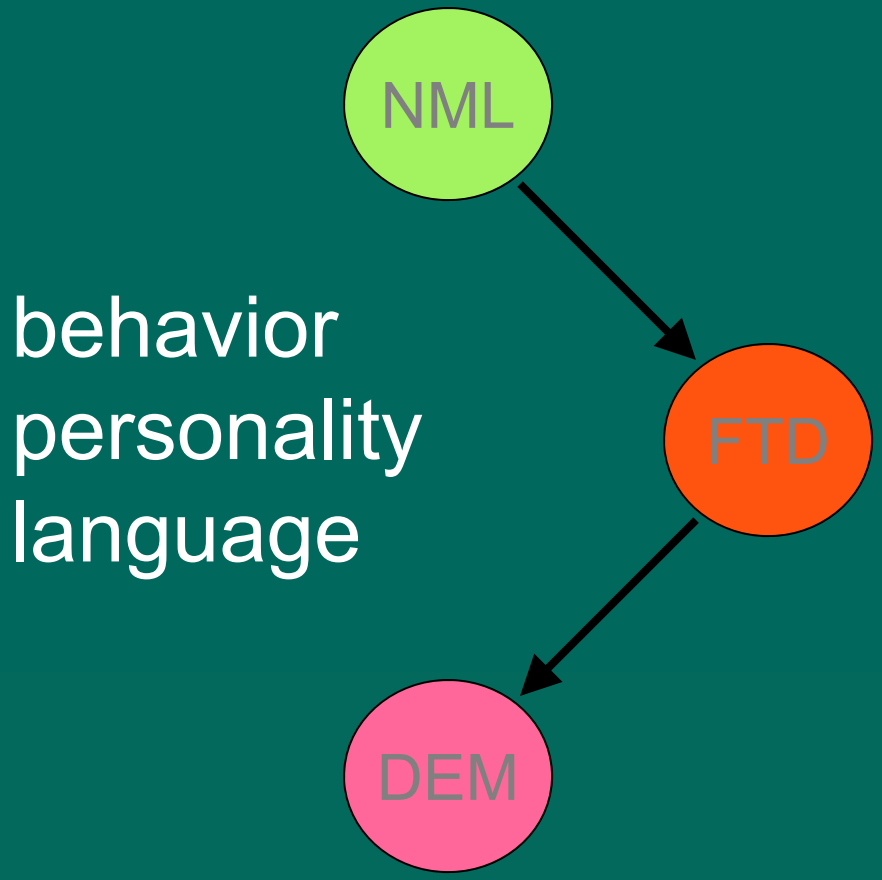
Key PPA distinguishing points

- Three variants
  - Nonverbal: Effortful, halting speech
  - Semantic: Impaired single-word comprehension
  - Logopenic: Impaired repetition

Frontotemporal dementia



Frontotemporal dementia



behavior
personality
language

Frontotemporal dementia

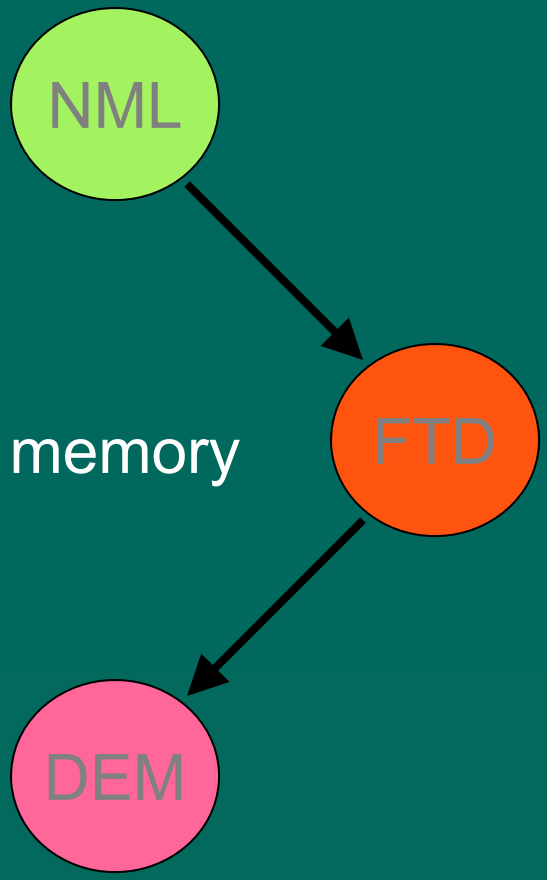
behavior

personality

language

relative sparing of memory

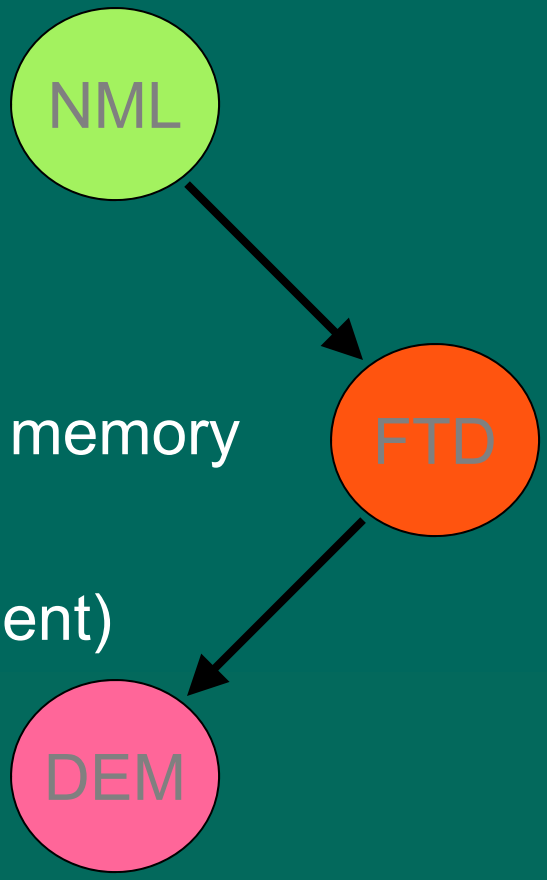
age <65



SIU

Frontotemporal dementia

behavior
personality
language
relative sparing of memory
age <65
(imaging requirement)



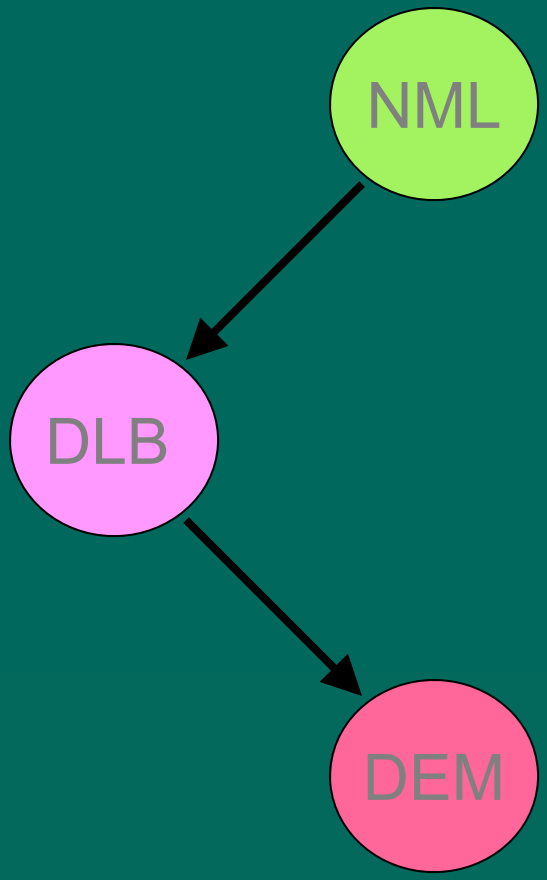
SIU

Frontotemporal dementia

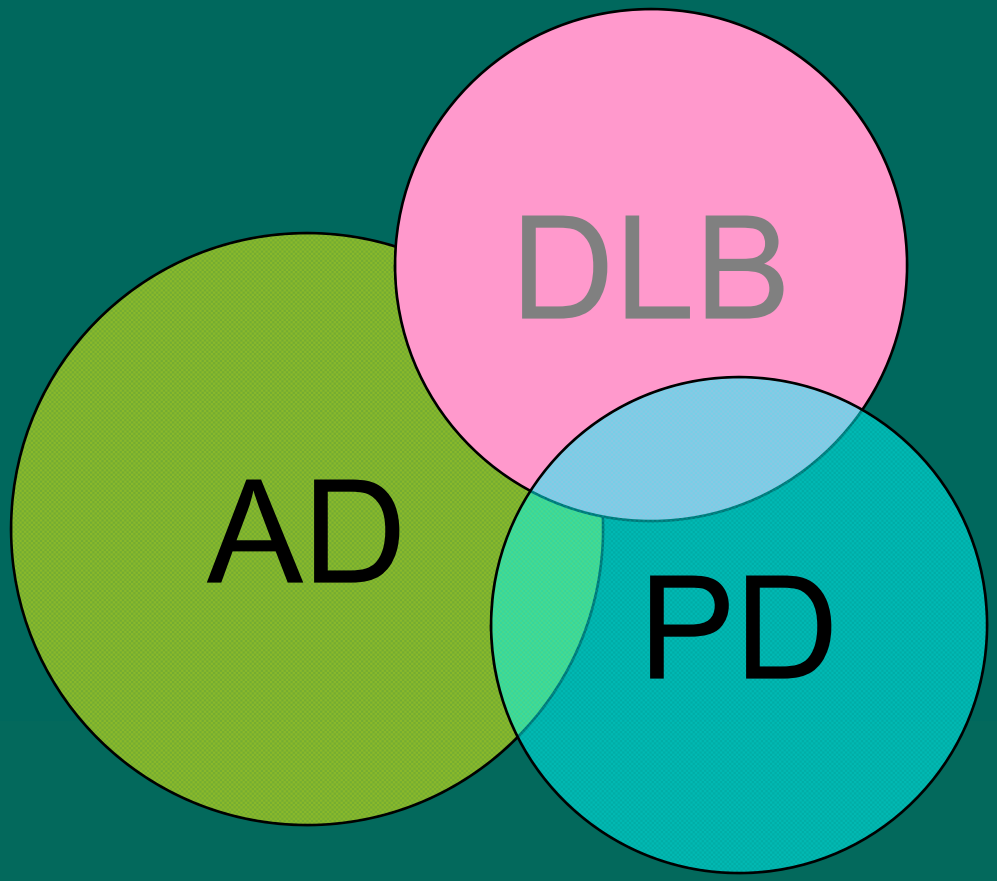
- Two variants
  - Behavioral variant
  - Language variant
- Relative sparing of memory
- Age usually <65
- Imaging requirement
- (Also consider Alzheimer's disease)

DLB

Dementia with Lewy bodies



One disease or two?



SIU

McKeith.
Neurology
2017;89:88.

Table 1 Revised[1,2] criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.

Core clinical features (***The first 3 typically occur early and may persist throughout the course.***)

Fluctuating cognition with pronounced variations in attention and alertness.
Recurrent visual hallucinations that are typically well formed and detailed.
REM sleep behavior disorder, *which may precede cognitive decline.*
One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.

Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

Indicative biomarkers

Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET.
Abnormal (low uptake) ^{123}iodine-MIBG myocardial scintigraphy.
Polysomnographic confirmation of REM sleep without atonia.

Supportive biomarkers

Relative preservation of medial temporal lobe structures on CT/MRI scan.
Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging.
Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Probable DLB can be diagnosed if:

a. Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or

b. Only one core clinical feature is present, but with one or more indicative biomarkers.

Probable DLB should not be diagnosed on the basis of biomarkers alone.

Possible DLB can be diagnosed if:

a. Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or

b. One or more indicative biomarkers is present but there are no core clinical features.

DLB is less likely:

a. In the presence of any other physical illness or brain disorder including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude a DLB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation, or

b. If parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia.

DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism. The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as Lewy body disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended.

SIU

DLB 4th consensus report

- Core features (≥ 2 required)
  - Fluctuating cognition
  - Visual hallucinations
  - REM sleep behavior disorder
  - Parkinsonism

McKeith. *Neurology* 2017;89:88.

SIU

DLB 4th consensus report

- Core features (≥ 2 required)
  - Fluctuating cognition
  - Visual hallucinations
  - REM sleep behavior disorder
  - Parkinsonism

McKeith. *Neurology* 2017;89:88.

SIU

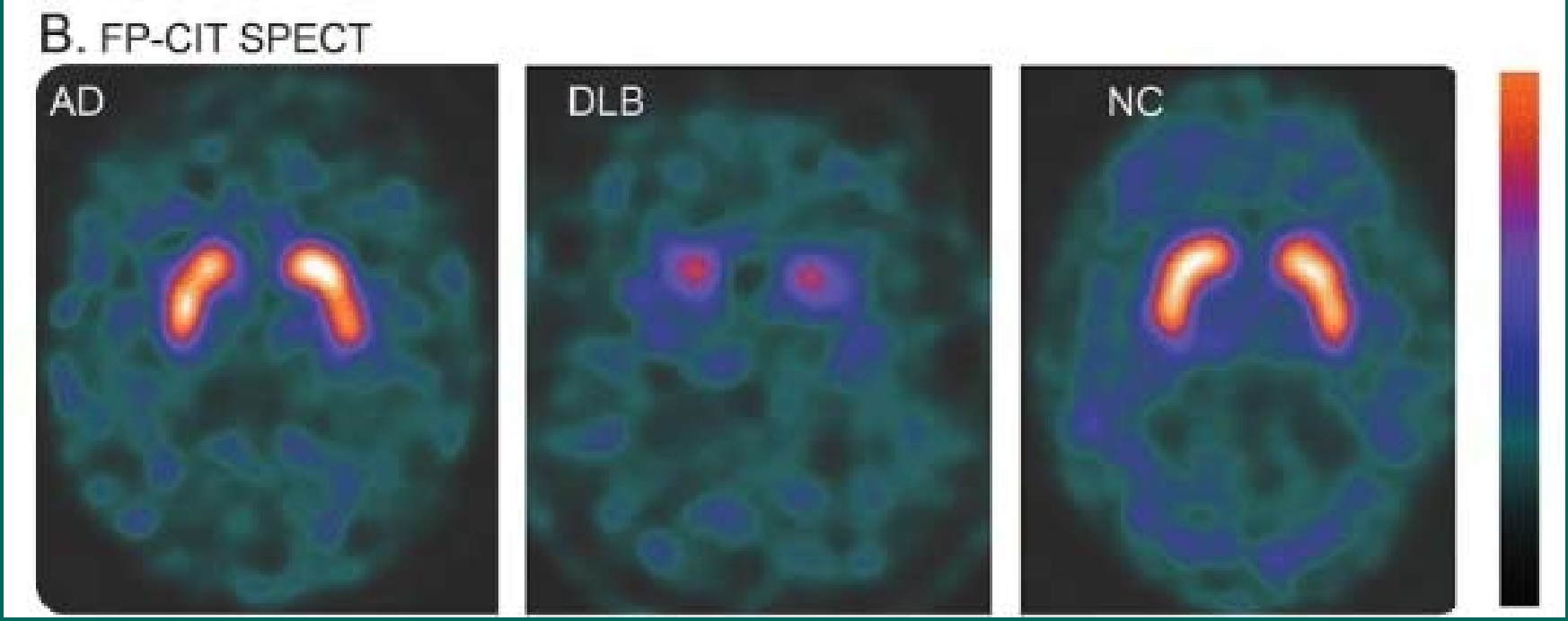
DLB 4th consensus report

- Indicative biomarkers
  - Reduced dopamine transporter uptake in basal ganglia by SPECT or PET
  - Abnormal ^{123}I-MIBG myocardial scintigraphy
  - Polysomnographic confirmation of REM sleep without atonia

McKeith. *Neurology* 2017;89:88.

SIU

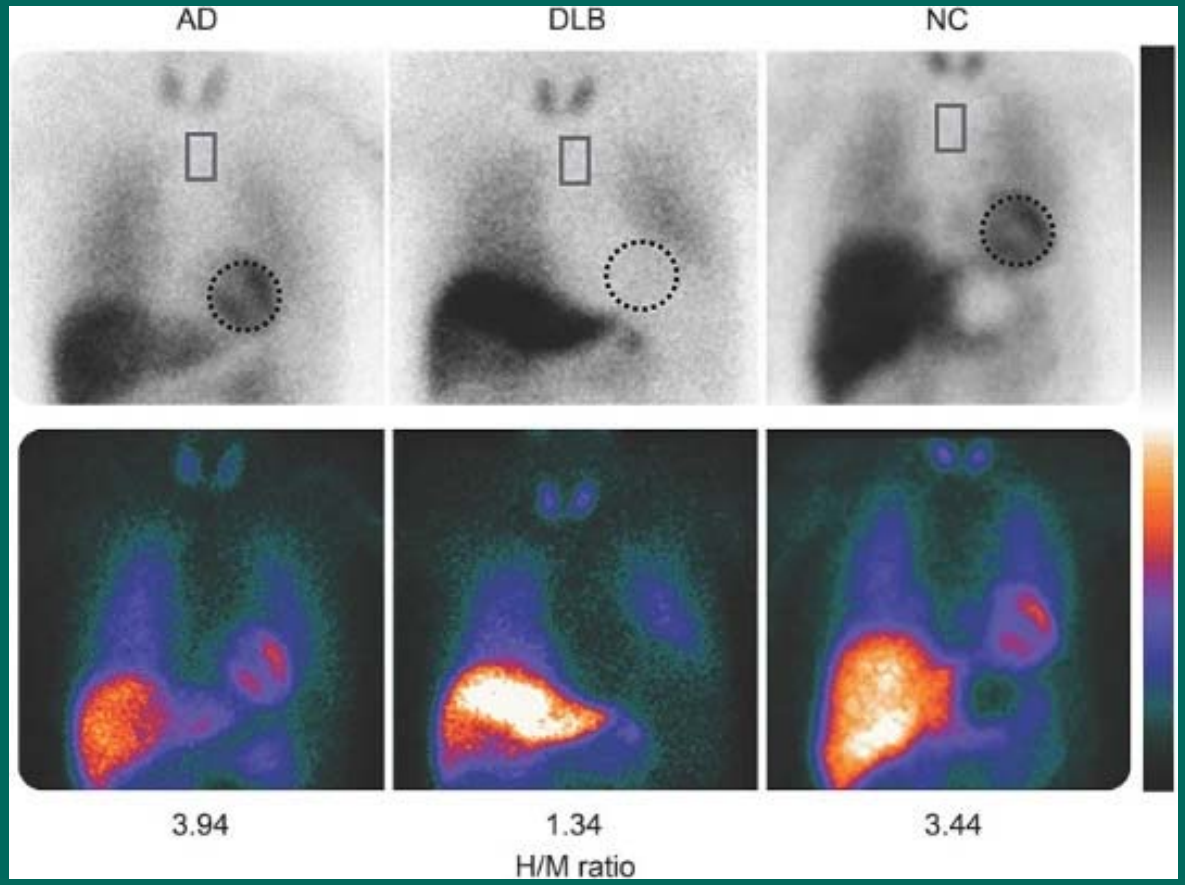
Dopamine transporter uptake (DAT scan)



^{123}iodine FP-CIT SPECT images in AD, DLB, and normal controls (NC)

McKeith. *Neurology* 2017;89:88.

^{123}I-MIBG myocardial scintigraphy

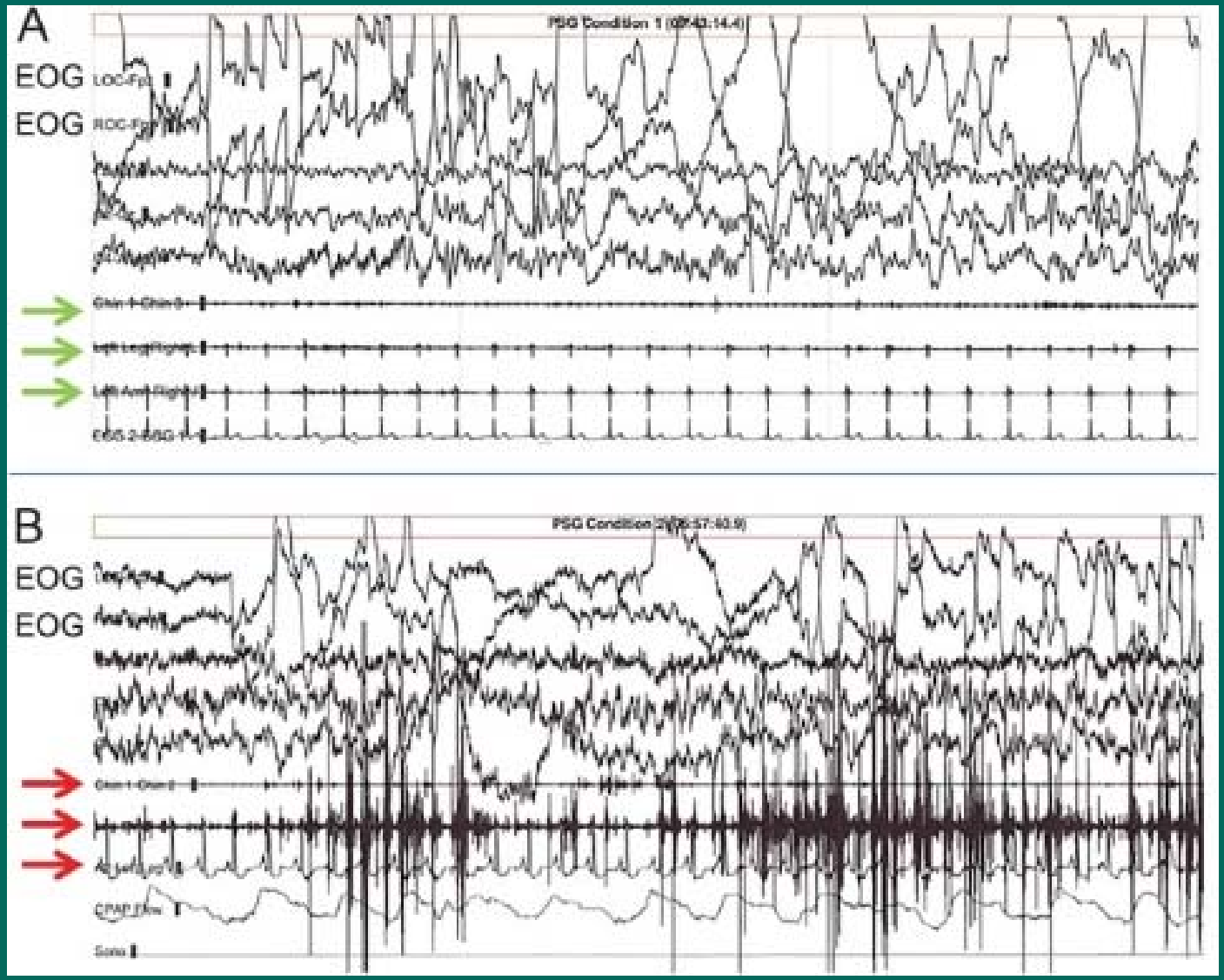


^{123}Iodine-metaiodobenzylguanidine myocardial imaging in patients with AD, DLB, and age-matched normal controls (NC). Images taken 3 hours after injection are shown in 2 color scales, and typical regions of interest are shown on the heart (dotted circle) and upper mediastinum (rectangle).

McKeith. *Neurology* 2017;89:88.

SIU

Polysomnographic recordings



Normal REM sleep

REM sleep without atonia

McKeith. *Neurology* 2017;89:88.

SIU

DLB 4th consensus report

- Probable DLB
  - Two or more core clinical features +/- indicative biomarkers
  - Only one core clinical feature + one or more indicative biomarkers
  - Cannot be diagnosed only with biomarkers

McKeith. *Neurology* 2017;89:88.

SIU

DLB 4th consensus report

- Possible DLB
  - Only one core clinical features with no indicative biomarkers
  - One or more indicative biomarkers without a core clinical feature

McKeith. *Neurology* 2017;89:88.

SIU

DLB 4th consensus report

- Supportive clinical features
  - Severe sensitivity to antipsychotics
  - Postural instability
  - Repeated falls
  - Syncope
  - Severe autonomic dysfunction
  - Hypersomnia
  - Hyposmia
  - Hallucinations in other modalities
  - Systematized delusions
  - Apathy, anxiety, and depression

McKeith. *Neurology* 2017;89:88.

SIU

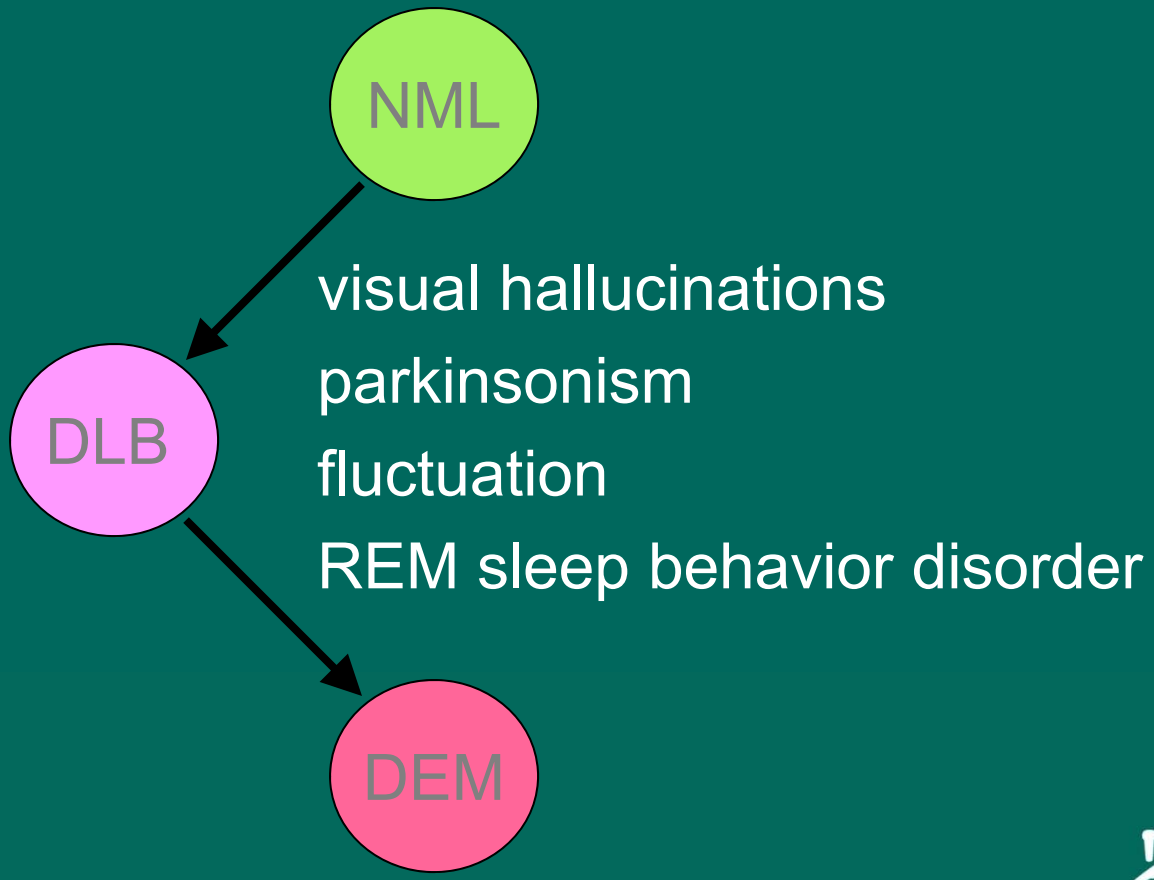
DLB 4th consensus report

- Supportive biomarkers
  - Relative preservation of medial temporal lobe structures on CT/MRI scan.
  - Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging.
  - Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

McKeith. *Neurology* 2017;89:88.

SIU

Dementia with Lewy bodies



SIU

DLB 4th consensus report

- Core features (≥ 2 required)
  - Fluctuating cognition
  - Visual hallucinations
  - REM sleep behavior disorder
  - Parkinsonism

McKeith. *Neurology* 2017;89:88.

SIU

DLB 4th consensus report

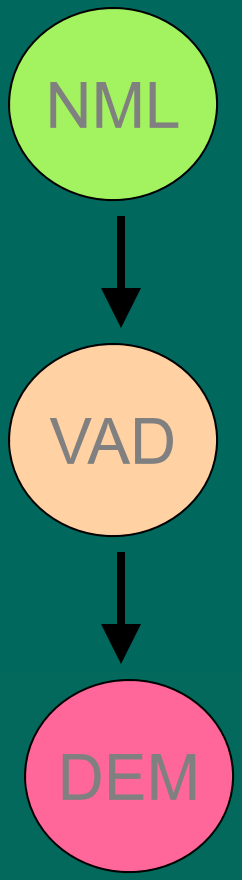
- Core features (≥ 2 required)
  - Fluctuating cognition
  - Visual hallucinations
  - REM sleep behavior disorder
  - Parkinsonism
  - (Cannot exclude concomitant AD)

McKeith. *Neurology* 2017;89:88.

SIU

VAD

Vascular dementia



VAD clinical diagnosis

- California criteria (Chui, 1992)
- NINDS-AIREN criteria (Roman, 1993)
- DSM-IV criteria (1994)

SIU

VAD clinical diagnosis

- California criteria (Chui, 1992)
- NINDS-AIREN criteria (Roman, 1993)
- DSM-IV criteria (1994)

Table 2. Criteria for the diagnosis of ischemic vascular dementia (IVD)

I. Dementia

Dementia is a deterioration from a known or estimated prior level of intellectual function sufficient to interfere broadly with the conduct of the patient's customary affairs of life, which is not isolated to a single narrow category of intellectual performance, and which is independent of level of consciousness.

This deterioration should be supported by historical evidence and documented by either bedside mental status testing or ideally by more detailed neuropsychological examination, using tests that are quantifiable, reproducible, and for which normative data are available.

II. Probable IVD

A. The criteria for the clinical diagnosis of PROBABLE IVD include ALL of the following:
   1. Dementia;
   2. Evidence of two or more ischemic strokes by history, neurologic signs, and/or neuroimaging studies (CT or T_1-weighted MRI);

      or

      Occurrence of a single stroke with a clearly documented temporal relationship to the onset of dementia;
   3. Evidence of at least one infarct outside the cerebellum by CT or T_1-weighted MRI.

B. The diagnosis of PROBABLE IVD is supported by
   1. Evidence of multiple infarcts in brain regions known to affect cognition;
   2. A history of multiple transient ischemic attacks;
   3. History of vascular risk factors (eg, hypertension, heart disease, diabetes mellitus);
   4. Elevated Hachinski Ischemia Scale (original or modified version).

C. Clinical features that are thought to be associated with IVD, but await further research, include
   1. Relatively early appearance of gait disturbance and urinary incontinence;
   2. Periventricular and deep white matter changes on T_2-weighted MRI that are excessive for age;
   3. Focal changes in electrophysiologic studies (eg, EEG, evoked potentials) or physiologic neuroimaging studies (eg, SPECT, PET, NMR spectroscopy).

D. Other clinical features that do not constitute strong evidence either for or against a diagnosis of PROBABLE IVD include
   1. Periods of slowly progressive symptoms;
   2. Illusions, psychosis, hallucinations, delusions;
   3. Seizures.

E. Clinical features that cast doubt on a diagnosis of PROBABLE IVD include
   1. Transcortical sensory aphasia in the absence of corresponding focal lesions on neuroimaging studies;
   2. Absence of central neurologic symptoms/signs, other than cognitive disturbance.

III. Possible IVD

A clinical diagnosis of POSSIBLE IVD may be made when there is
   1. Dementia;

      and one or more of the following:

   2a. A history or evidence of a single stroke (but not multiple strokes) without a clearly documented temporal relationship to the onset of dementia;

      or

   2b. Binswanger's syndrome (without multiple strokes) that includes all of the following:
      i. Early-onset urinary incontinence not explained by urologic disease, or gait disturbance (eg, parkinsonian, magnetic, apraxic, or "senile" gait) not explained by peripheral cause,
      ii. Vascular risk factors, and
      iii. Extensive white matter changes on neuroimaging.

IV. Definite IVD

A diagnosis of DEFINITE IVD requires histopathologic examination of the brain, as well as
A. Clinical evidence of dementia;
B. Pathologic confirmation of multiple infarcts, some outside of the cerebellum.

Note: If there is evidence of Alzheimer's disease or some other pathologic disorder that is thought to have contributed to the dementia, a diagnosis of MIXED dementia should be made.

V. Mixed dementia

A diagnosis of MIXED dementia should be made in the presence of one or more other systemic or brain disorders that are thought to be *causally* related to the dementia.

The degree of confidence in the diagnosis of IVD should be specified as possible, probable, or definite, and the other disorder(s) contributing to the dementia should be listed. For example: mixed dementia due to probable IVD and possible Alzheimer's disease or mixed dementia due to definite IVD and hypothyroidism.

VI. Research classification

Classification of IVD for RESEARCH purposes should specify features of the infarcts that may differentiate subtypes of the disorder, such as

Location:	cortical, white matter, periventricular, basal ganglia, thalamus
Size:	volume
Distribution:	large, small, or microvessel
Severity:	chronic ischemia versus infarction
Etiology:	embolism, atherosclerosis, arteriosclerosis, cerebral amyloid angiopathy, hypoperfusion.

Chui. *Neurology* 1992;42:473

SIU

VAD California criteria

- Dementia
- Either:
  - Two or more strokes by history, exam or CT/MRI, or
  - One stroke with temporal relationship to the dementia onset
- At least one stroke outside the cerebellum on CT/MRI
- Doubtful if aphasia without stroke on CT/MRI or normal exam

Chui. *Neurology* 1992;42:473

SIU

Criteria for the diagnosis of vascular dementia. VaD is a complex disorder characterized by cognitive impairment resulting from ischemic or hemorrhagic stroke or from ischemic-hypoxic brain lesions. The clinical criteria for the diagnosis of probable, possible, and definite vascular dementia are here summarized.

I. The criteria for the clinical diagnosis of *probable* vascular dementia include *all* of the following:

1. *Dementia* defined by cognitive decline from a previously higher level of functioning and manifested by impairment of memory and of two or more cognitive domains (orientation, attention, language, visuospatial functions, executive functions, motor control, and praxis), preferably established by clinical examination and documented by neuropsychological testing; deficits should be severe enough to interfere with activities of daily living not due to physical effects of stroke alone.

Exclusion criteria: cases with disturbance of consciousness, delirium, psychosis, severe aphasia, or major sensorimotor impairment precluding neuropsychological testing. Also excluded are systemic disorders or other brain diseases (such as AD) that in and of themselves could account for deficits in memory and cognition.

2. *Cerebrovascular disease,* defined by the presence of focal signs on neurologic examination, such as hemiparesis, lower facial weakness, Babinski sign, sensory deficit, hemianopia, and dysarthria consistent with stroke (with or without history of stroke), and evidence of relevant CVD by brain imaging (CT or MRI) including *multiple large-vessel infarcts* or a *single strategically placed infarct* (angular gyrus, thalamus, basal forebrain, or PCA or ACA territories), as well as *multiple basal ganglia* and *white matter lacunes* or *extensive periventricular white matter lesions*, or combinations thereof.

3. *A relationship between the above two disorders,* manifested or inferred by the presence of one or more of the following: (a) onset of dementia within 3 months following a recognized stroke; (b) abrupt deterioration in cognitive functions; or fluctuating, stepwise progression of cognitive deficits.

II. Clinical features consistent with the diagnosis of *probable* vascular dementia include the following:

(a) Early presence of a gait disturbance (small-step gait or marche à petits pas, or magnetic, apraxic-ataxic or parkinsonian gait); (b) history of unsteadiness and frequent, unprovoked falls; (c) early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease; (d) pseudobulbar palsy; and (e) personality and mood changes, abulia, depression, emotional incontinence, or other subcortical deficits including psychomotor retardation and abnormal executive function.

III. Features that make the diagnosis of vascular dementia uncertain or unlikely include (a) early onset of memory deficit and progressive worsening of memory and other cognitive functions such as language (transcortical sensory aphasia), motor skills (apraxia), and perception (agnosia), in the absence of corresponding focal lesions on brain imaging; (b) absence of focal neurologic signs, other than cognitive disturbance; and (c) absence of cerebrovascular lesions on brain CT or MRI.

IV. Clinical diagnosis of *possible* vascular dementia may be made in the presence of dementia (section I-1) with focal neurologic signs in patients in whom brain imaging studies to confirm definite CVD are missing; or in the absence of clear temporal relationship between dementia and stroke; or in patients with subtle onset and variable course (plateau or improvement) of cognitive deficits and evidence of relevant CVD.

V. Criteria for diagnosis of *definite* vascular dementia are (a) clinical criteria for *probable* vascular dementia; (b) histopathologic evidence of CVD obtained from biopsy or autopsy; (c) absence of neurofibrillary tangles and neuritic plaques exceeding those expected for age; and (d) absence of other clinical or pathologic disorder capable of producing dementia.

VI. Classification of vascular dementia for research purposes may be made on the basis of clinical, radiologic, and neuropathologic features, for subcategories or defined conditions such as cortical vascular dementia, subcortical vascular dementia, BD, and thalamic dementia.

The term "AD *with* CVD" should be reserved to classify patients fulfilling the clinical criteria for possible AD and who also present clinical or brain imaging evidence of relevant CVD. Traditionally, these patients have been included with VaD in epidemiologic studies. The term "mixed dementia," used hitherto, should be avoided.

Roman. *Neurology* 1993;43:250

SIU

VAD NINDS-ARIEN criteria

- Dementia
- Abnormal exam consistent with stroke
- Ischemic vascular disease on CT/MRI
- Temporal relationship between the above
- Doubtful if early memory impairment without stroke on CT/MRI or normal exam

Roman. *Neurology* 1993;43:250

SIU

Vascular dementia

- Dementia associated with a clinical stroke*
- Strokes on CT or MRI
- Abnormal neurological exam

* Within three months

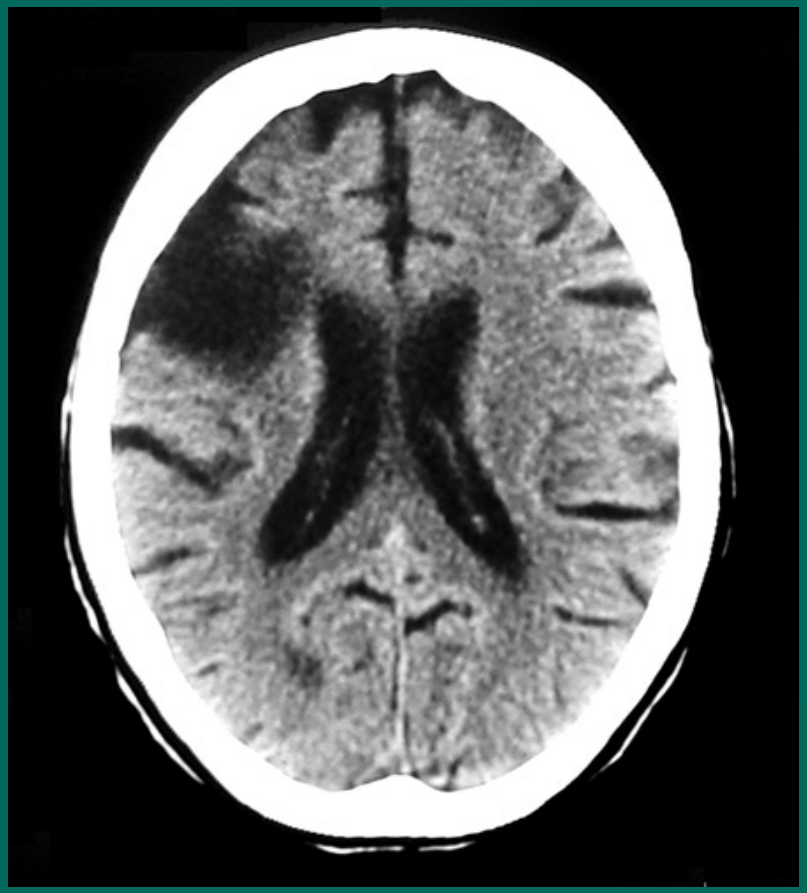
Vascular dementia

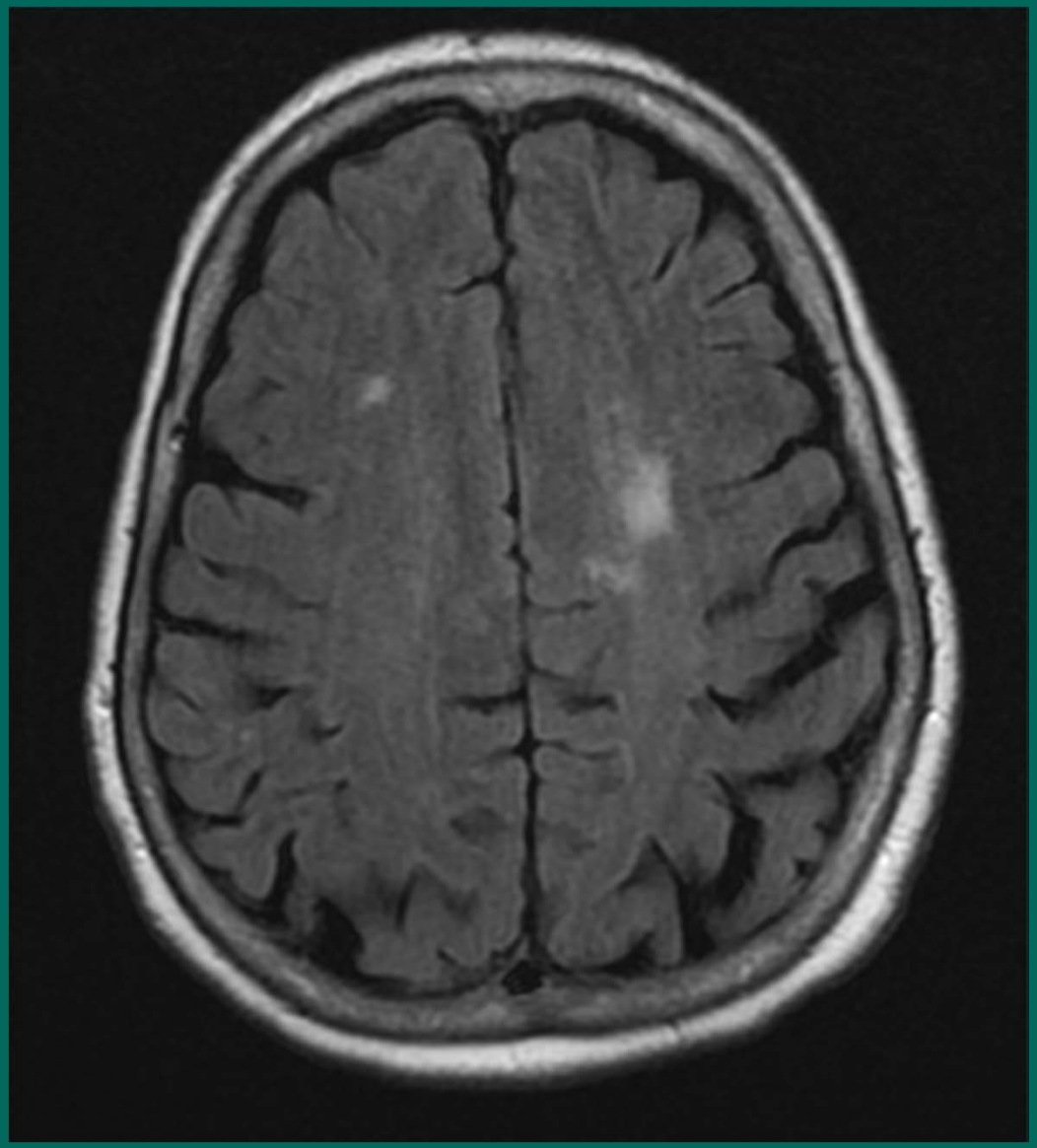
- Dementia associated with a clinical stroke
- Strokes on CT or MRI
- Abnormal neurological exam
- (Presence of vascular disease risk factors)

VAD key point

- Strokes seen on CT or MRI

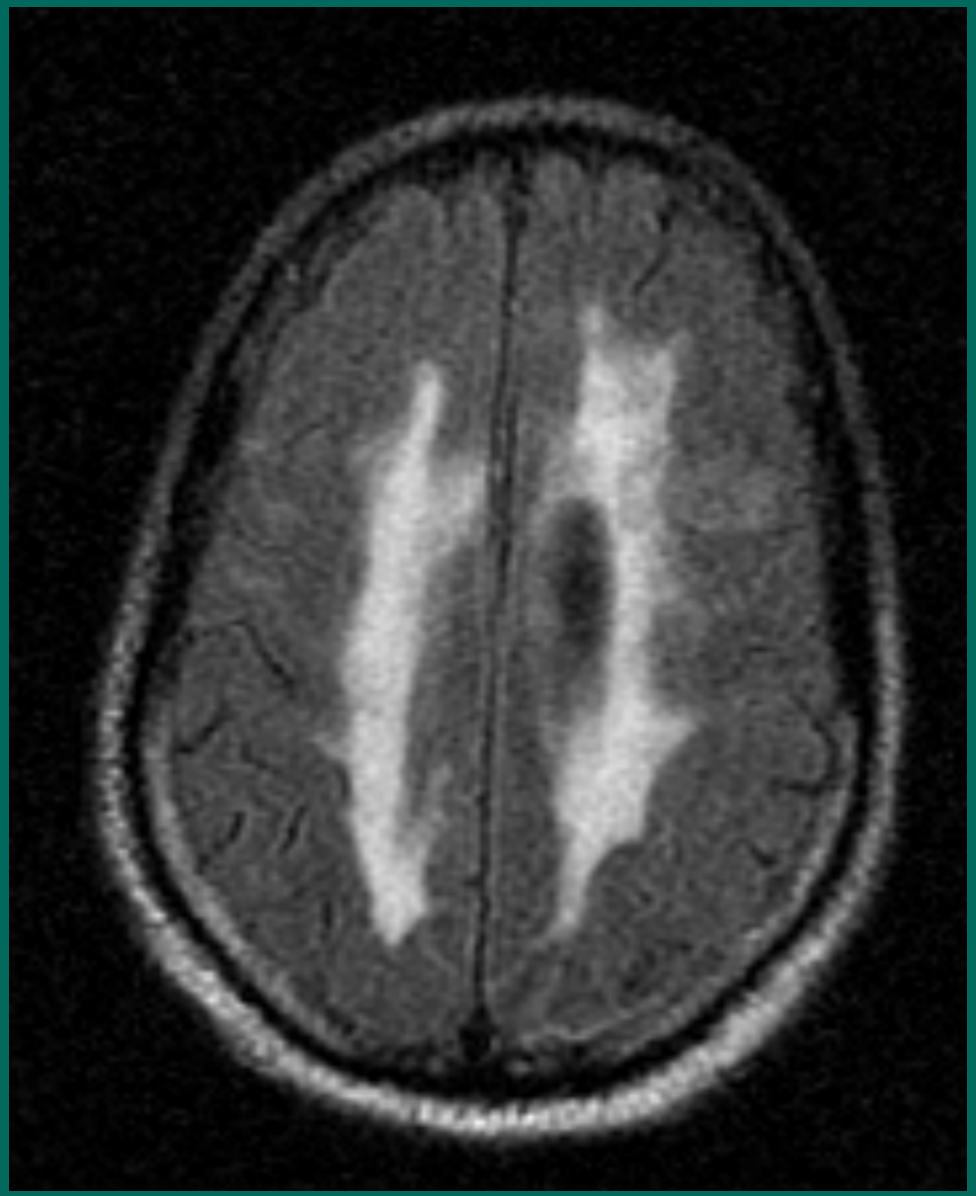
Stroke on CT



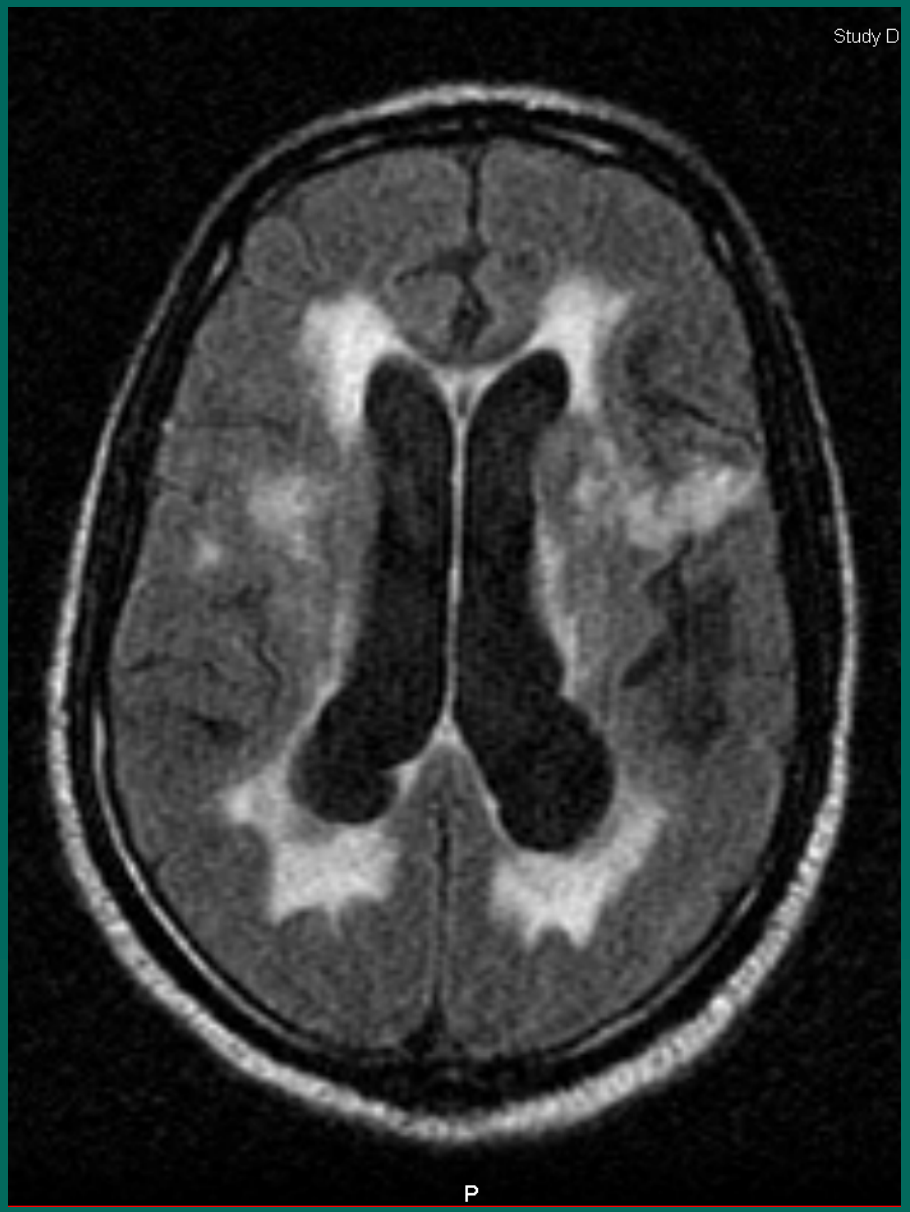


Non-specific white matter change

SIU



Possible exception: extensive perivascular white matter lesions



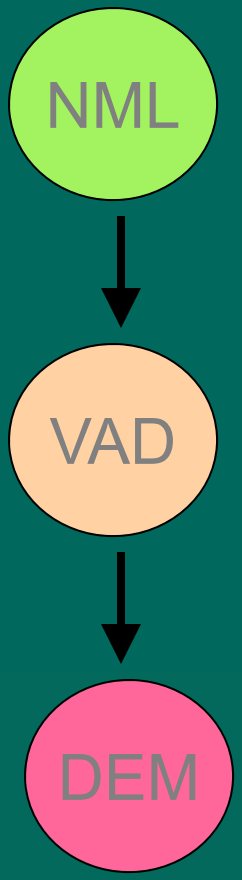
Possible exception: extensive perivascular white matter lesions

SIU

White matter disease

- Does not prove that a patient is demented
- Does not prove vascular dementia
- Is associated with dementia
- Vascular disease risk factors should be optimized.

Vascular dementia



strokes on CT or MRI

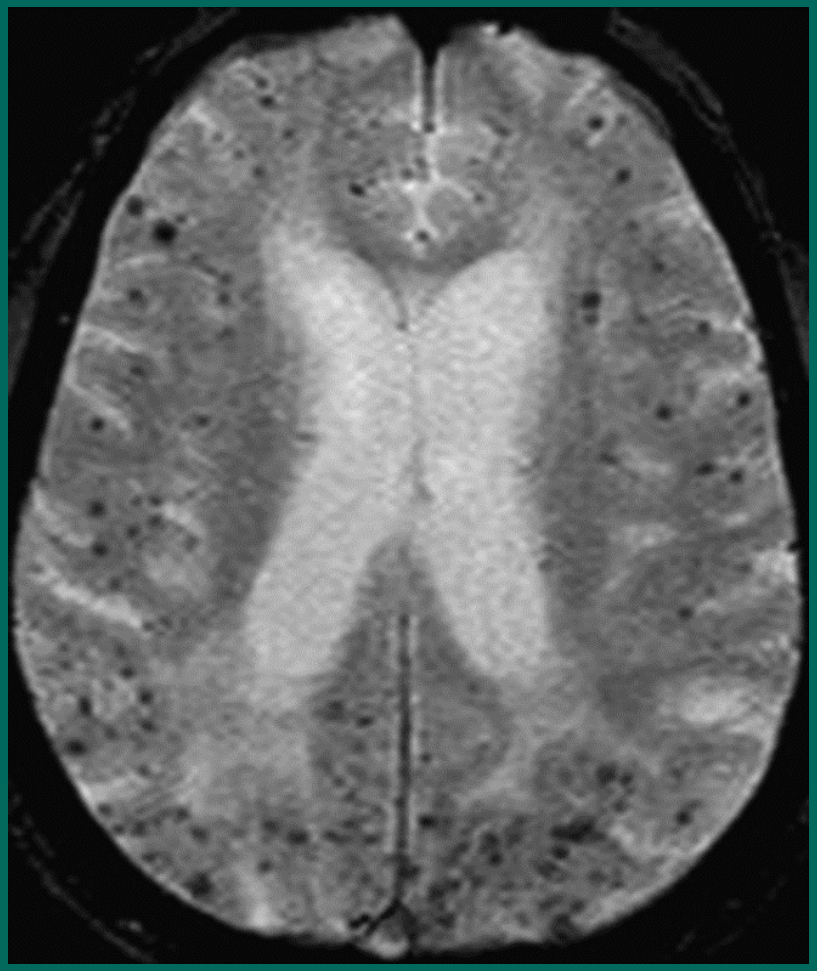
SIU

Vascular dementia

- Dementia associated with a clinical stroke
- Radiological infarcts
- Abnormal neurological exam
- (Stroke risk factors)
- (Cannot exclude concomitant Alzheimer's disease)

Cerebral amyloid angiopathy

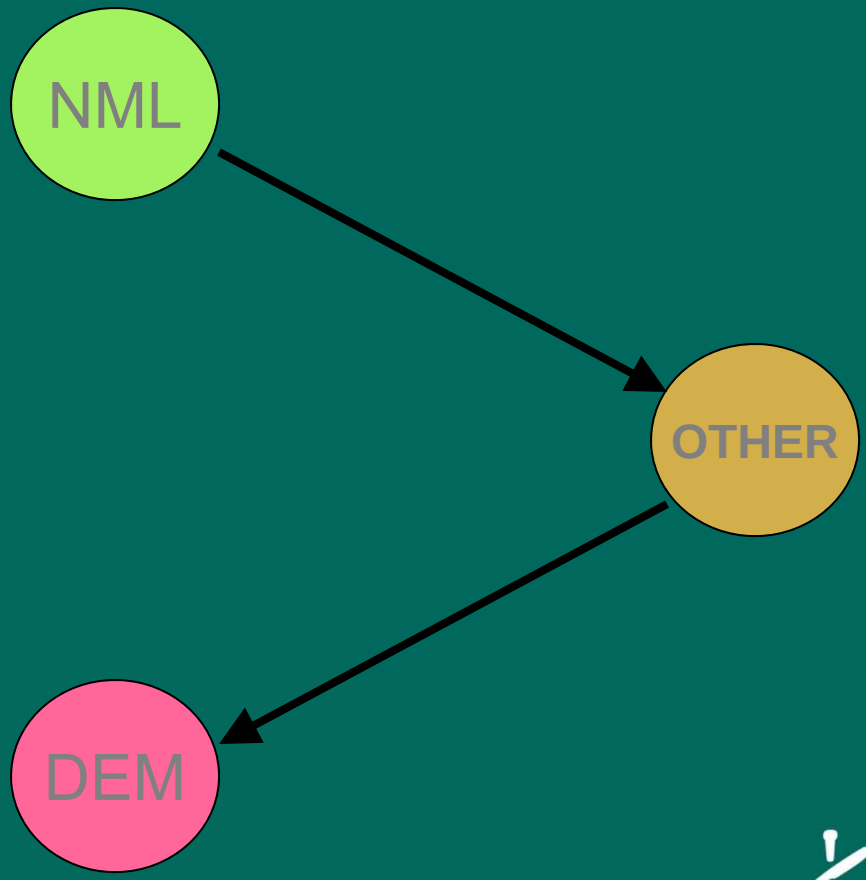
Overlap between AD and VAD?



Robinson. *Cambridge University Press* 2015; 212.

SIU

Other dementias



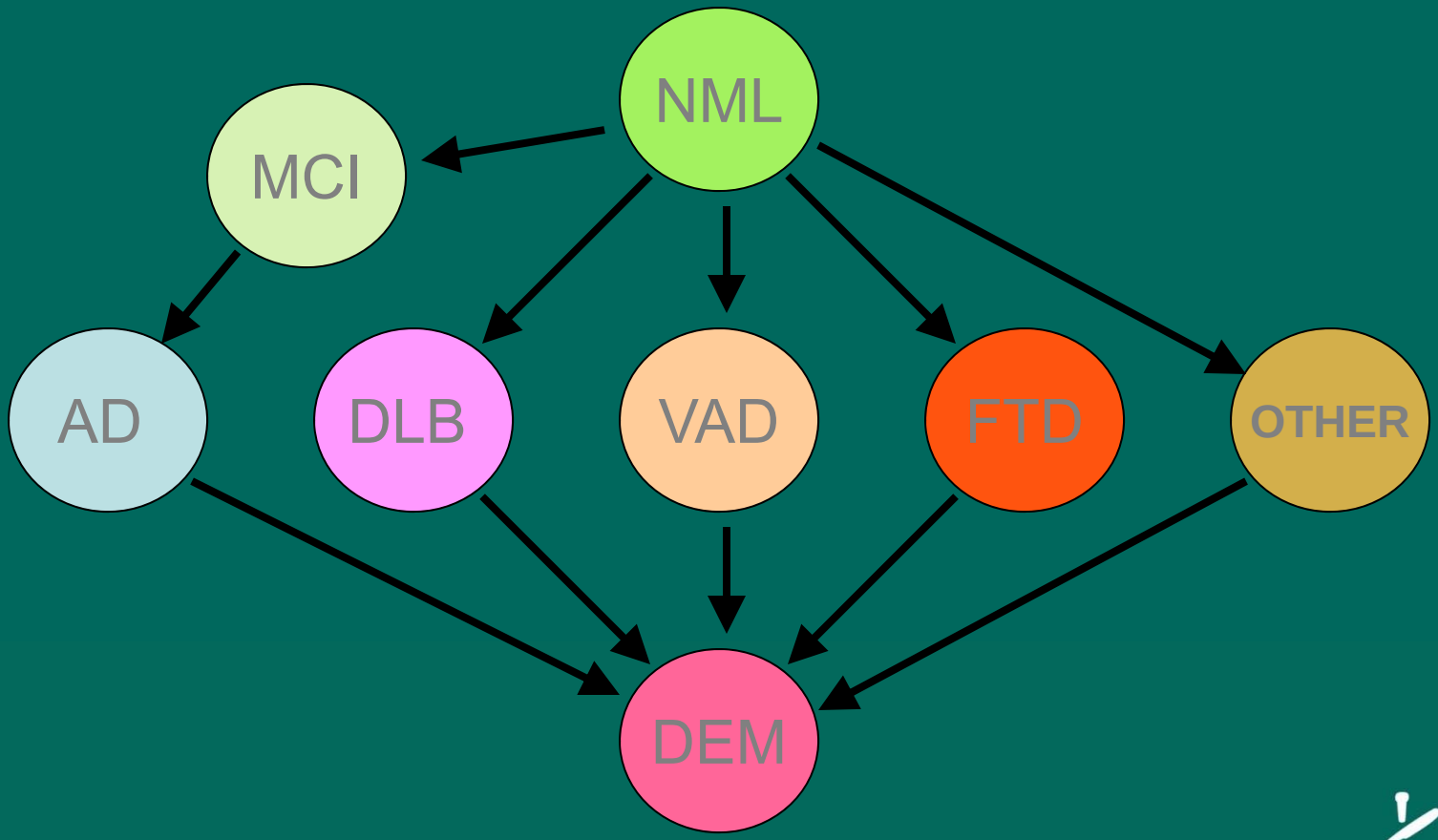
Most common other dementias

- Other neurodegenerative disease
  - Parkinson disease
  - progressive supranuclear palsy
  - other movement disorders

Parkinson plus syndromes

- All have
  - bradykinesia
  - rigidity
  - gait disorder
  - negative family histories

The final common pathway



SIU

LATE disease

- Limbic-predominant
- Age-related
- TDP-43
- Encephalopathy

doi:10.1093/brain/awz099 BRAIN 2019: 142; 1503–1527 | 1503

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW

Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report

Peter T. Nelson,[1] Dennis W. Dickson,[2] John Q. Trojanowski,[3] Clifford R. Jack Jr.,[4] Patricia A. Boyle,[5] Konstantinos Arfanakis,[5,6] Rosa Rademakers,[2] Irina Alafuzoff,[7] Johannes Attems,[8] Carol Brayne,[9] Ian T.S. Coyle-Gilchrist,[9] Helena C. Chui,[10] David W. Fardo,[1] Margaret E. Flanagan,[11] Glenda Halliday,[12] Suvi R.K. Hokkanen,[9] Sally Hunter,[9] Gregory A. Jicha,[1] Yuriko Katsumata,[1] Claudia H. Kawas,[13] C. Dirk Keene,[14] Gabor G. Kovacs,[15] Walter A. Kukull,[14] Allan I. Levey,[16] Nazanin Makkinejad,[6] Thomas J. Montine,[17] Shigeo Murayama,[18] Melissa E. Murray,[2] Sukriti Nag,[5] Robert A. Rissman,[19] William W. Seeley,[20] Reisa A. Sperling,[21] Charles L. White III,[22] Lei Yu[5] and Julie A. Schneider[5]

Treatment of Alzheimer's

- There have been no new FDA-approved drugs to treat AD in the past 17 years.

FDA-approved drugs for Alzheimer's Disease

donepezil

rivastigmine

galantamine

memantine

donepezil +
memantine

SIU

FDA-approved drugs for Alzheimer's Disease

- donepezil
- rivastigmine
- galantamine

} increase acetylcholine acetylcholine esterase inhibitors (AChEIs)

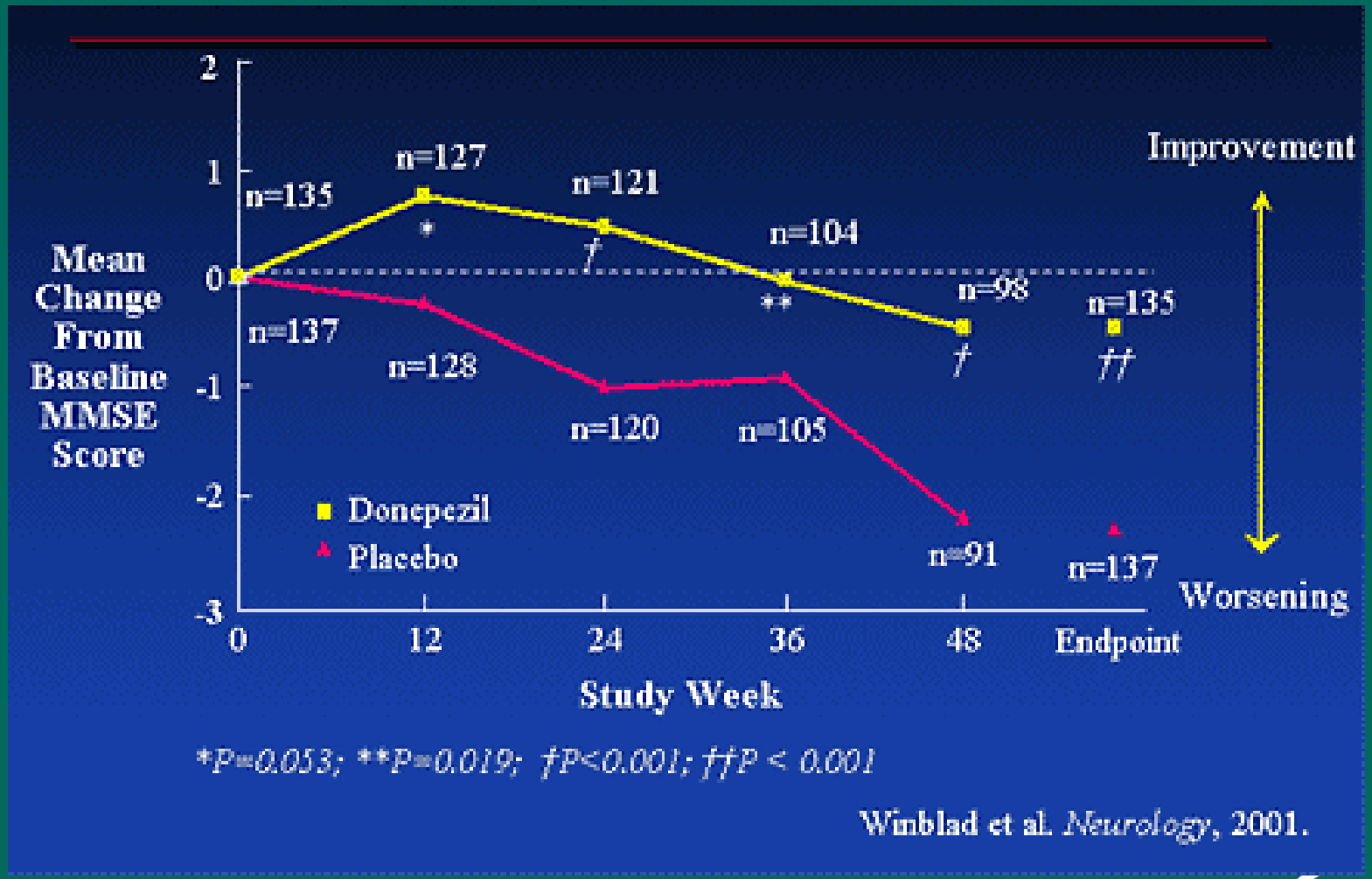
- memantine — interferes with glutamate

SIU

FDA-approved drugs for Alzheimer's

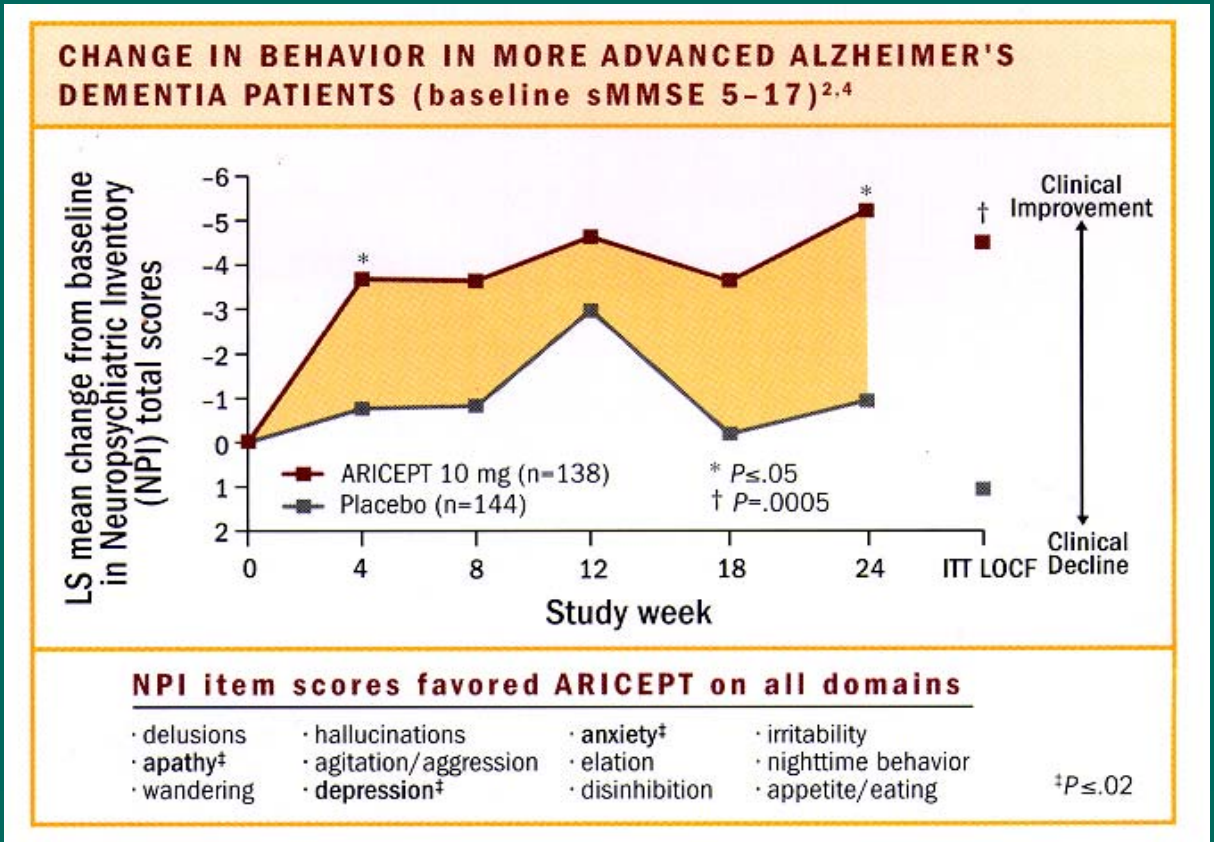
- Alter the balance of chemicals in the brain
  - donepezil (Aricept®)
  - galantamine (Razadyne®)
  - rivastigmine (Exelon®)
  - memantine (Namenda®)

THESE DRUGS CAN IMPROVE COGNITION IN ALZHEIMER'S



SIU

THESE DRUGS CAN IMPROVE BEHAVIOR IN ALZHEIMER'S

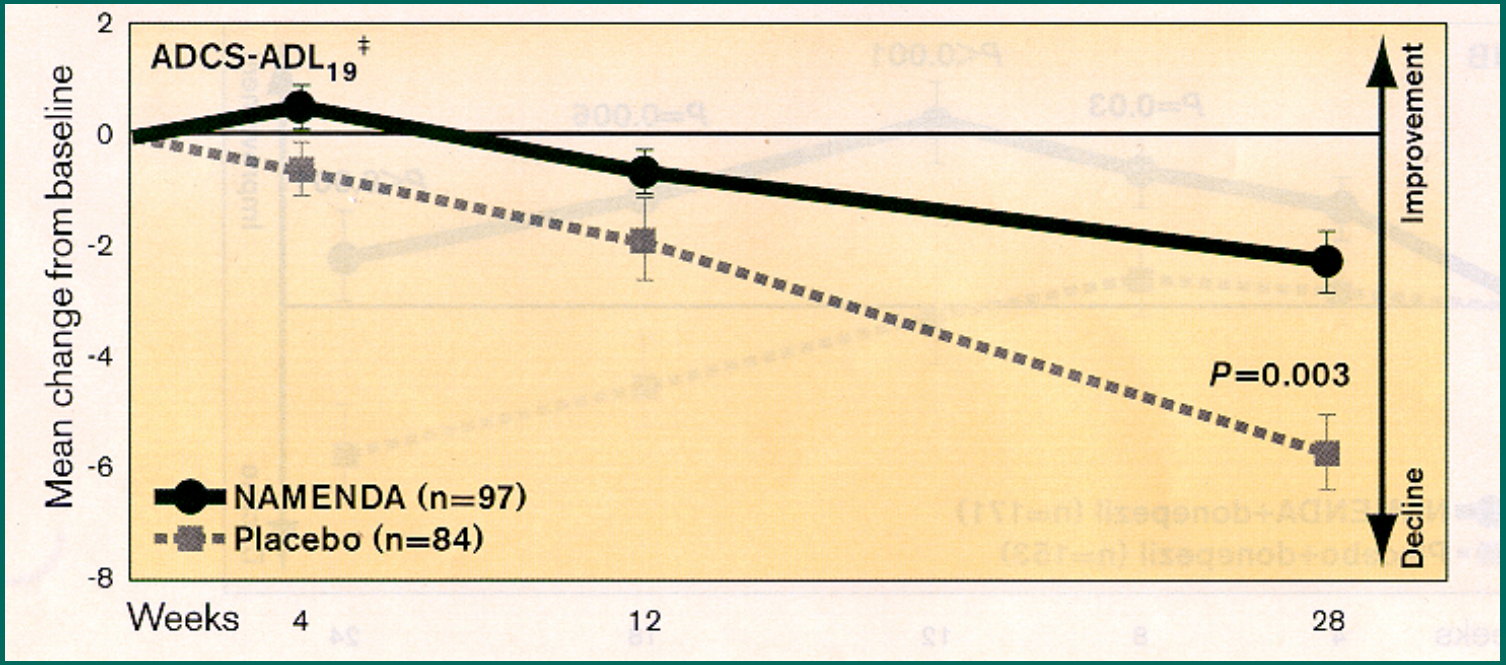


Neuropsychiatric Inventory Scale

Feldman. Neurology 2001;57:613

SIU

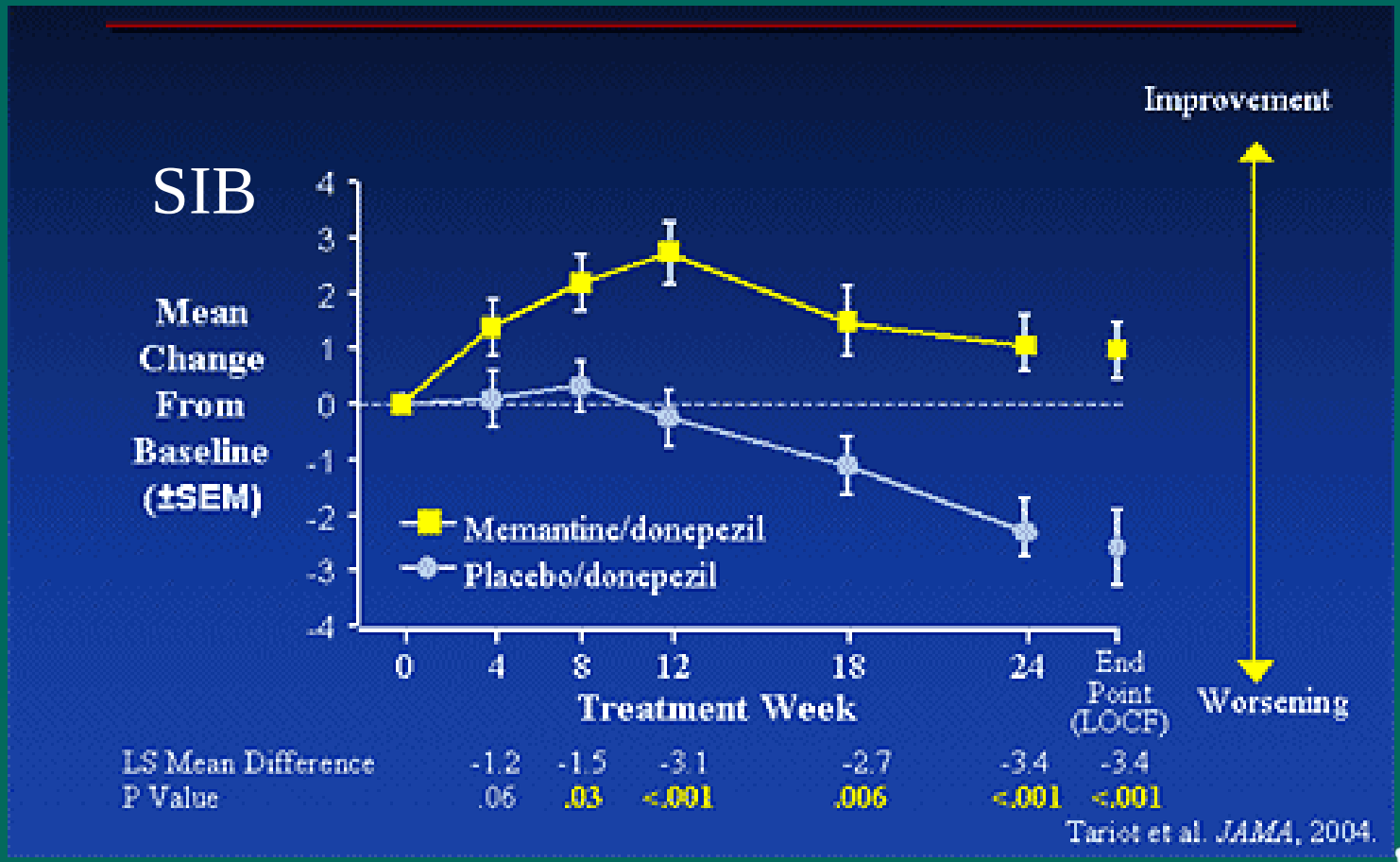
THESE DRUGS CAN IMPROVE ACTIVITIES OF DAILY LIVING IN ALZHEIMER'S



Reisberg. NEJM 2003;348:1333

SIU

Combination therapy



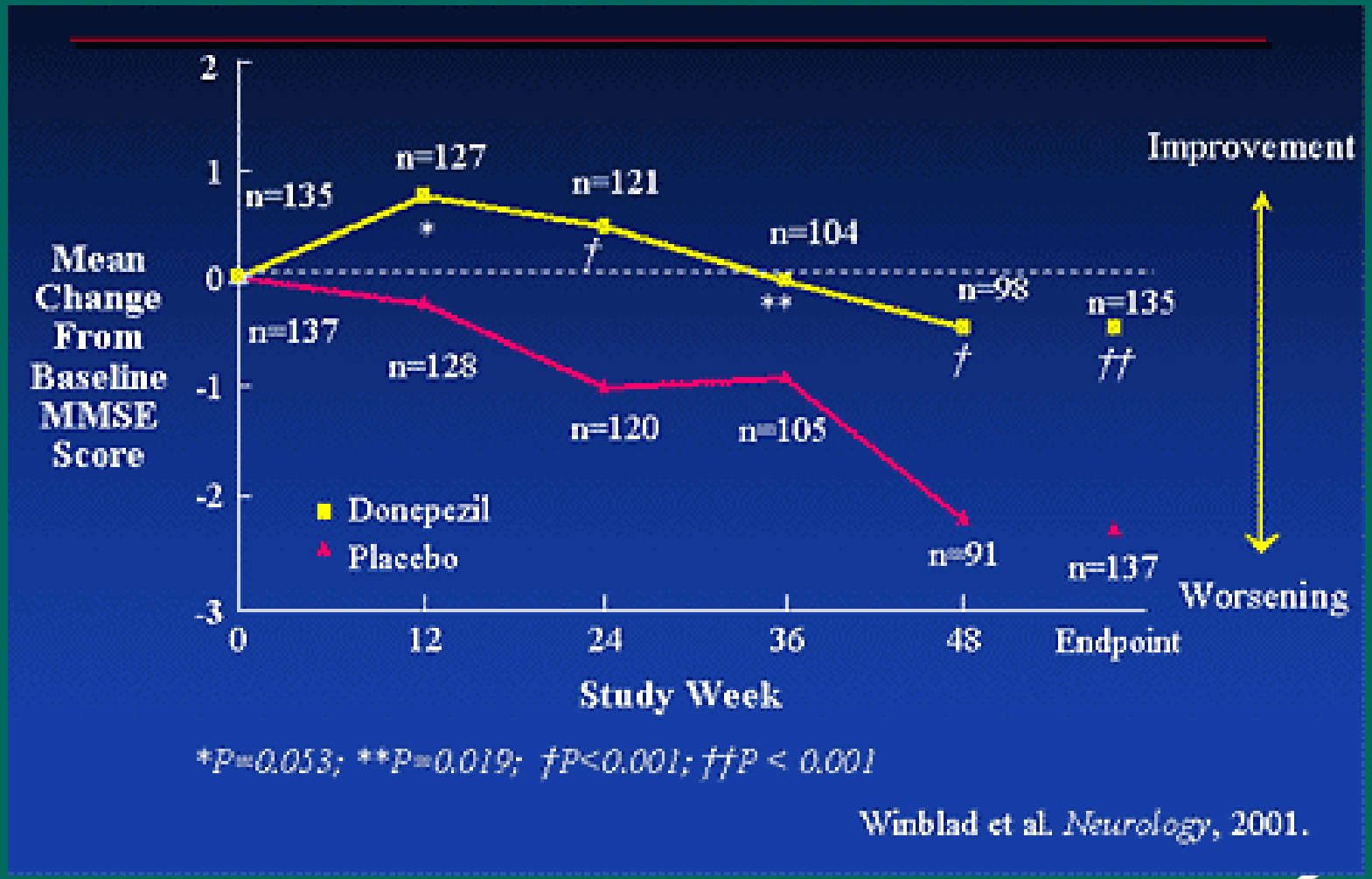
Trey Sunderland. www.medscape.org/viewarticle/481063

SIU

Treatment of Alzheimer's

- There have been no new FDA-approved drugs to treat AD in the past 17 years.
- The drugs that have been approved offer modest *symptomatic* benefit.

THESE DRUGS CAN IMPROVE COGNITION IN ALZHEIMER'S



SIU

Treatment of Alzheimer's

- There have been no new FDA-approved drugs to treat AD in the past 17 years.
- The drugs that have been approved offer modest *symptomatic* benefit.
- They do not slow or stop the progression of Alzheimer's.

The benefit of these drugs

- The average patient functions a little better.

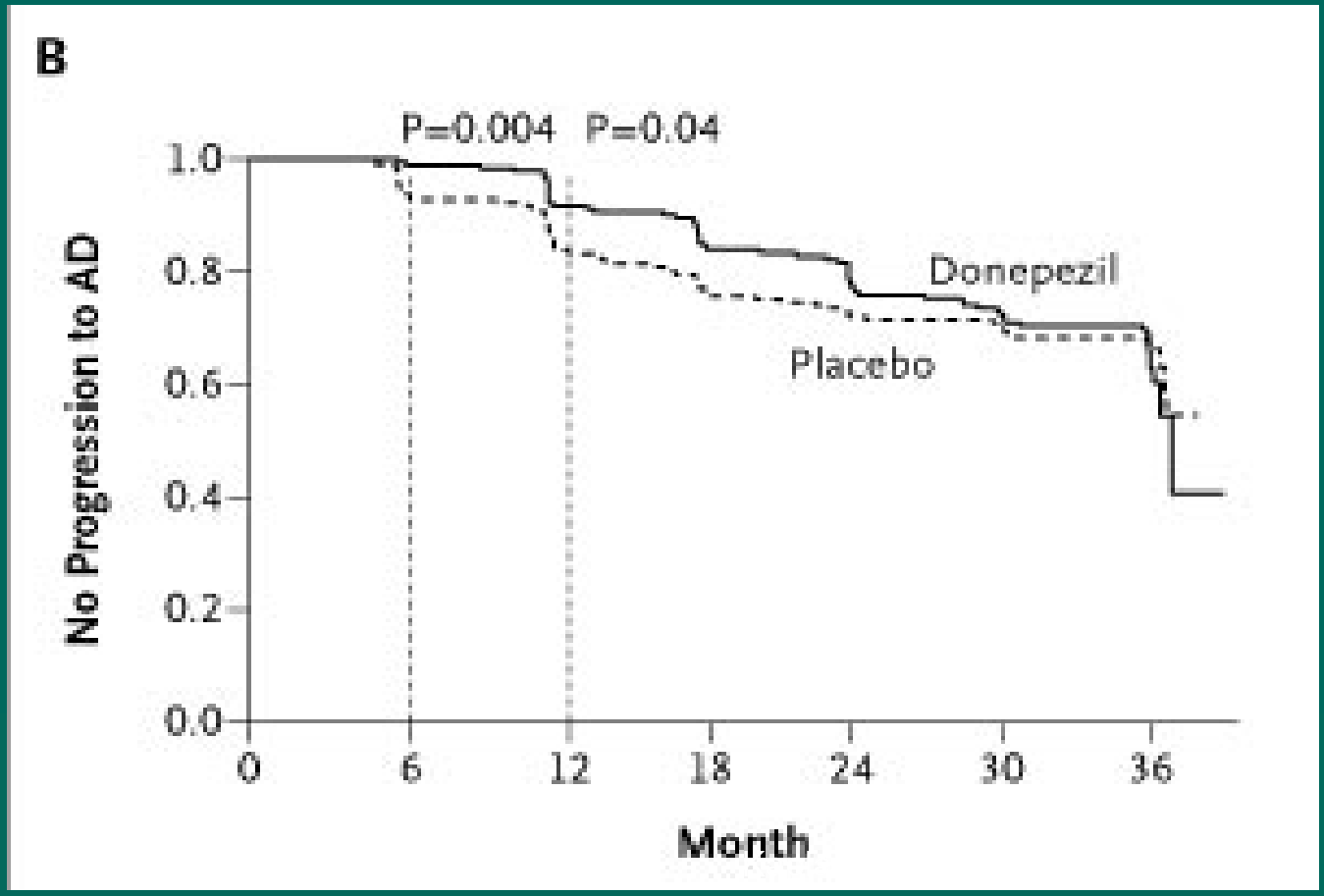
THE BENEFIT OF THESE DRUGS

- The average patient functions a little better.
- A few patients do significantly better.

The benefit of these drugs

- The average patient functions a little better.
- A few patients do significantly better.
- They delay the conversion to Alzheimer's disease.

Rate of progression from MCI to AD



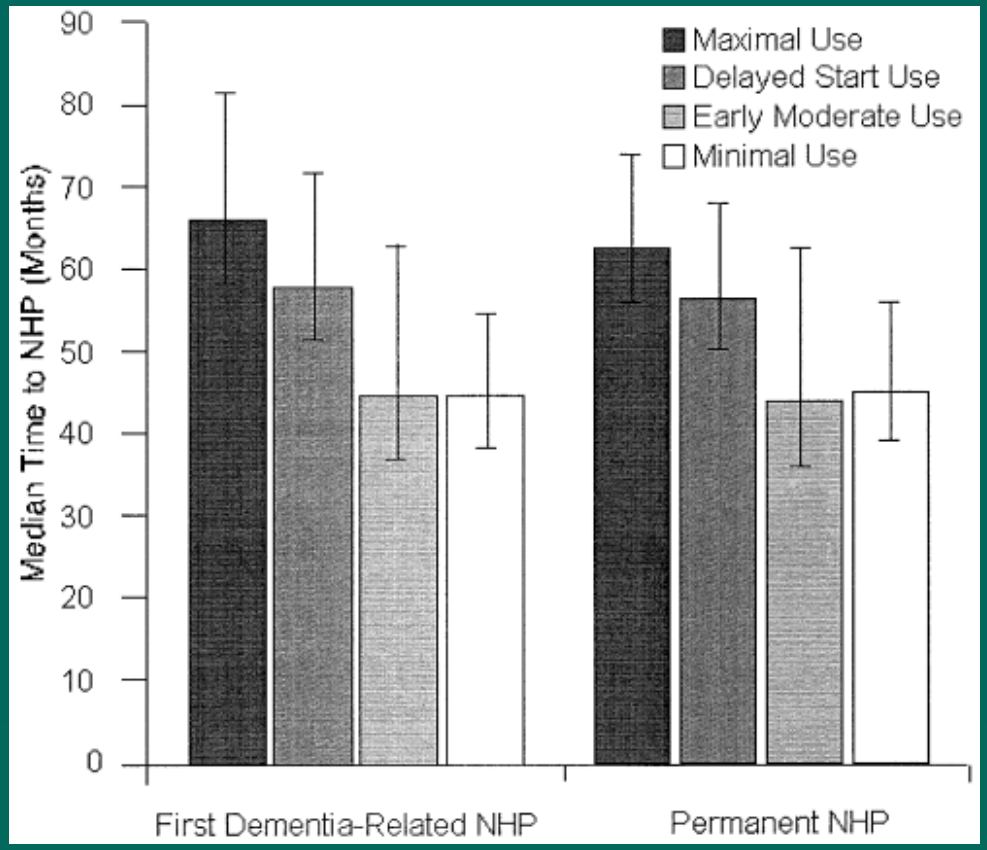
Petersen. NEJM 2005; 352:2379

SIU

The benefit of these drugs

- The average patient functions a little better.
- A few patients do significantly better.
- They delay the conversion to Alzheimer's disease.
- They help keep the patient out of the nursing home.

Delaying nursing home placement



When donepezil was taken at an effective dose for at least 9 to 12 months, conservative estimates of the time gained before NHP were 21.4 months for first dementia-related NHP and 17.5 months for permanent NHP.

Geldmacher. JAGS. 2003;51:937.

SIU

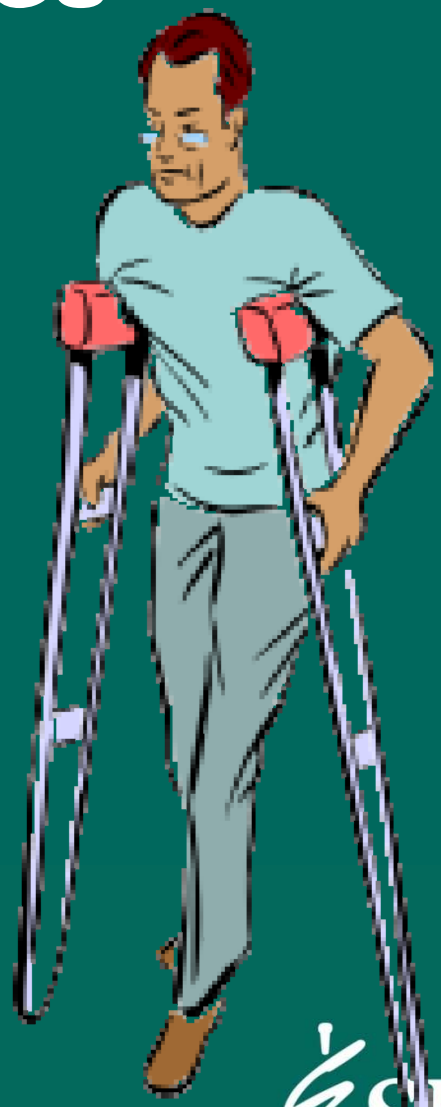
Treatment of Alzheimer's

Donepezil, galantamine, rivastigmine, memantine treat the ABCs of AD:

- **A**ctivities of daily living
- **B**ehavior
- **C**ognition

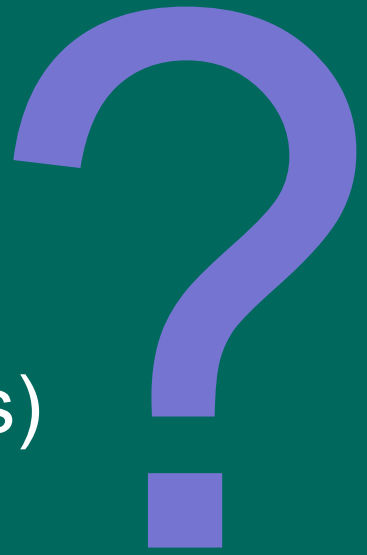
THE BENEFIT OF THESE DRUGS

Like using a crutch if we have severe leg pain...



Over-the-counter medicine

- Prevagen®
- Cognium® (Natrol®)
- Resveratrol
- Ginkgo biloba
- Curcumin (curry spice turmeric)
- Fish oil (DHA, omega-3 fatty acids)
- Vitamin E
- Coenzyme Q10
- Huperzine A
- Many others



SIU

symptoms of dementia

- Agitation
- Depression
- Anxiety
- Disordered sleep
- Psychosis
- Combativeness
- Many others

Treatments for the SYMPTOMs of dementia

- Non-pharmacological treatment first!

Non-pharmacological treatment

- Education about Alzheimer's/dementia
- Nutrition
- Exercise
- Take care of yourself.
- What's good for the heart is good for the brain.
- If you don't use it, you lose it.
  - (applies to the body and the brain)

Treatments for the SYMPTOMs of dementia

- Non-pharmacological treatment first!
- Pharmacological

Drugs to treat the SYMPTOMs

- Anti-agitation
- Anti-depressants
- Anti-anxiety (anxiolytics)
- Anti - no sleep (hypnotics)
- Anti-psychotics
- Anti - caregiver burn-out
- Others

SIU

Drugs to treat the complications

- Anti-agitation
- Anti-depressants
- Anti-anxiety (anxiolytics)
- Anti - no sleep (hypnotics)
- Anti-psychotics
- Anti - caregiver burn-out
- Others

Start low and go slow!

DISEASE-MODIFYING DRUGS?

“Four immunotherapies now banish amyloid from the brain”

- donanemab (NP3G, LY3002813)
- BAN2401
- gantenerumab
- aducanumab

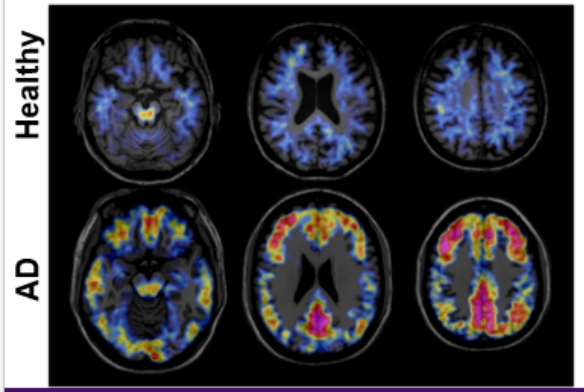
https://www.alzforum.org/print-series/1030941

SIU

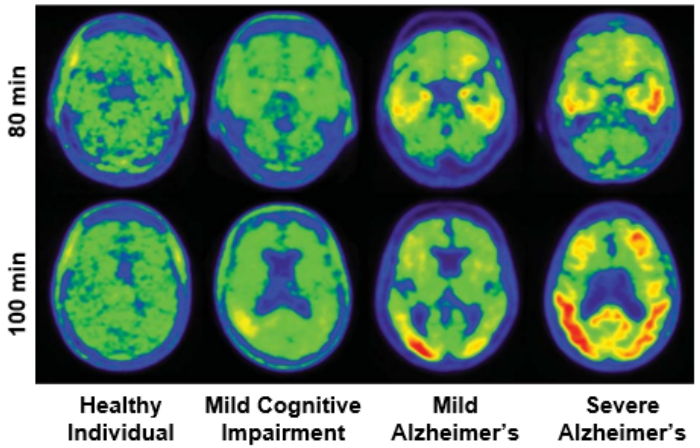
Biomarkers Are Changing the Game

Saliva Biofluid

Amyloid-β PET Imaging



Tau PET Imaging



Optical Evaluation

Blood Test

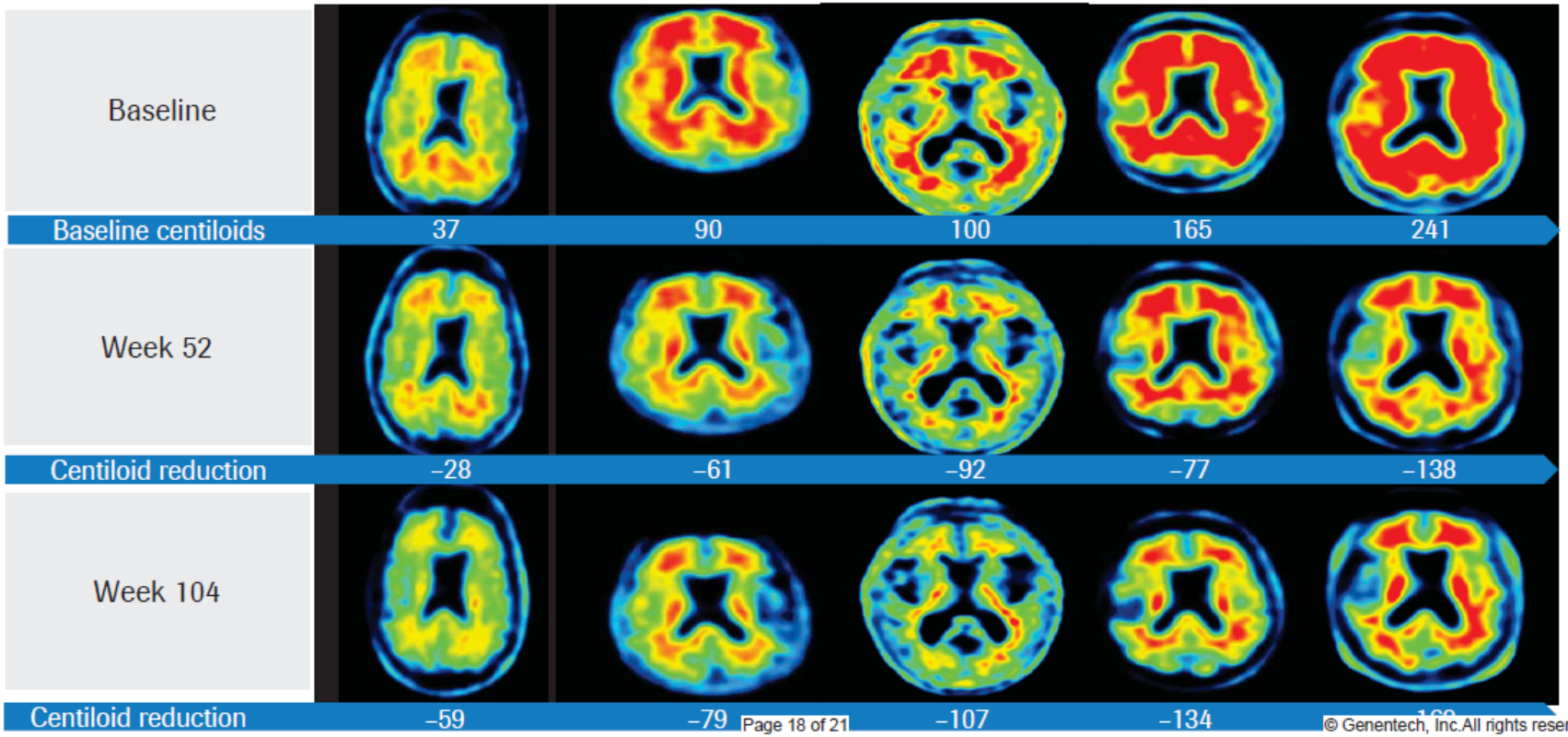
CSF – Lumbar Puncture

alzheimer's association

SIU

Continued amyloid reduction during gantenerumab second year

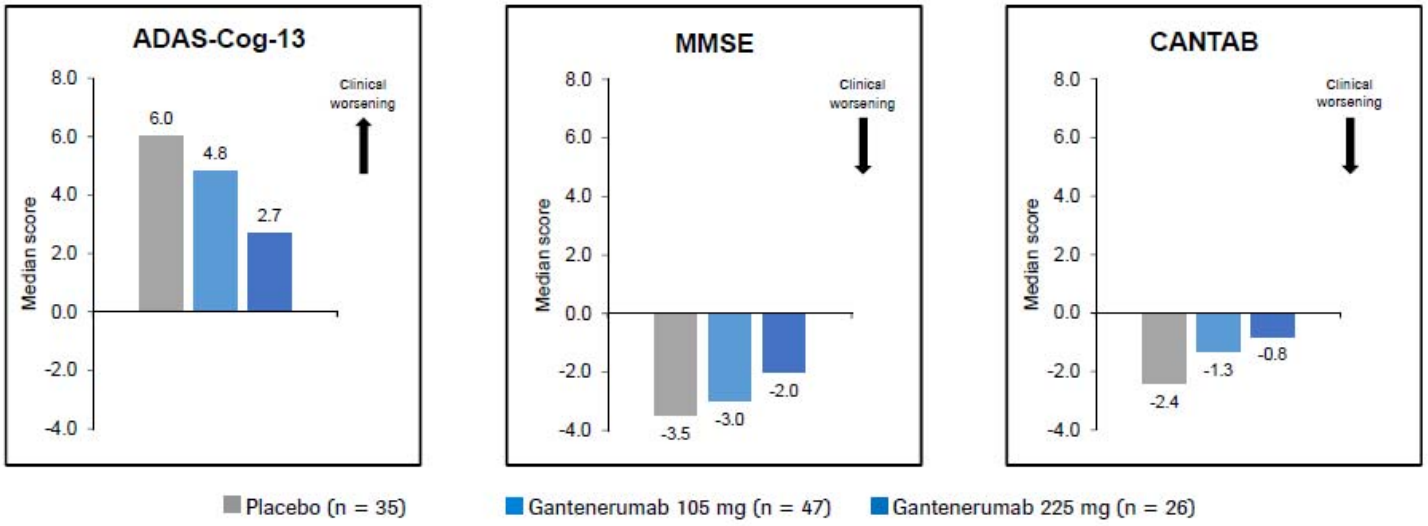
Examples from five patients in OLEs



BUT do these antibody treatments affect cognition?

SCarlet RoAD double-blind study efficacy signal

Dose-dependent effect on slowing cognitive decline in fast progressors[1*]



- Participants from SCarlet RoAD with prodromal AD, *post hoc* analyses
- *Fast progressors defined as baseline CDR-SB ≥ 2, FAQ ≥ 4 and hippocampal volume < median[2]
- No trend for CDR-SB

ADAS-Cog-13, 13-item Alzheimer's Disease Assessment Scale – Cognitive Subscale; CANTAB, Cambridge Neuropsychological Test Automated Battery; FAQ, Functional Activities Questionnaire; MMSE, Mini-Mental State Examination.

1. Ostrowitzki S, et al. Alzheimers Res Ther 2017 9:95; 2. Delor I, et al. CPT Pharmacometrics Syst Pharmacol. 2013;2, e78.

9

LOOKS GOOD, BUT HAS IT BEEN PROVEN?

DISEASE-MODIFYING DRUGS?

“Four immunotherapies now banish amyloid from the brain”

- donanemab (NP3G, LY3002813)
- BAN2401
- gantenerumab
- aducanumab has applied for FDA-approval

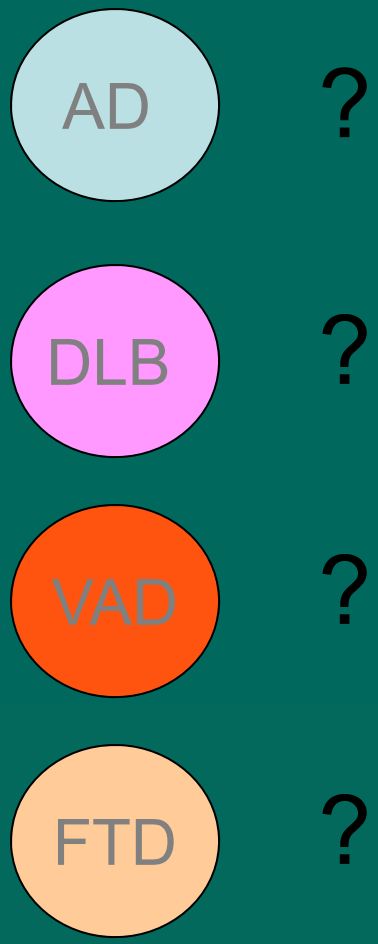
https://www.alzforum.org/print-series/1030941

SIU

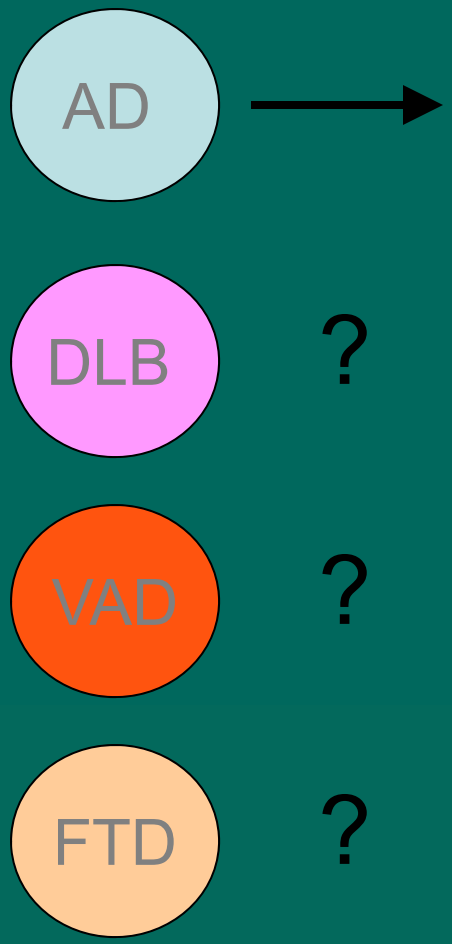
Treatment of dementia

- Specific
- Symptomatic
  - Antidepressants
  - Anxiolytics
  - Neuroleptics
  - Hypnotics
  - Others

Treatment



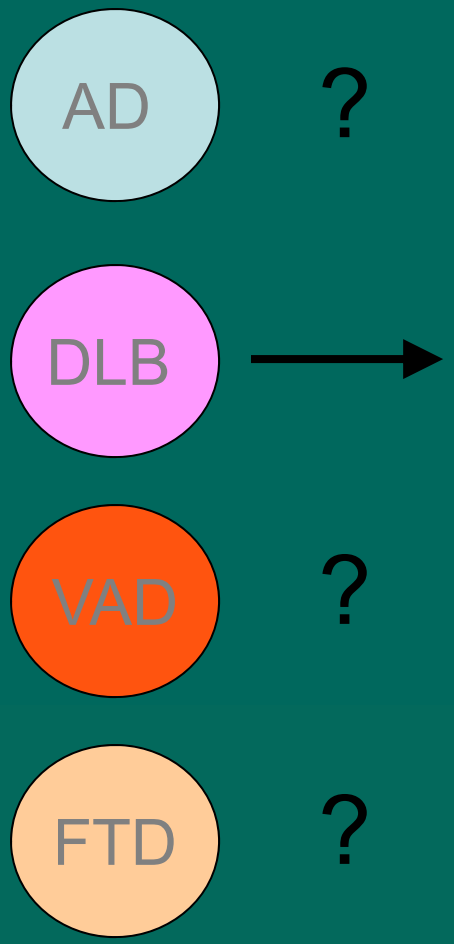
Treatment



donepezil, rivastigmine,
galantamine, memantine

SIU

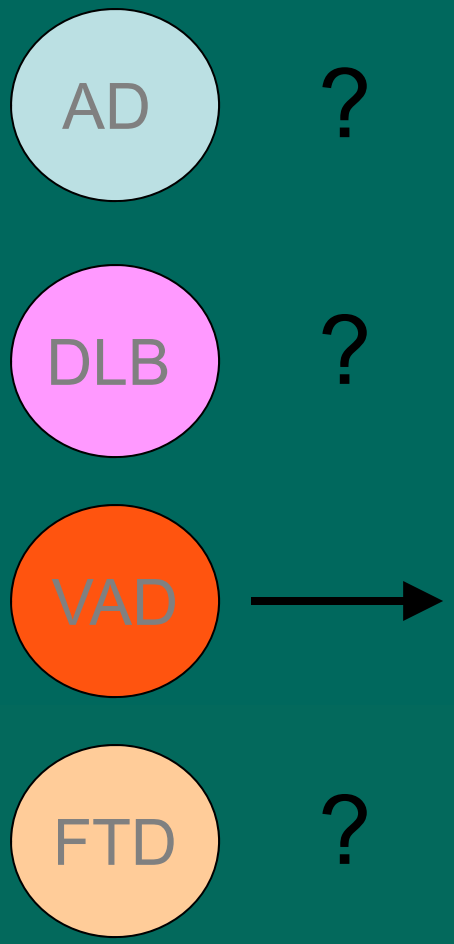
Treatment



donepezil, rivastigmine,
galantamine, memantine

SIU

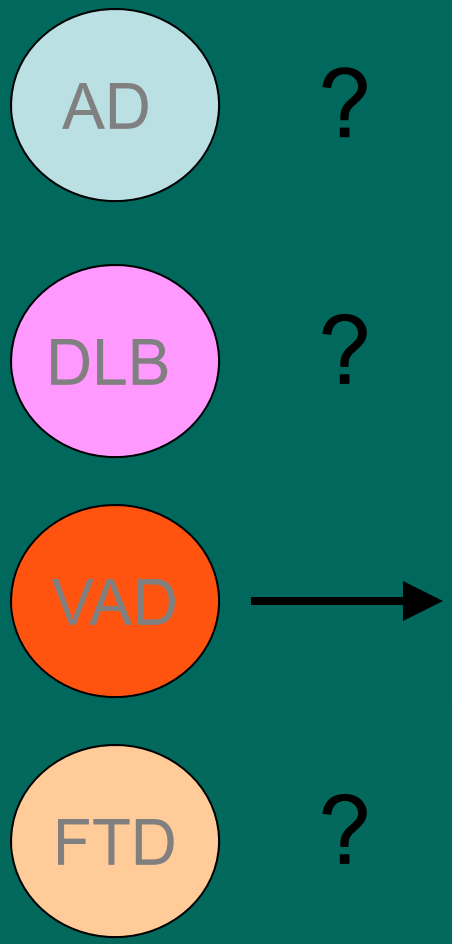
Treatment



donepezil, rivastigmine,
galantamine, memantine

SIU

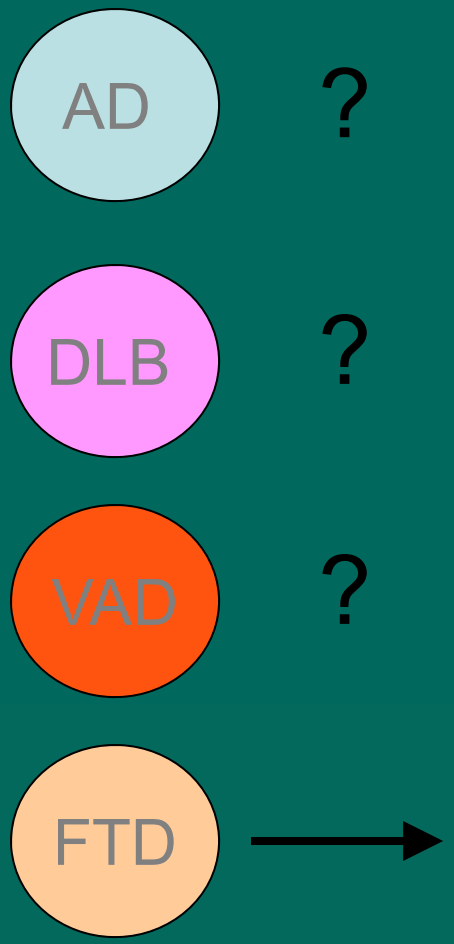
Treatment



donepezil, rivastigmine, galantamine, memantine, and prevent strokes

SIU

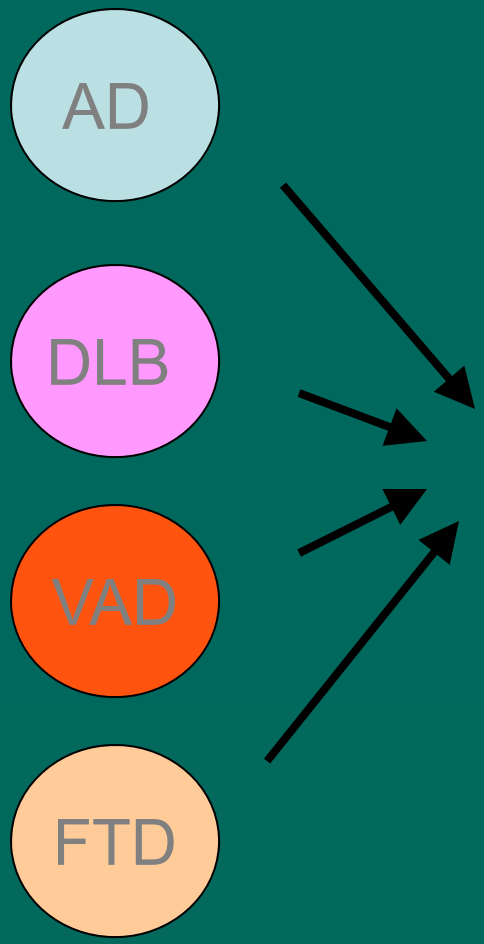
Treatment



donepezil, rivastigmine,
galantamine, memantine

SIU

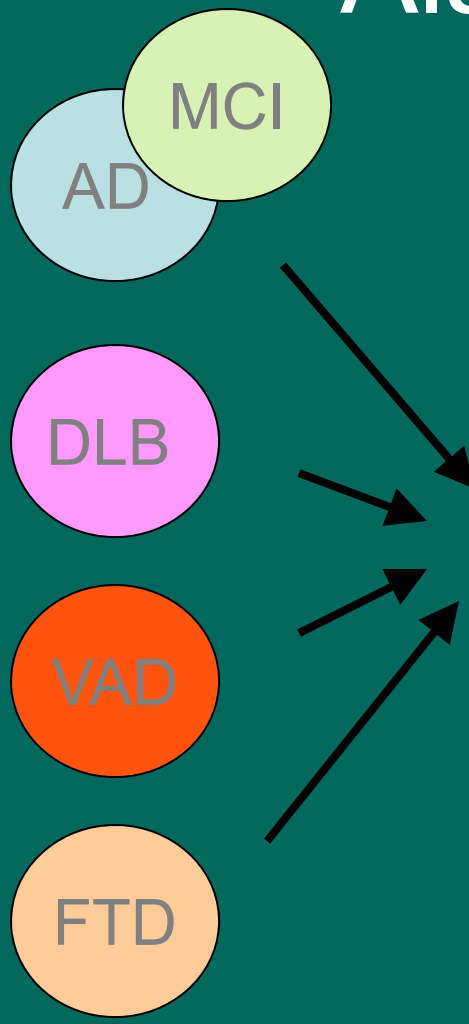
Ala's Treatment



donepezil, rivastigmine,
galantamine, memantine

SIU

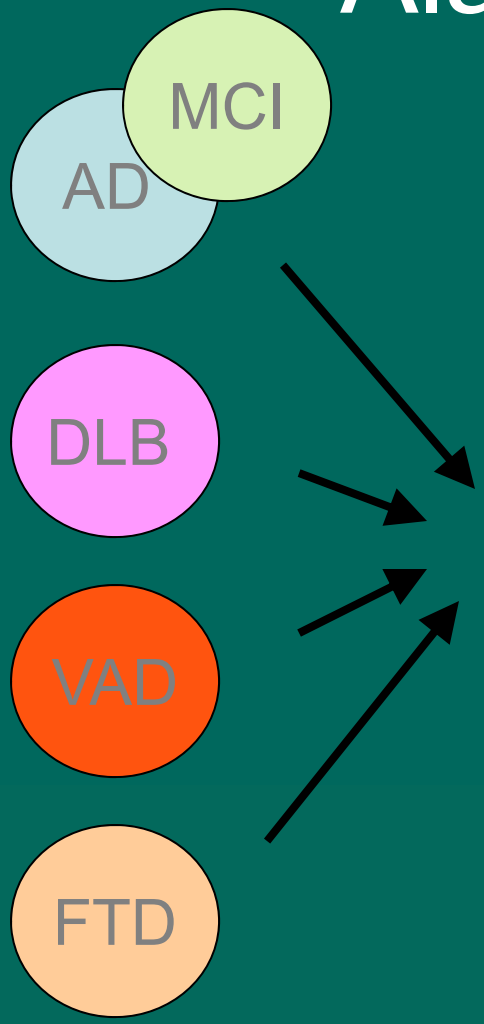
Ala's Treatment



donepezil, rivastigmine,
galantamine, memantine

SIU

Ala's Treatment



donepezil, rivastigmine, galantamine, memantine, and prevent strokes

SIU

Treatment of dementia

- Non-pharmacologic methods:
  - treatment of complicating factors
  - exercise
  - nutrition
  - education of the caregiver!

The Ala shortcut

- Is progressive cognitive impairment likely?

The Ala shortcut

- Is progressive cognitive impairment likely?
- If yes, 95% chance it is due to a degenerative dementing illness.

The Ala shortcut

- Cognitive impairment is likely?
- If yes, 95% chance it is due to a degenerative dementing illness.
- Therefore,

donepezil, rivastigmine, galantamine, memantine, prevent strokes, and education

The end

Thank you!