



Phenotyping Alzheimer's Disease

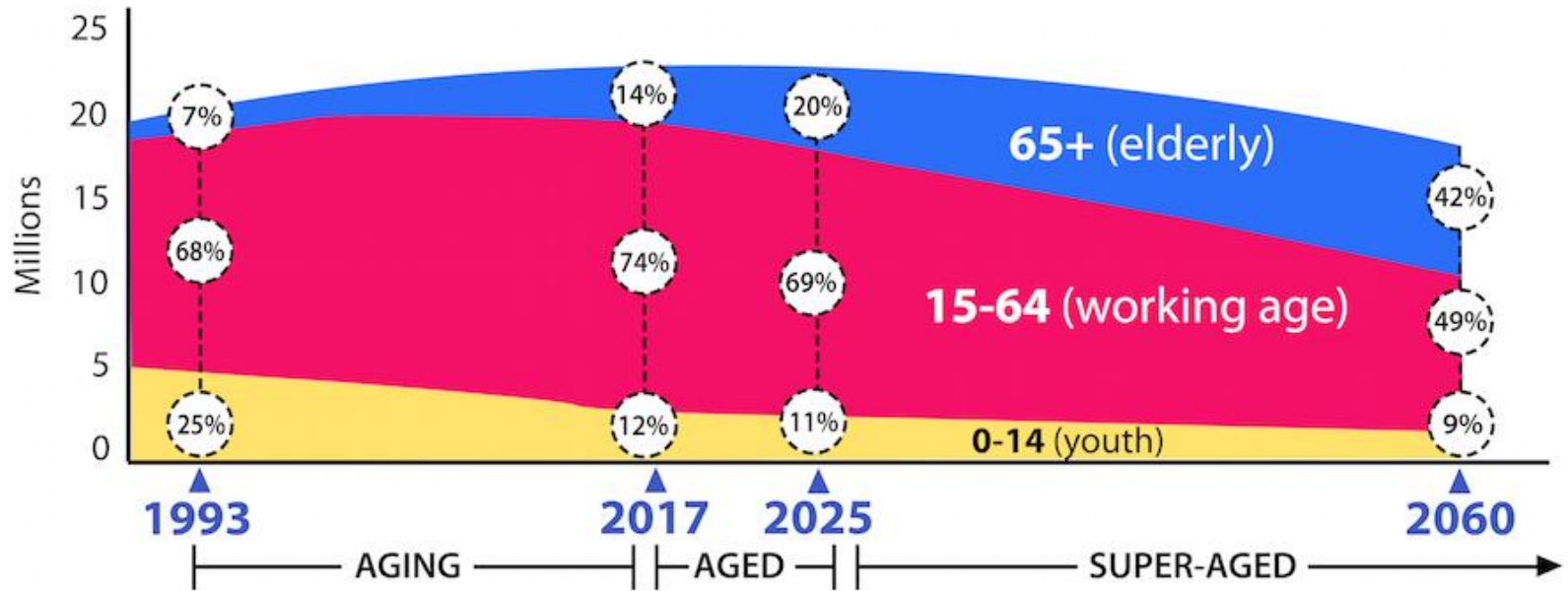
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TAIWAN'S AGING POPULATION Original Data: CEPD / NDC



Percentage of Taiwan's population classified as "elderly" (65+) in **2015**

12%

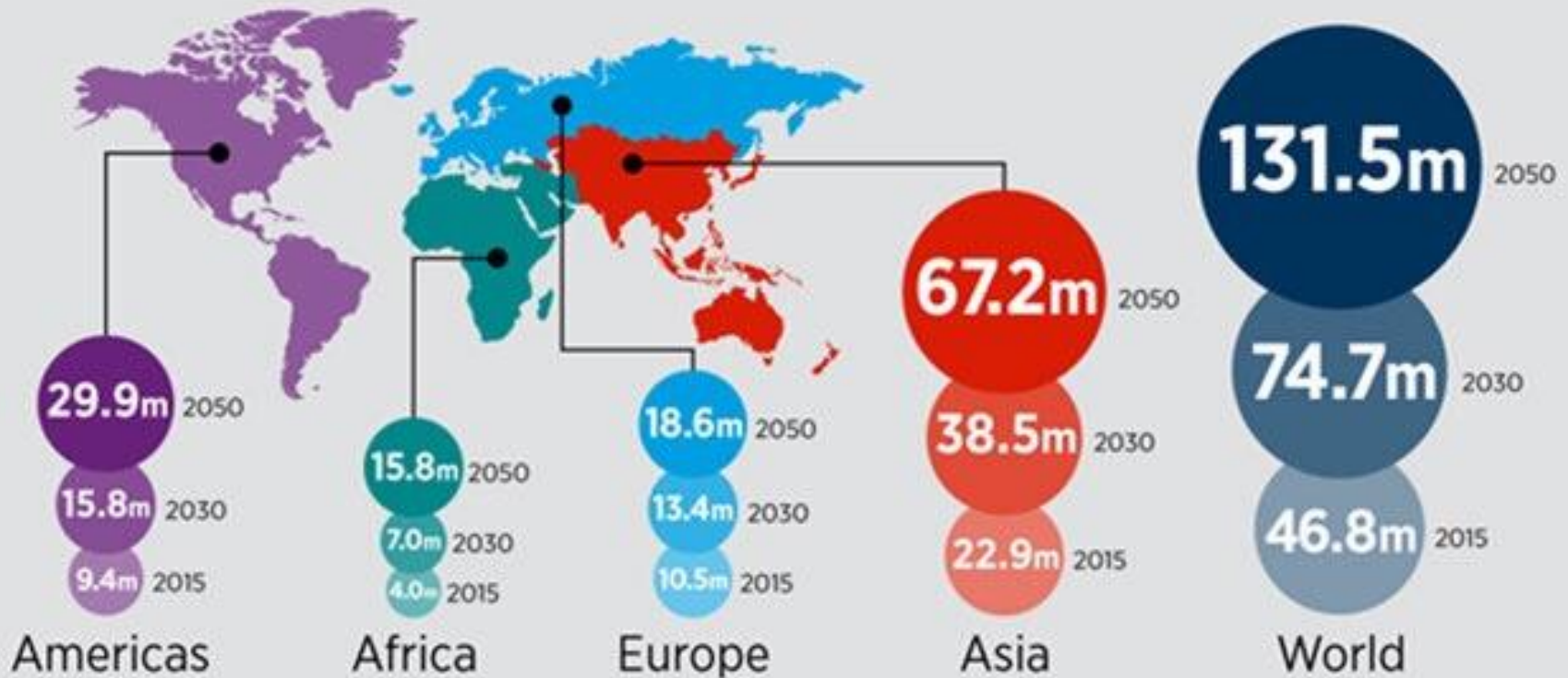


42%

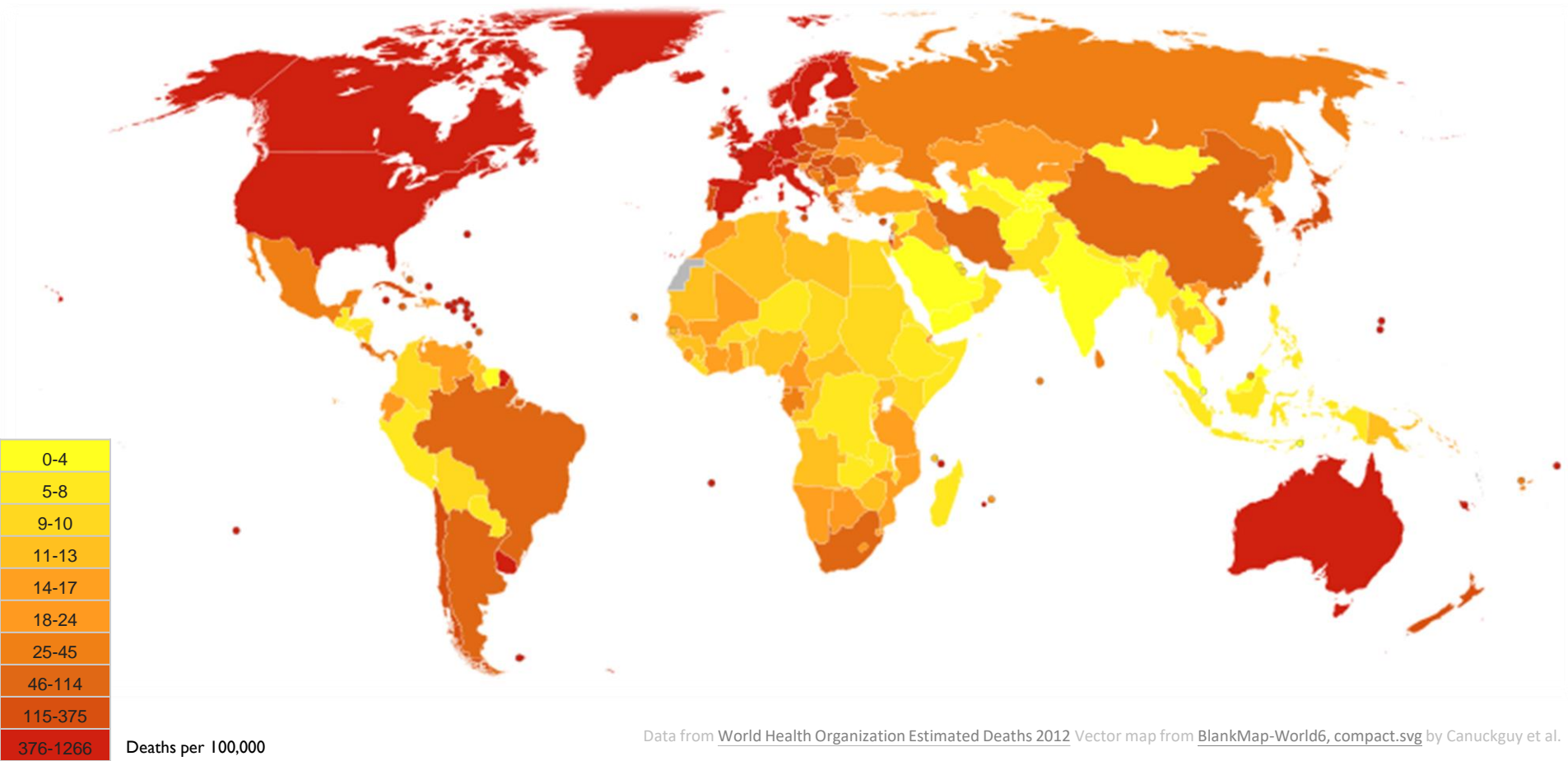
Projected percentage of Taiwan's population classified as "elderly" (65+) in **2060**

Dementia around the World

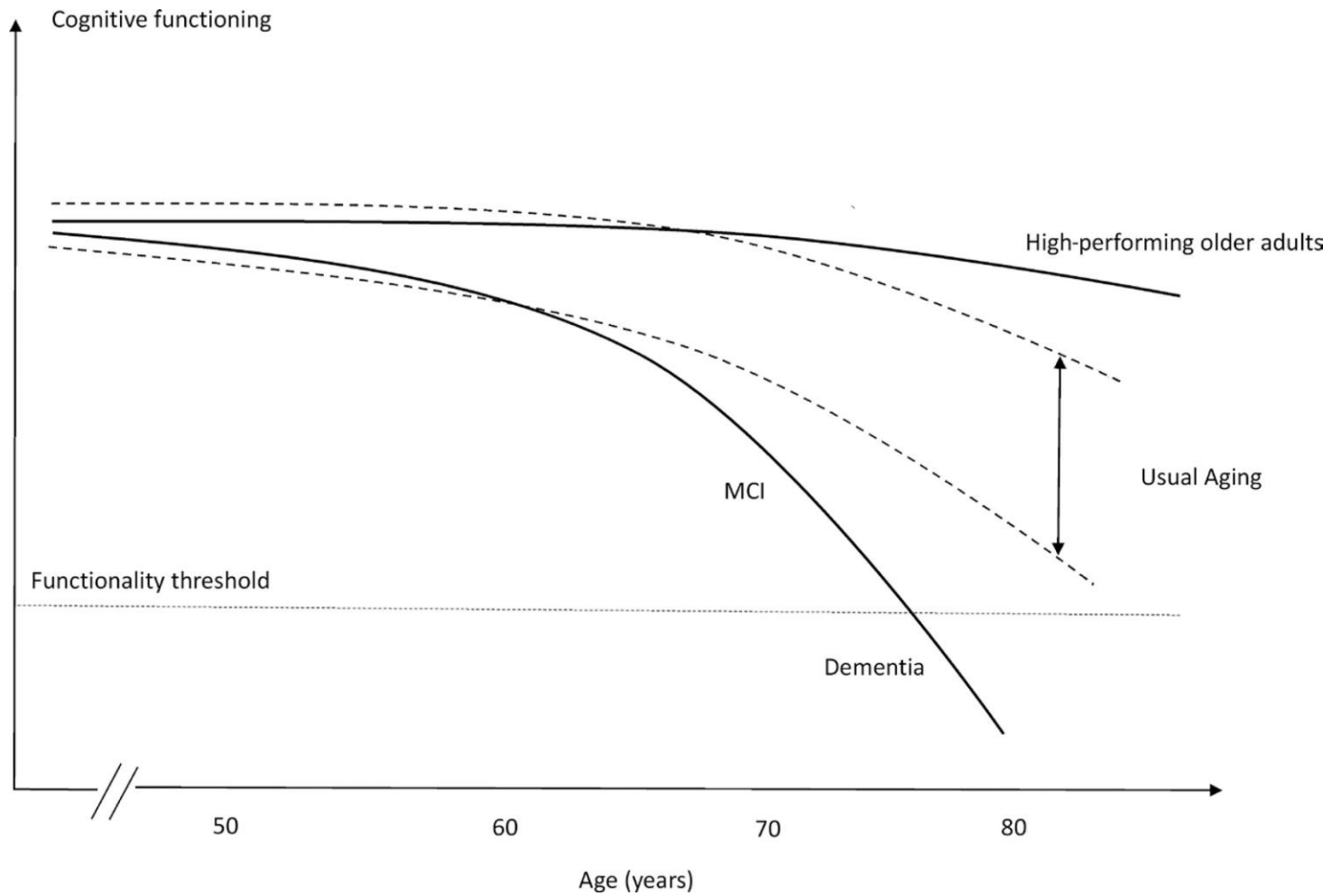
People living with **dementia** around the world



Global Deaths from Dementia per 100,000 people



Normal Aging \neq Dementia



Normal Aging vs. Dementia

NORMAL AGING	DEMENTIA
Independent in all activities of daily living (ADL)	Dependent on others for ADL
Patient claims of memory loss but can recall incidents of forgetfulness	May report memory loss if asked, unable to recall instances of forgetfulness
Patient more concerned about memory loss	Close family members more concerned about memory loss
Recent memory of events and conversations intact	Notable decline in memory of recent events and conversations
Occasional difficulty in finding words (expressive aphasia)	Frequently experiences difficulty in finding words with or without difficulty of understanding (expressive and receptive aphasia)
No history of getting lost in familiar territory, may pause briefly to reorient	History of getting lost in familiar territory while walking or driving
Able to operate common appliances	Unable to operate common appliances
Normal interpersonal and social skills	Loss of interpersonal and social skills, lack of interest in social activities or inappropriate behavior

Types of Dementia

The causes of dementia



Alzheimer's disease

A physical disease caused by changes in the structure of the brain and a shortage of important chemicals that help with transmission of messages.



Vascular dementia

Caused by problems in the supply of blood to the brain, commonly caused by a stroke or series of small strokes.



Mixed dementia

A type of dementia where a person has a diagnosis of both Alzheimer's disease and vascular dementia.



Dementia with Lewy bodies

One of the less common forms of dementia, it is caused by irregularities in brain cells, leading to symptoms similar to Alzheimer's disease and Parkinson's disease.



Rarer causes of dementia

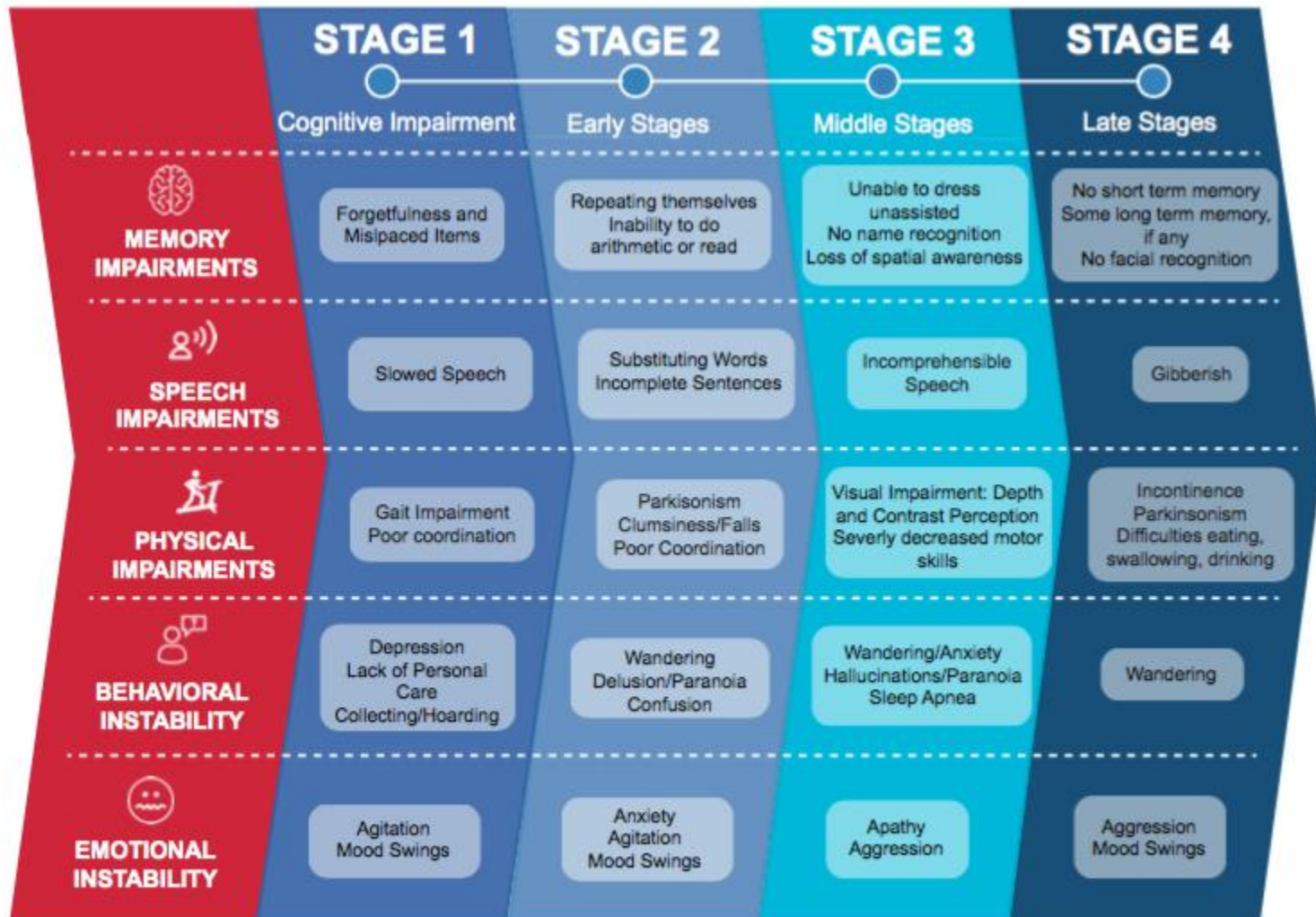
There are many rarer diseases and syndromes that can lead to dementia or dementia-like symptoms, including Corticobasal degeneration and Creutzfeldt-Jakob disease.



Fronto-temporal dementia

Rare when all ages are taken into account but relatively common in people under 65, it is a physical disease that affects the brain.

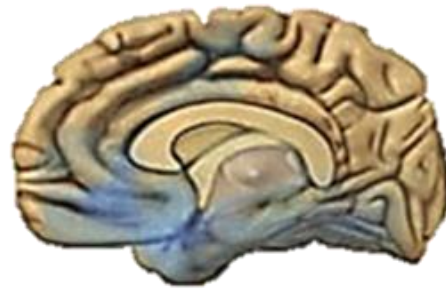
Progression of Dementia



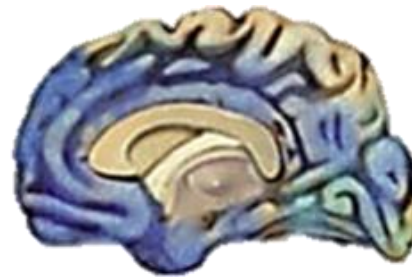
Course of Dementia



Mild
Cognitive
Impairment

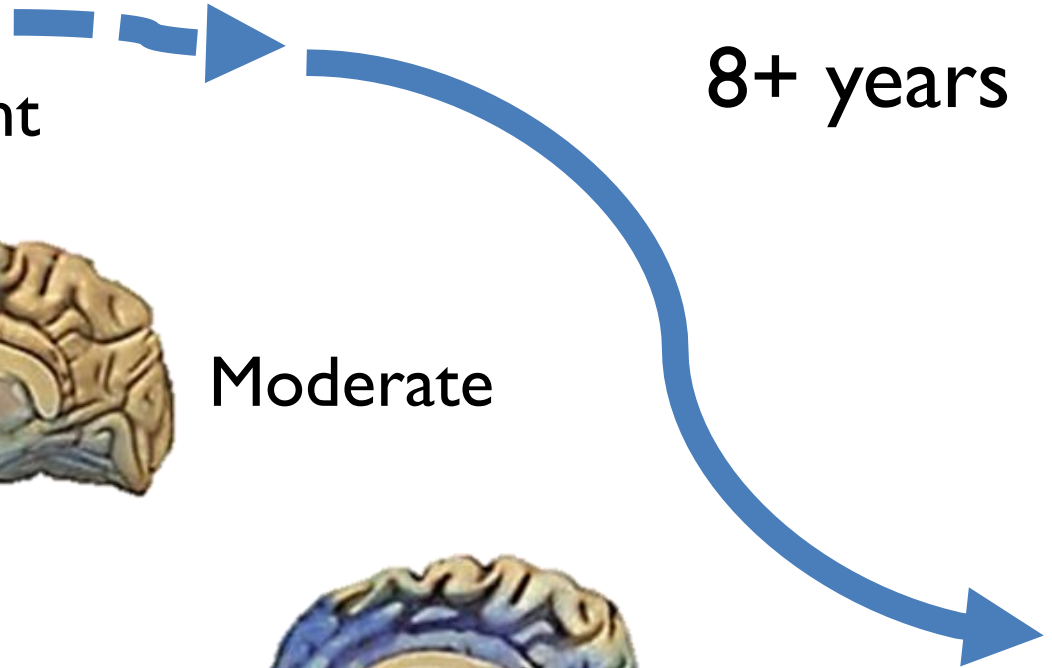


Moderate

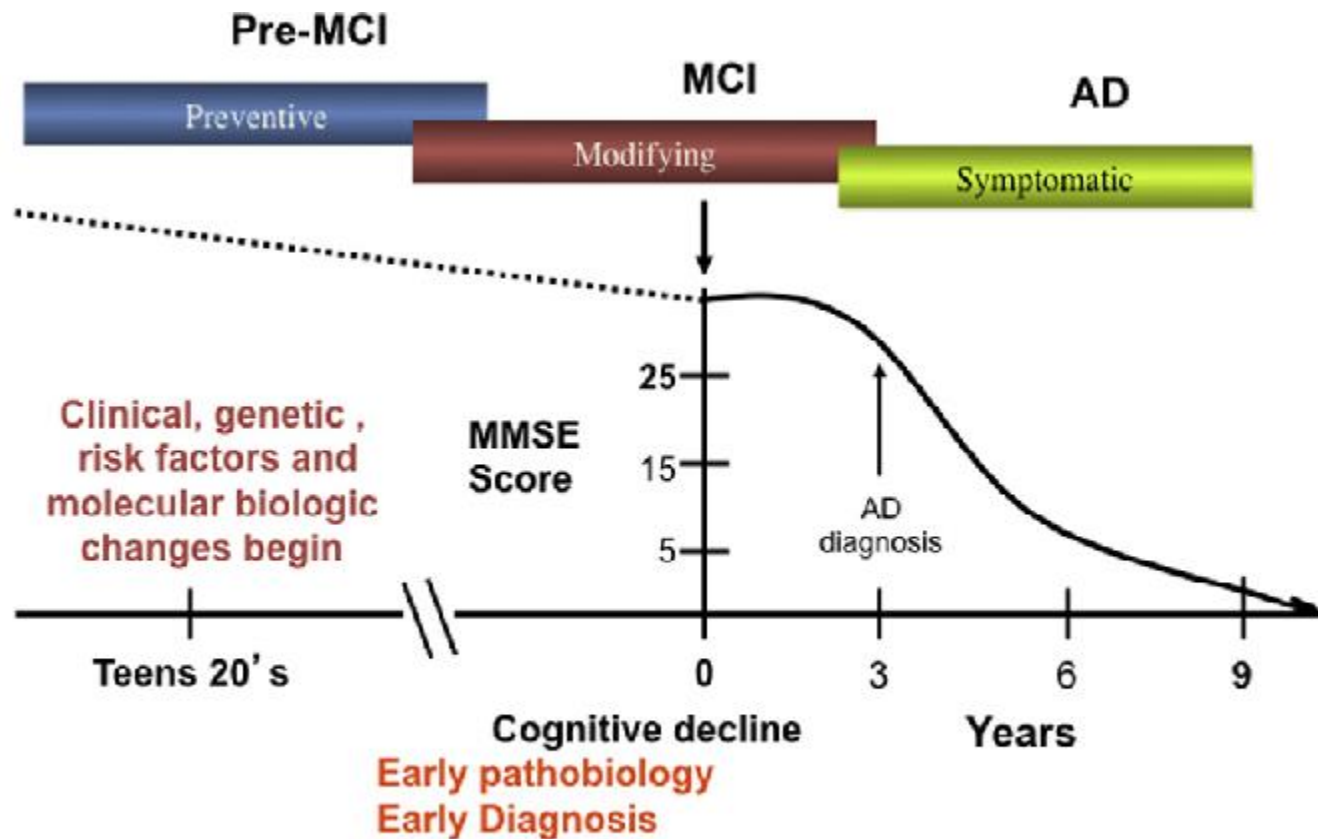


Severe

8+ years



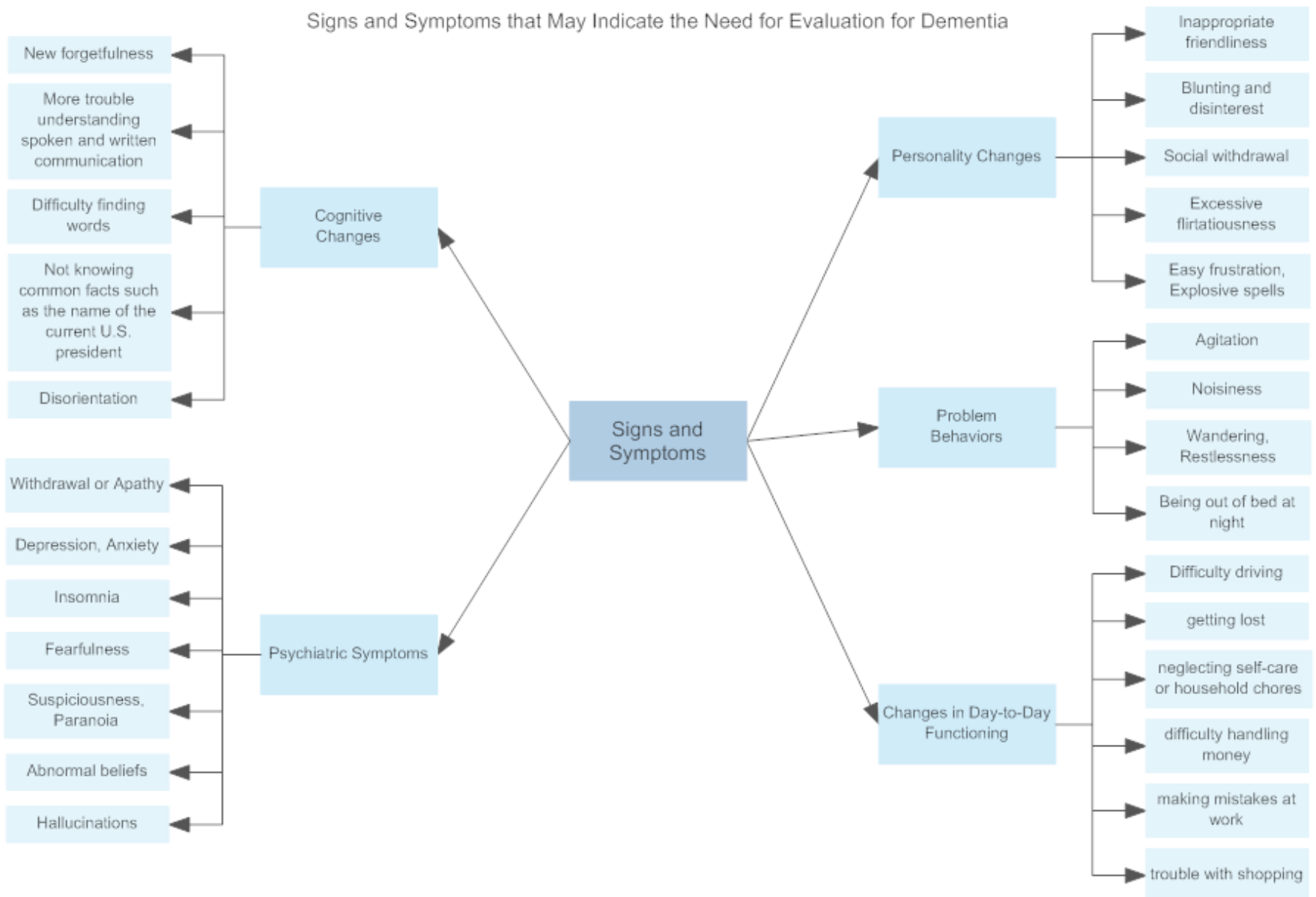
Course of Alzheimer's Disease



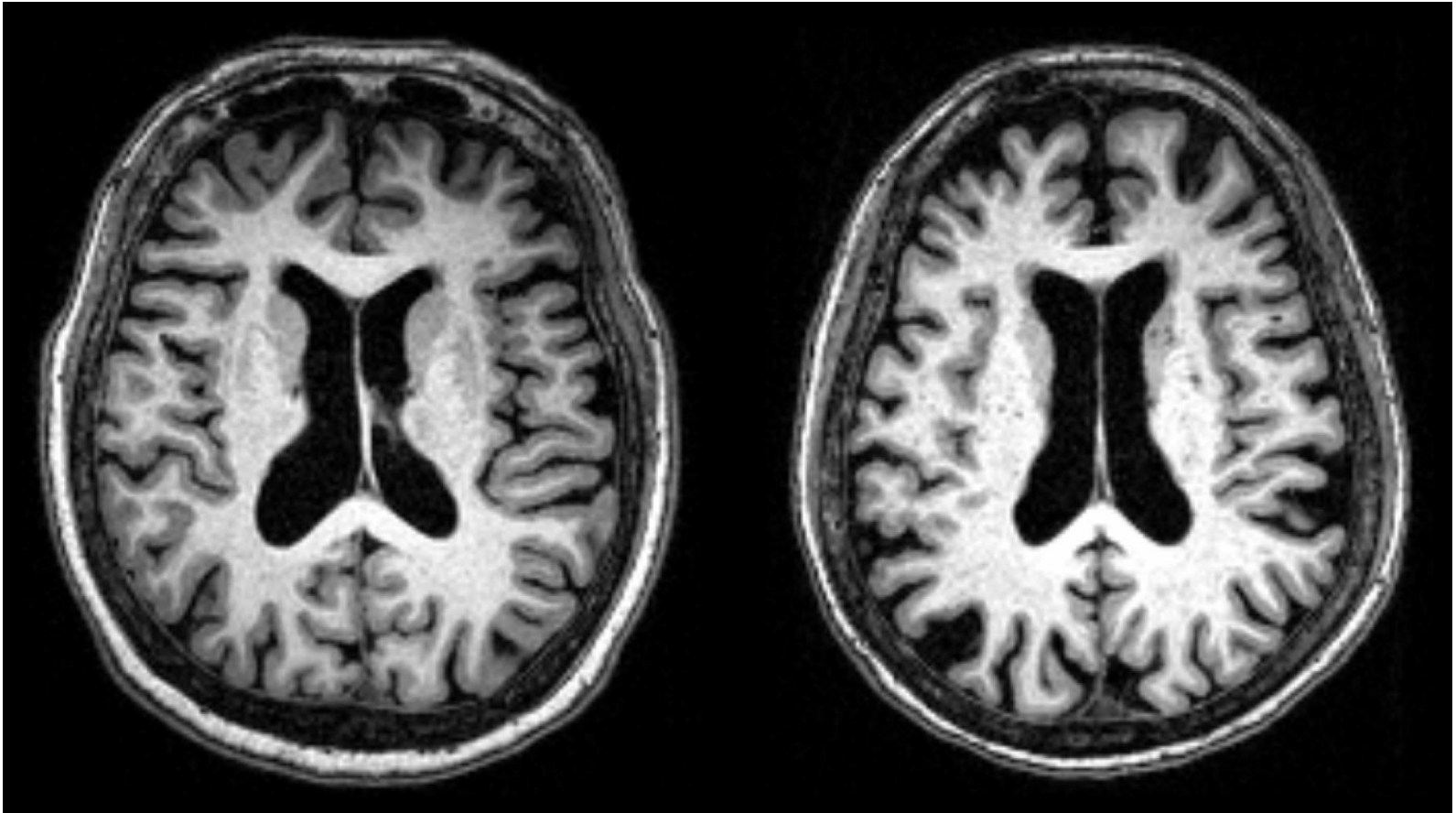
Modified from Swerdlow, Neurobiology of Aging, 2007

Early Symptoms of Dementia

Signs and Symptoms that May Indicate the Need for Evaluation for Dementia



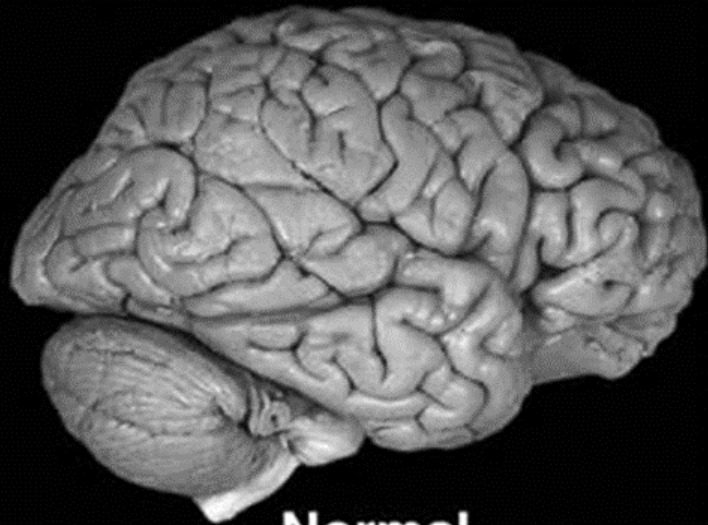
Which Brain is Demented?



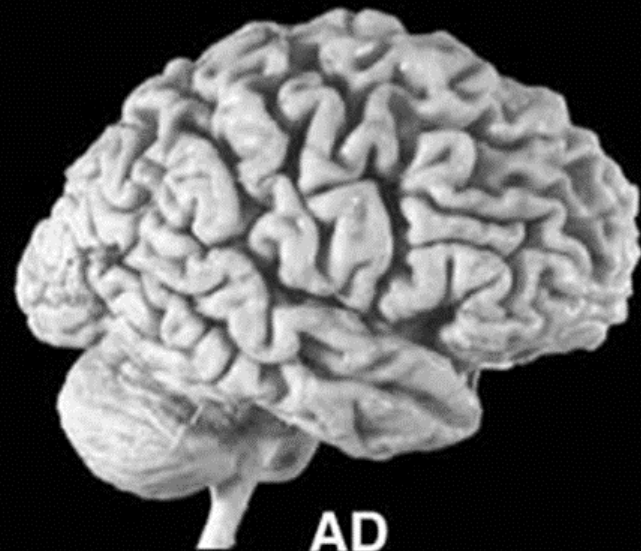
Non-demented (Age 70)

Demented (Age 70)

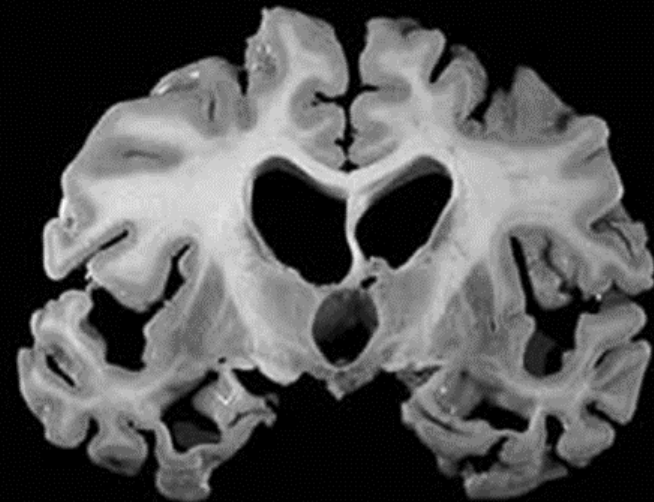
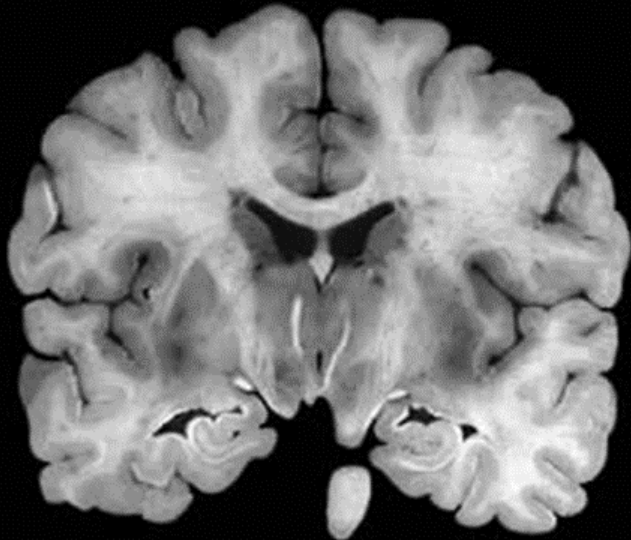
Brain Atrophy in Advanced Alzheimer's Disease



Normal



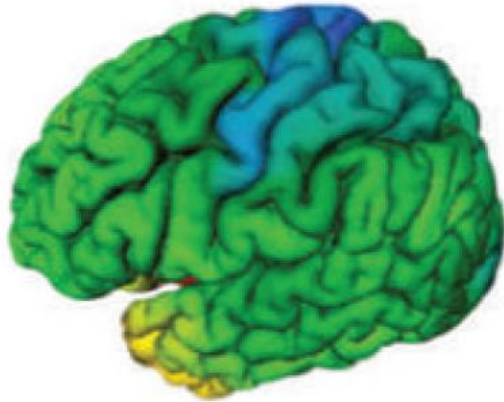
AD



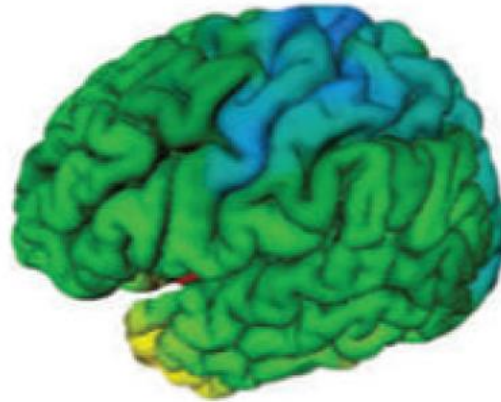
Structural Neuroimaging

Grey Matter Loss

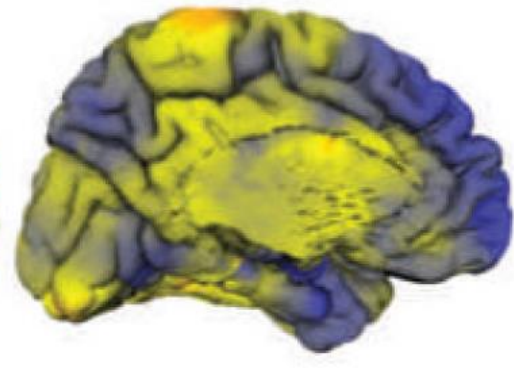
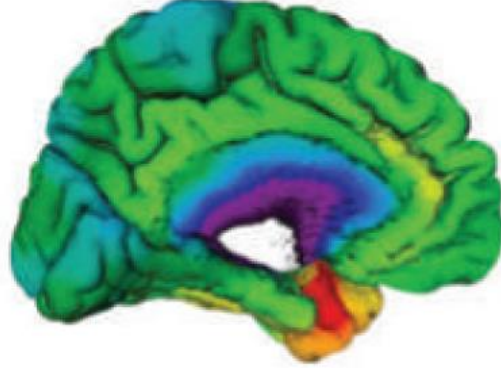
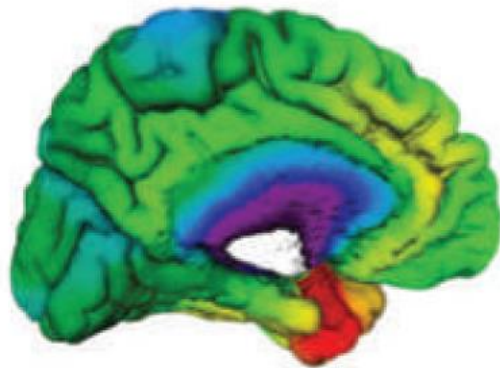
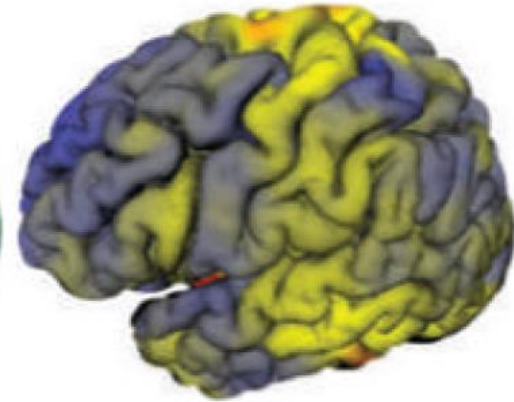
Cortical Thickness
at Month 0



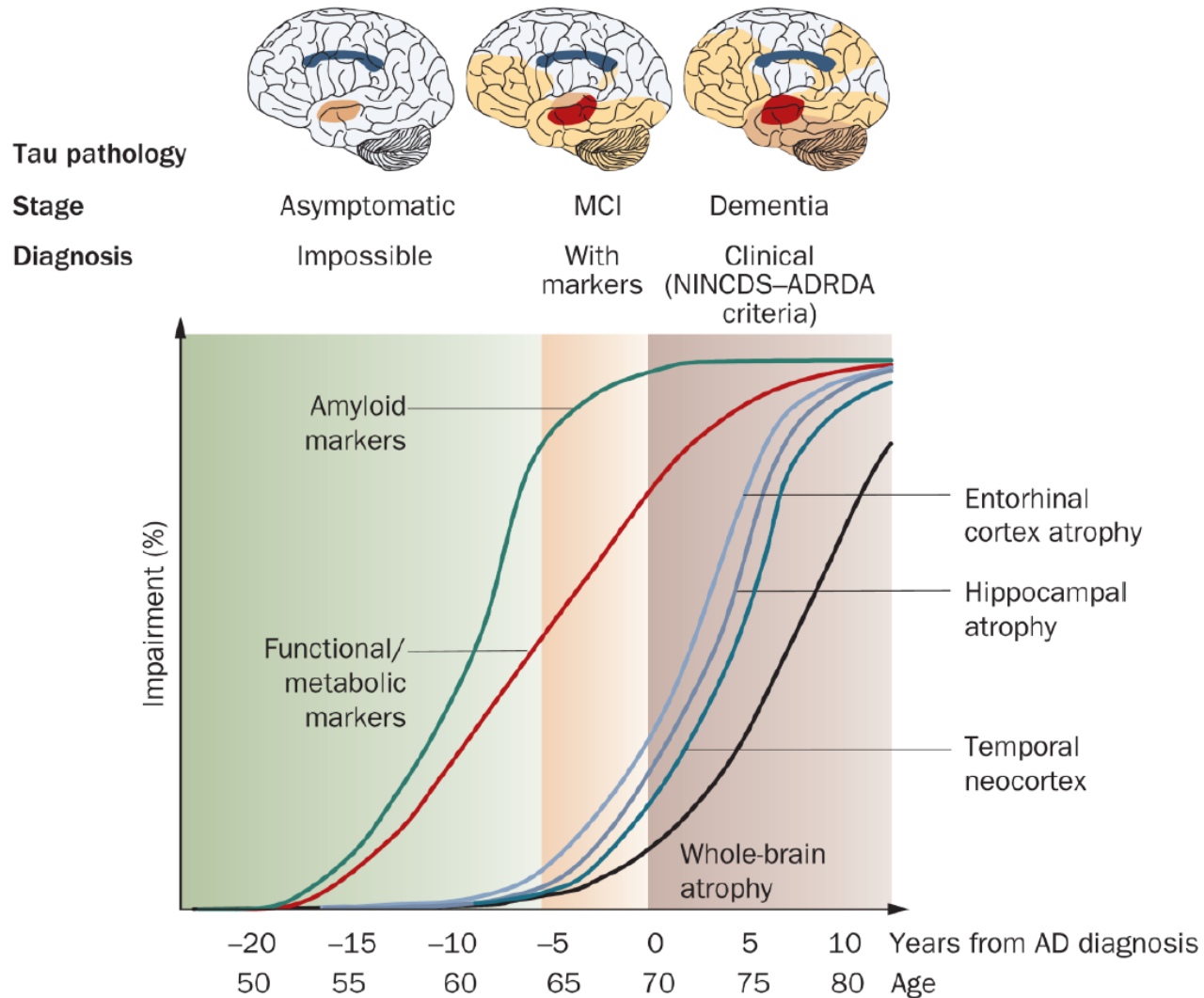
Cortical Thickness
at Month 12



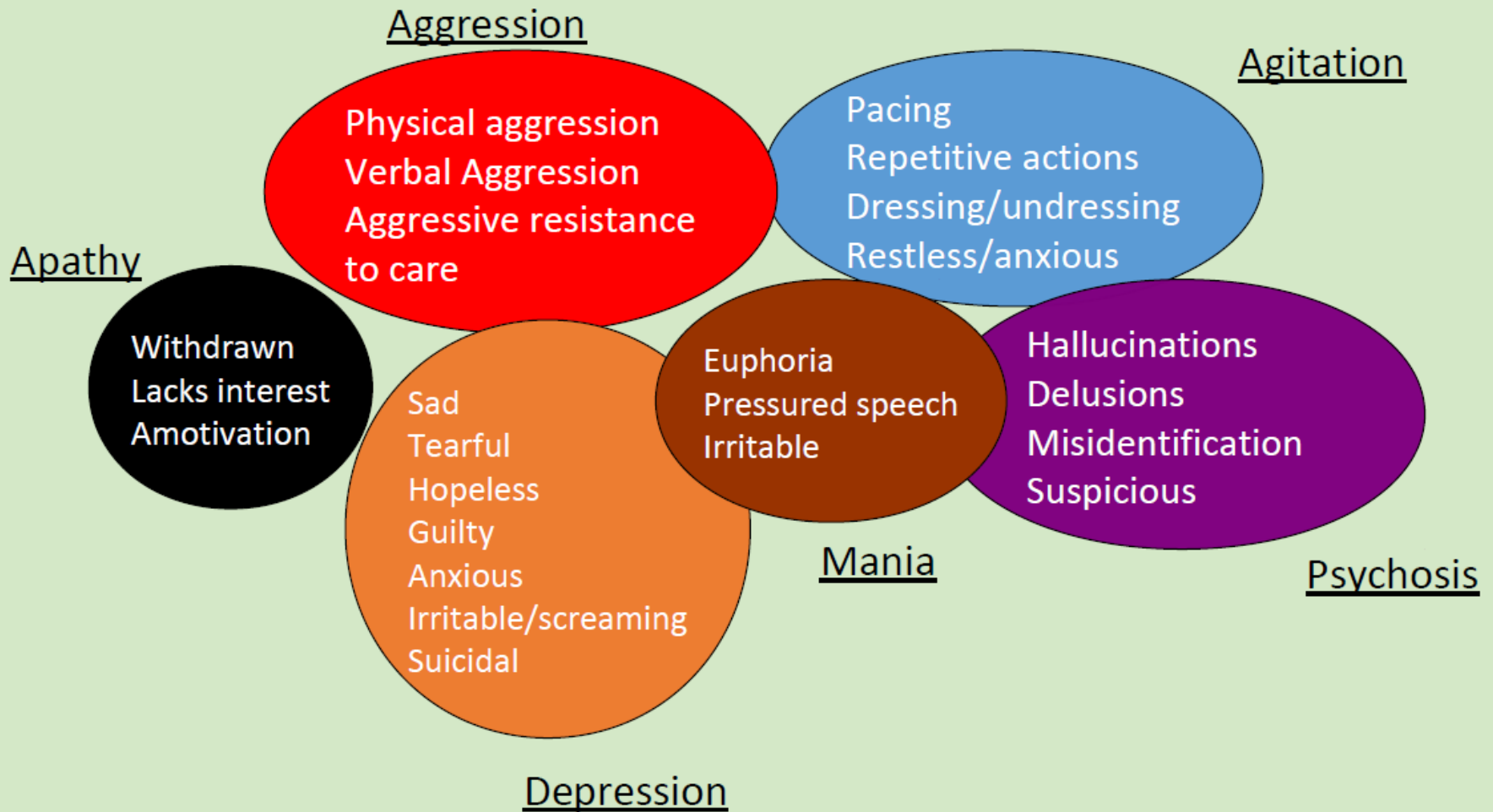
Difference Map



Functional vs. Structural Marker



Neuropsychiatric Clusters in Dementia



Behavioral and Psychiatric Symptom of Dementia

失智症精神行為症狀

近的記不住，舊的一直講
躺著睡不著，坐著打瞌睡
到處漫遊走，出門就迷路
東西一不見，直覺被偷走
問話重覆說，行為反覆做
情緒欠穩定，憂鬱最早現
當面對質問，謾罵攻擊出

Prevalence of BPSD

95% of patients affected by dementia will experience BPSD that are severe enough to be labeled as a problem during the course of their illness.

NPI BPSD Items	Point Prevalence at Baseline (%)	Five year Period Prevalence (%)
Delusions	18	60
Hallucinations	10	38
Agitation/Aggression	14	45
Depression/Dysphoria	29	77
Apathy/Indifference	20	71
Elation/Euphoria	1	6
Anxiety	14	62
Disinhibition	7	31
Irritability/Lability	20	57
Aberrant Motor Behavior	7	52
Any Symptom	56	97

Impact of BPSD

- 50 – 90% of caregivers considered physical aggression as the most serious problem they encountered and a factor leading to institutionalization.
 - (Rabins et al. 1982)
- Front-line staff working in LTC (long term care) report that physical assault contributes to significant work related stress
 - (Wimo et al. 1997)
- Agitation, depression, anxiety, paranoid ideation cause significant suffering.

Etiology of BPSD

- **Functional neuroimaging studies**: suggest that BPSD are not random consequences of diffuse brain illness, but are fundamental expressions of regional cerebral pathology.
- **Disruptions of circadian rhythms** can result in BPSD and lead to agitation during the day and restlessness at night.
 - “Sundowning syndrome.”

Untreatable BPSD

- Wandering
- Inappropriate urination/defecation
- Inappropriate dressing/undressing
- Annoying repetitive activities (perseveration) or vocalization
- Hiding/hoarding
- Eating inedibles
- Tugging at/removal of restraints
- Pushing wheelchair bound co-residents

Treatable BPSD

- Anxiety
- Depressive symptoms
- Sleep disturbance
- Manic-like symptoms
- Persistent and distressing delusions or hallucinations
- Persistent verbal and physical aggression
- Sexually inappropriate behavior

The World Alzheimer Report 2019: Attitudes to dementia

Key findings

Knowledge

- 95% of the public think they will develop dementia in their lifetime
- 78% are concerned about developing dementia at some point
- 1 in 4 people think that there is nothing you can do about dementia
- 2 out of 3 think dementia is caused by normal ageing
- 62% of healthcare practitioners think that dementia is a normal part of ageing
- 82% of people would take a genetic test to learn about their risk
- 54% of respondents think that lifestyle factors play a part in developing dementia
- Just under 40% of the general public think that there are adequate community services for people living with dementia and for carers
- Just under 70% of the general public think there are adequate competent physicians for the diagnosis and treatment of dementia

Behaviour

- Over 85% of respondents living with dementia stated that their opinion had not been taken seriously
- Around 40% of the general public think doctors and nurses ignore people with dementia
- 67% of people living with dementia in Africa, and 63% in South East Asia, said their dementia symptoms were joked about by others
- Between 35% in high income countries and 57% in low-middle income countries reported being treated unfairly in dating and intimate relationships
- Around 30% of people in Europe are willing to have a person with dementia move in with them, rising to 62% in South East Asia and 71% in the Eastern Mediterranean region



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The Global Voice on Dementia

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The World Alzheimer Report 2019: Attitudes to dementia

Attitudes

- 91% of respondents say that people should not hide the fact they have dementia and the vast majority of carers never hide the person with dementia
- However, around 20% of respondents would keep their own dementia a secret when meeting people
- Concealment of dementia varied regionally - with the general public in Europe (25.7%) and the Americas (24.5%) reporting they would keep their dementia a secret. Healthcare practitioners also reported higher levels of concealment in Europe (19%) and the Americas (17.4%)
- Respondents stating they would hide their dementia when meeting people was highest in Russia (66.7%), Poland (57.9%), and Puerto Rico (51.1%),
- 45% of people living in South-East Asia and 48% of healthcare practitioners in the region feel that people with dementia are dangerous.
- 60% of people felt it was important to remove responsibilities of people living with dementia

Carers

- Majority of carers expressed positive sentiments about their caring role
- 52% of carers said their health had suffered
- 49% of carers said their work had suffered
- 62% of carers said their social life had suffered
- Over 35% of carers globally have hidden the diagnosis of a person with dementia

Recommendations

- 1 Targeted public health awareness campaigns
- 2 Promotion of timely diagnosis and better post diagnostic support
- 3 Global evolution of dementia friends programmes and dementia friendly/inclusive communities - with people living with dementia and carers at the heart of their design, implementation and evaluation
- 4 Increased public advocacy of people living with dementia – amplifying the voice of lived experience
- 5 Increase advocacy focused on carers experiences – whilst improving the understanding of first-hand experience
- 6 Specialised education about dementia-related stigma and person-centred care practice for healthcare practitioners
- 7 Call for local governments to increase the funding, range and quality of community services for people living with dementia
- 8 Changes to public policy relating to employment, health and insurance for both people living with dementia and their carers
- 9 Full adoption of a rights-based approach to dementia including full compliance with the Convention of Rights of Persons with Disabilities (CRPD)
- 10 Increase funded research – for both a disease-modifying drug as well as further understanding of stigma. We know from other high stigma illnesses, including cancer and HIV-AIDS, that medical treatment breakthroughs can be a catalyst to stigma reduction – and we also need to better understand the complex role stigma plays throughout society in order to tackle it and change hearts and minds.

Approvals for AI-based Assessment

- **2017.01 Cantab Mobile**
memory assessment for the elderly

Cambridge Cognition (2002)

AD, ADHD, Autism, Depression, Dawn Syndrome, Huntington Disease, OCD, PD, Schizophrenia, Stroke, etc





Cantab Mobile

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Device Classification Name	Computerized Cognitive Assessment Aid
510(K) Number	K161328
FOIA Releasable 510(K)	K161328
Device Name	Cantab Mobile
Applicant	CAMBRIDGE COGNITION LTD., US AGENT: CLEMENTI ASSOCIATES LTD. TUNBRIDGE COURT, TUNBRIDGE LANE Bottisham, GB Cb25 9tu
Applicant Contact	Nancy D. Clementi
Correspondent	CLEMENTI ASSOCIATES LTD 919 CONESTOGA RD, BUILDING 3, SUITE 312 Rosemont, PA 19010
Correspondent Contact	Nancy D. Clementi
Regulation Number	882.1470
Classification Product Code	PKQ
Date Received	05/12/2016
Decision Date	01/13/2017
Decision	Substantially Equivalent (SESE)
Regulation Medical Specialty	Neurology
510k Review Panel	Neurology
Statement	Statement
Type	Traditional
Reviewed By Third Party	No
Combination Product	No

Biological Subtype of Alzheimer's Disease

