

Untangling Alzheimer's Promising Advances

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alzheimer's  association®

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- I have no relevant financial relationship with the manufacturers of any commercial products and/or providers of commercial services discussed in this CME activity
- Neither I nor any member of my immediate family has a financial relationship or interest with any proprietary entity producing health care goods or services related to the content of this CME activity
- My content will include reference to commercial products; however, generic and alternative products will be discussed wherever possible
- Drug reps really don't like me

What is Dementia?

- Dementia is a clinical syndrome, diagnosed when there is a decline in thinking ability (often memory and other areas of thinking) that is bad enough to interfere with the ability to function in daily life
- Diagnosing the presence of dementia is a clinical exercise—there is no blood test or brain scan that can diagnose dementia, and there is no simple test a doctor can perform that will diagnose dementia
- Dementia can be caused by many things, including several neurological diseases
- Alzheimer Disease is the most common cause of dementia

How is “Dementia” Different from “Alzheimer Disease”?

- Dementia is the syndrome of cognitive decline
- Alzheimer Disease is a disease, defined by the type of pathological changes in the brain (specifically, deposits of amyloid and tau proteins, along with degeneration of loss of neurons (brain cells))
- Alzheimer Disease is the most common cause of dementia

The Diagnostic Journey with Dementia

- Detection of cognitive impairment
- Medical evaluation with assessment of cognition
- Diagnostic testing to rule out reversible causes of dementia
- Diagnosis of the etiology (the cause) of dementia
- Disclosure of diagnosis
- Discussion of management
- Follow-up to re-assess level of impairment, and symptoms present
- Changes in management follow changes in symptoms and function

Who Should Diagnose Dementia?

- Most people have more contact with Primary Care Providers (MDs, DOs, Nurse Practitioners in Family Medicine or Internal Medicine)
- Studies show PCPs often are uncomfortable making a diagnosis of dementia, may avoid dealing with the problem of dementia, and typically make the diagnosis rather late
- Diagnosis of dementia, including diagnosis of the cause of dementia (eg, Alzheimer Disease, Dementia with Lewy Bodies, etc.) is usually fairly straightforward, for a provider with knowledge about dementia
- Those best-equipped through training, to deal with dementia, include some Neurologists (especially Behavioral Neurologists), Psychiatrists, and Geriatricians

The Behavioral Neurology Approach to Memory Loss

- Step One: Is dementia present?

How Presence of Dementia is Determined

- A thorough history is taken from patient and from informant(s)
- Cognition is assessed, usually with screening instruments
 - Mini-Mental State Exam (MMSE)
 - St. Louis University Mental Status Exam (SLUMS)
 - Montreal Cognitive Assessment (MoCA)
- The clinician must take into account many factors from the history and the exam to determine if criteria for dementia are met:
 - Is there evidence of cognitive decline?
 - Does that cognitive decline interfere with daily function?

The Behavioral Neurology Approach to Memory Loss

- Step One: Is dementia present?
- If dementia is present, follow steps to determine the etiology of dementia
- If dementia is not present, is memory abnormal on testing of cognition?
 - If dementia is not present and memory is normal on testing, then this is Subjective Cognitive Decline (SCD)
 - Risk for dementia only slightly elevated
 - If dementia is not present and memory is impaired on testing, then this is Mild Cognitive Impairment (MCI)
 - Risk for dementia elevated

What Do You Do with SCD/MCI?

- There are no drugs proven effective for either SCD or MCI
- There are no drugs which improve memory
- There are no vitamins or diet supplements which have been shown to improve memory or prevent or delay dementia
- There are drugs to delay decline in full-blown dementia, but they have not proven effective against MCI and have no effect in SCD

What Do You Do with SCD/MCI?

- There are lifestyle changes or modifications, which may reduce risk of developing dementia, so are hoped to reduce decline toward dementia:
 - Regular, aerobic physical exercise (150 minutes/week)
 - Eating a “heart healthy” diet (eg, Mediterranean diet, DASH diet)
 - Engage in cognitively stimulating activity
- We recommend regularly re-evaluating people with MCI, and many people with SCD, to detect changes that may signal progression to full-blown dementia
- If dementia develops, standard treatments for dementia should be started

The Behavioral Neurology Approach to Dementia

- Determine whether a reversible cause could be present
- Obtain diagnostic tests to exclude (“rule out”) reversible causes
- If no reversible cause is present, apply diagnostic criteria to determine the cause of dementia
- Disclose diagnosis of etiology of dementia to patient and caregiver
- Discuss management of dementia, including drug treatment and support services
- Send report of evaluation to Primary Care Provider

What Are the Reversible (Fixable) Causes of Dementia?

- Drugs (medications) can cause dementia, including: opioids (narcotics), benzodiazepines (sedatives), sleeping pills, and anticholinergic medicines (medicines like diphenhydramine (Benadryl®))
- Some medical conditions can cause dementia, including low thyroid function
- Depression can cause dementia, and may improve with treatment
- Occasionally, benign brain tumors have caused dementia, which improved when the tumor was removed
- Normal Pressure Hydrocephalus (NPH), a condition where the fluid-containing cavities of the brain are enlarged, can cause cognitive impairment that hypothetically could improve with treatment

What Diagnostic Tests Are Recommended?

- General laboratory tests to assess electrolytes, renal function, liver enzymes, calcium level
- Tests of thyroid function and vitamin B12 level
- Brain imaging with CT or MRI
 - Comparative studies show no advantage for MRI over CT in diagnosing the cause of dementia
 - CT has advantages including: it's cheaper, faster, less risky, and easier to tolerate

Diagnostic Tests Commonly Done (but Should Not Be Routine)

- PET scans
- Lumbar puncture with tests of spinal fluid
- Genetic testing
- EEG (“brainwave testing”)
- Carotid Dopplers (testing the arteries in the neck for blockage)
- Neuropsychological Testing

What Are the Common Causes of Dementia?

- Alzheimer Disease (AD)
- Dementia with Lewy bodies (DLB)
- Vascular Dementia (VaD)
- Frontotemporal Lobar Degeneration, including Frontotemporal Dementia (FTD)

Diagnostic Criteria for Alzheimer Disease

- Meets criteria for dementia
- Insidious onset
- Evidence of progression
- Neurological exam is usually normal except for cognition
- Not due to another condition

Core Features of Dementia with Lewy bodies

- Fluctuating cognition with pronounced variations in attention and alertness
- Well-formed visual hallucinations
- REM sleep behavior disorder (may precede other symptoms by many years)
- Spontaneous Parkinsonism (bradykinesia, rigidity, rest tremor)

Diagnostic Criteria for Vascular Dementia

- Meets criteria for dementia
- Evidence of significant cerebrovascular disease relevant to dementia:
 - Sudden onset of dementia in temporal association with stroke
 - Presence of multiple cortical infarcts or severe White Matter Hyperintensities on imaging

Frontotemporal Lobar Degeneration

- Three common presentations:
 - Behavioral Variant FTD (bvFTD)
 - Primary Progressive Aphasia (PPA):
 - Nonfluent/Agrammatic Variant
 - Semantic Variant

Diagnostic Criteria for bvFTD

- “Possible” bvFTD: 3 of the following behavioral/cognitive symptoms must be present:
 - Early behavioral disinhibition
 - Early apathy or inertia
 - Early loss of sympathy or empathy
 - Early perseverative, stereotyped, or ritualistic behavior
 - Hyperorality and dietary changes
 - Neuropsych profile with executive deficits and sparing of memory and visuospatial functions

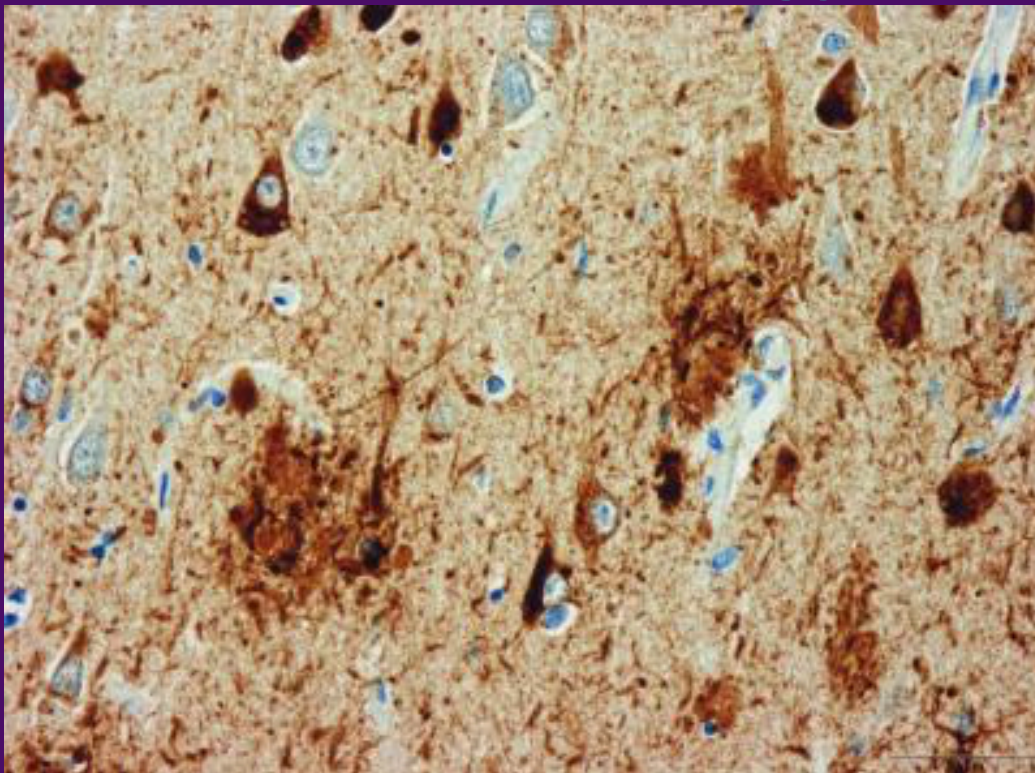
Diagnostic Criteria for bvFTD

- “Probable” bvFTD: All of the following must be present:
 - Meets criteria for “possible” bvFTD
 - Exhibits significant functional decline
 - Imaging results consistent with bvFTD:
 - Frontal and/or temporal atrophy on MRI/CT
 - Frontal and/or temporal deficits on PET

Alzheimer Disease Research

- Changes in diagnostic criteria for research studies
- Advances in diagnostic tools
 - Imaging
 - Blood-based biomarkers
- Treatments
 - Nonpharmacological
 - New drugs

Alzheimer Disease Pathology



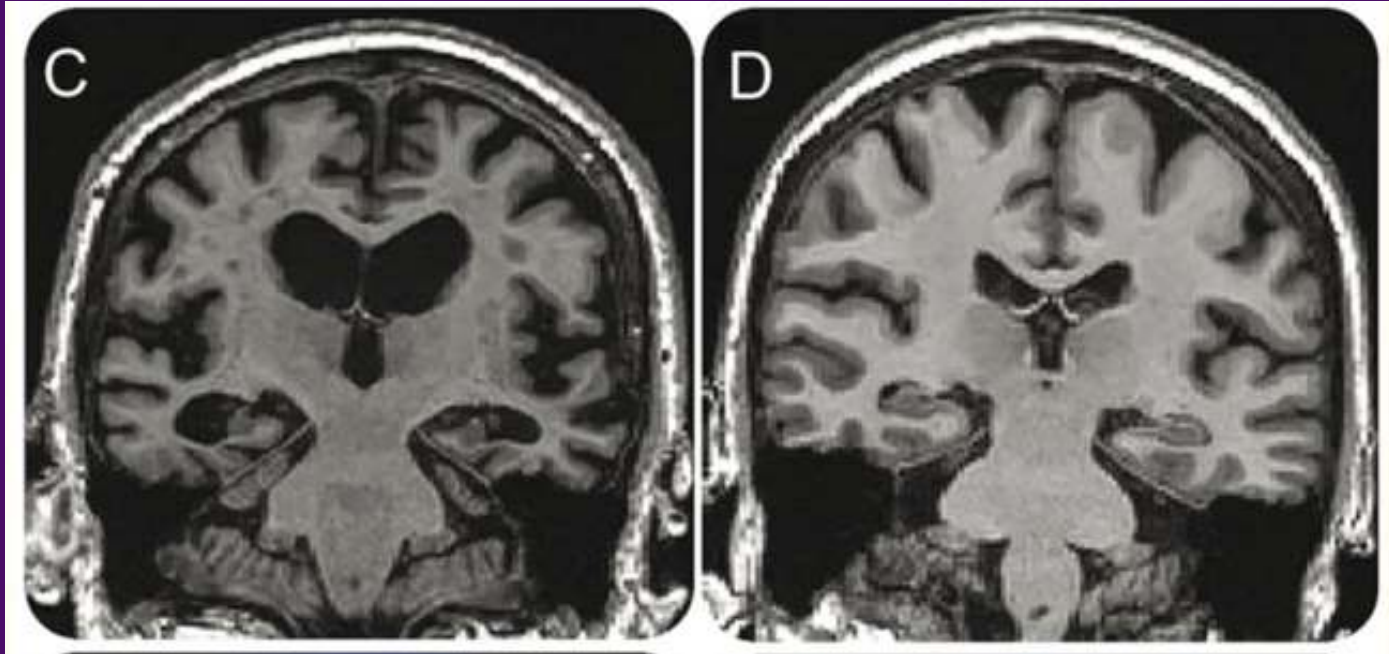
Alzheimer Disease Research Diagnostic Criteria

- NIA/AA Criteria
- International Working Group (IWG) Criteria
- A / T / N Criteria

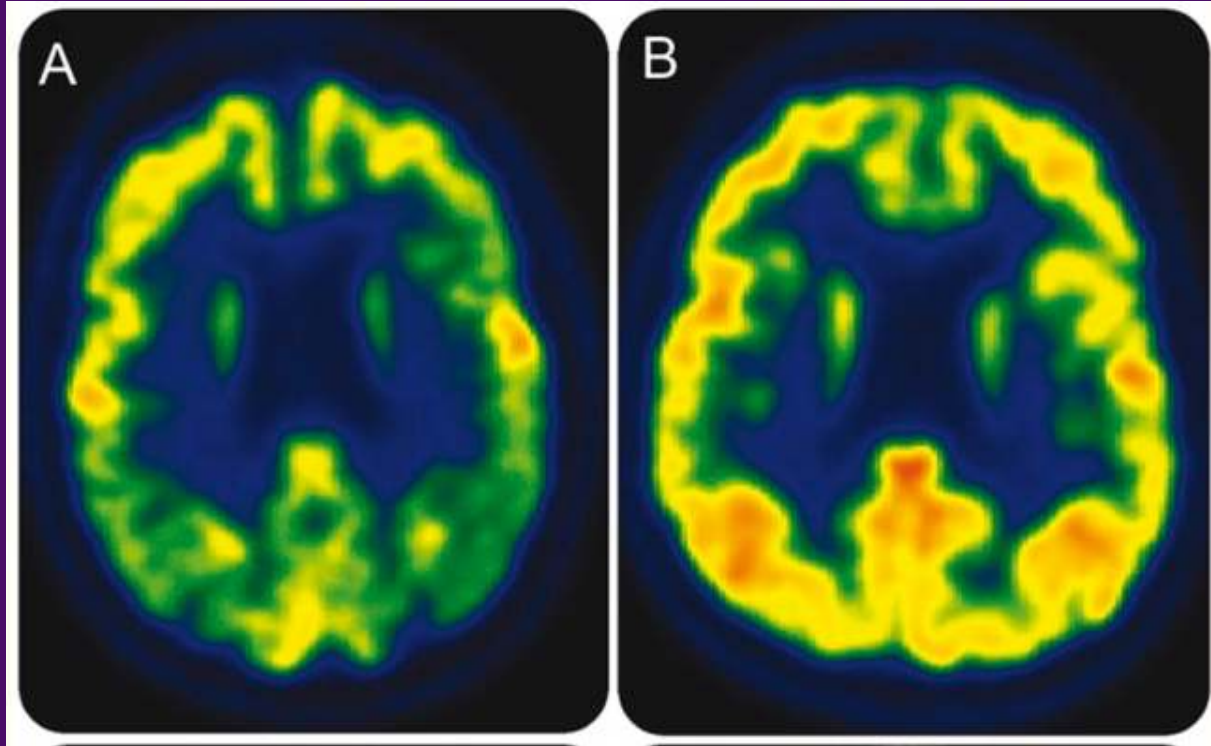
Alzheimer Disease Imaging

- Structural
 - Atrophy on MRI
- Functional
 - FDG-PET
 - Amyloid PET
 - Tau PET

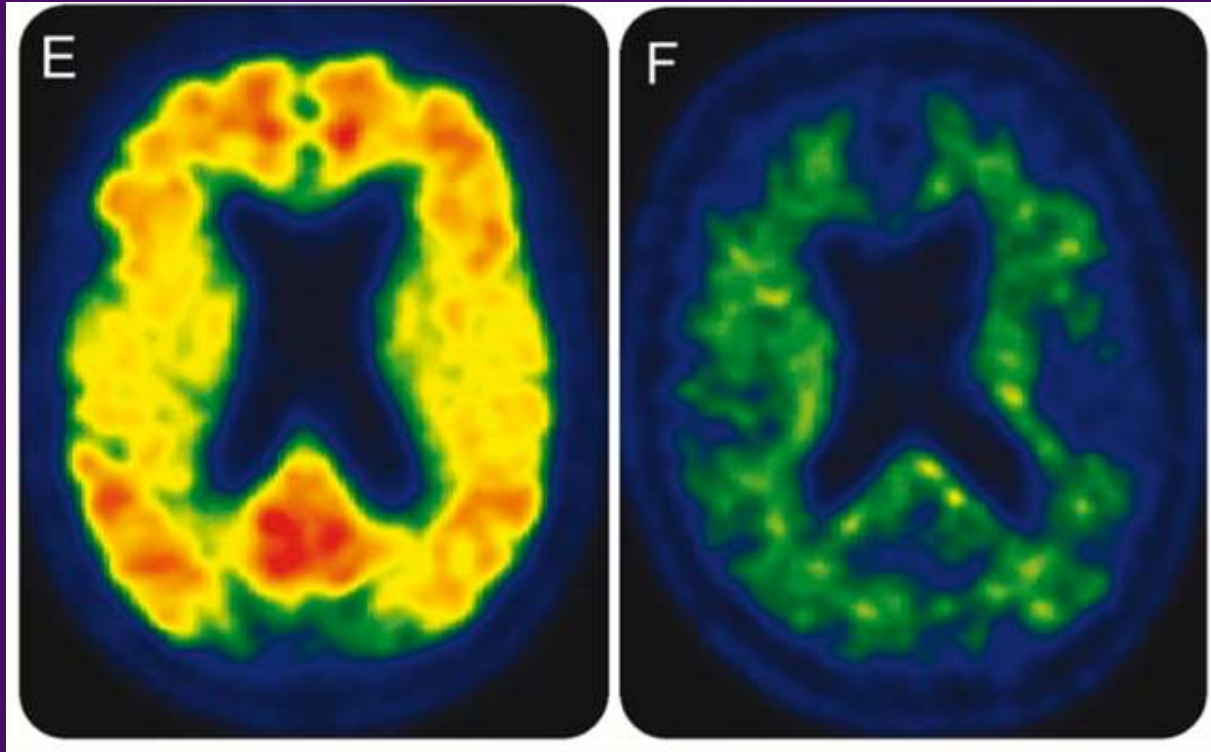
Alzheimer Disease Imaging: MRI



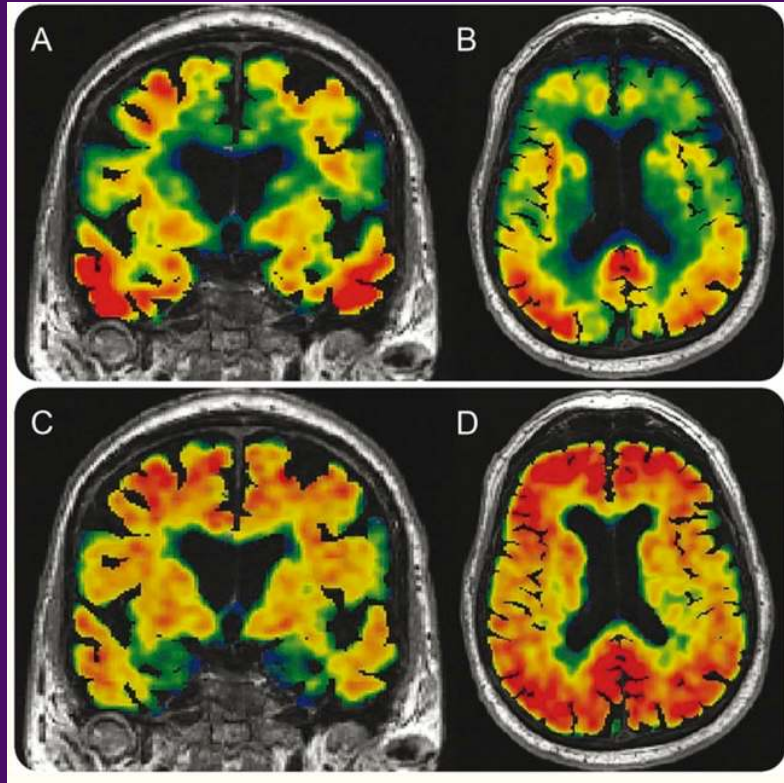
Alzheimer Disease Imaging: FDG-PET



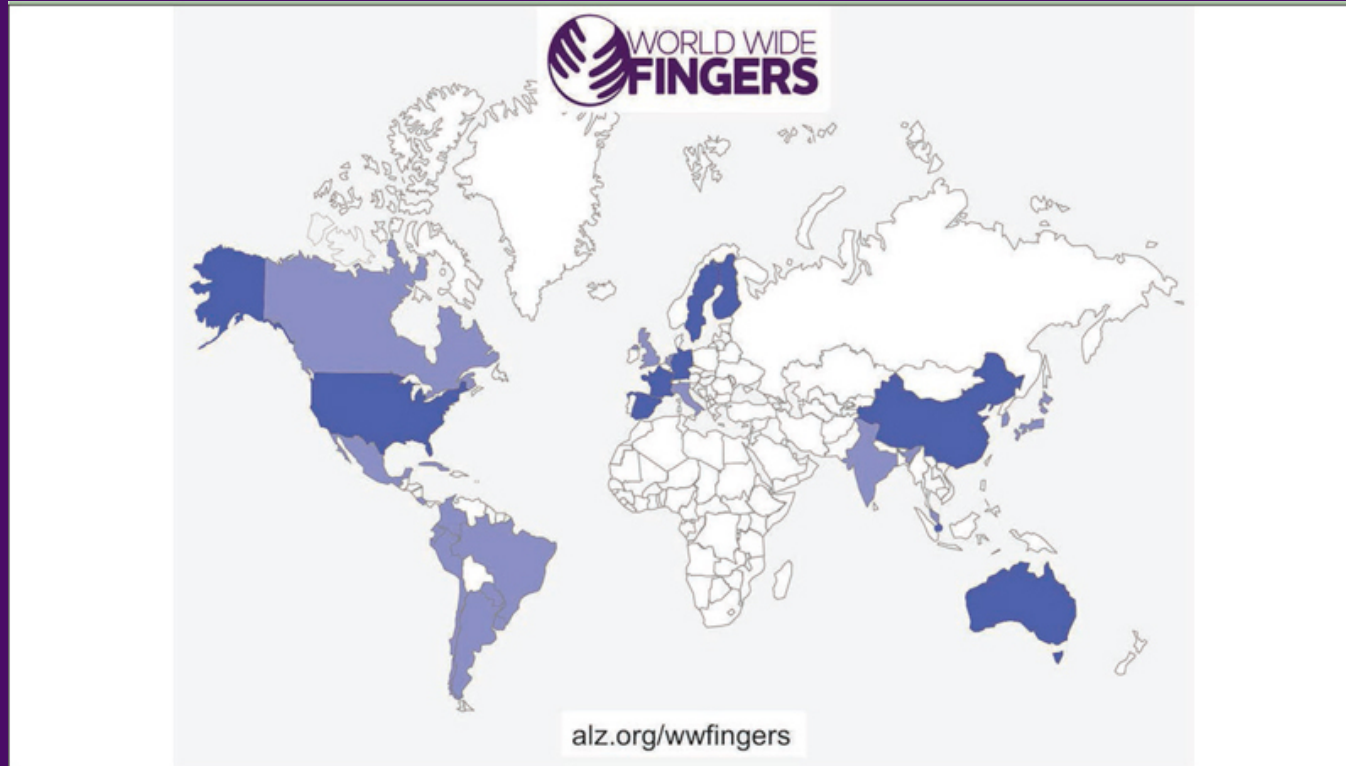
Alzheimer Disease Imaging: Amyloid PET



Alzheimer Disease Imaging: Tau & Amyloid PET

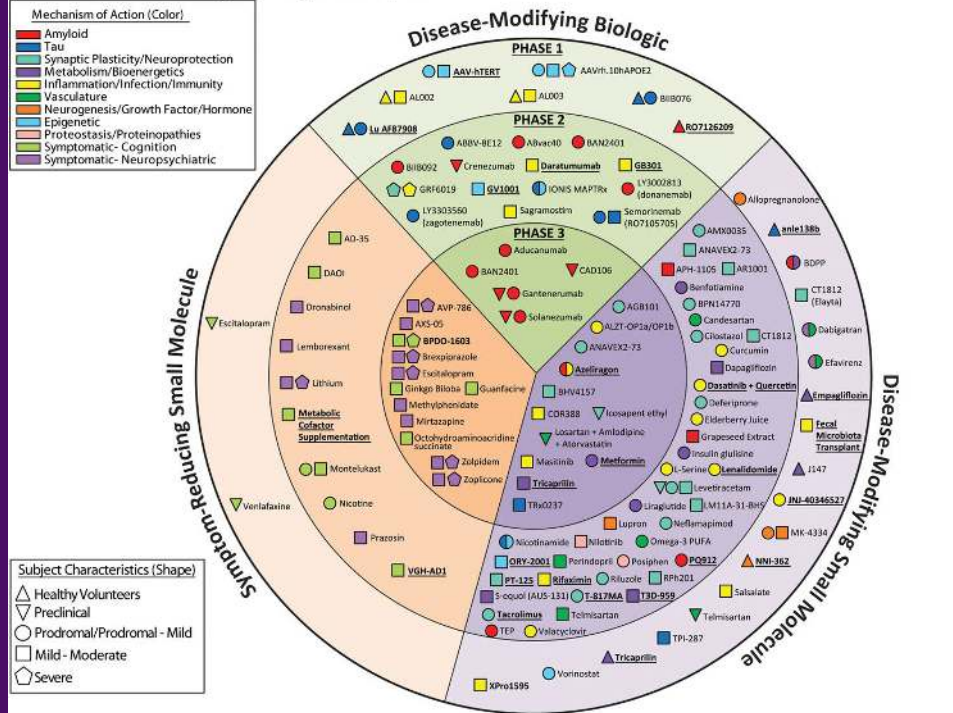


Multidomain Interventions for Alzheimer Disease



Alzheimer Disease Drug Pipeline

2020 Alzheimer's Drug Development Pipeline



Alzheimer Disease Drugs: Coming Soon?

- Aducanumab
- BAN2401
- Donenumab