

4th International
Alzheimer's Disease
Conference



مؤتمر ألزهايمر الدولي الرابع ٢٠٢٠

Strategic Supporting Partner



2-4 Jumada II 1441 / 27-29 January 2020
Conference Hall – KACST HQ
Riyadh, Saudi Arabia

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Alzheimer's Stages: How the Disease progresses ?

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Objectives:

- **Benefits for staging.**
- **the disease progression.**
- **Different staging scales.**

Benefits for staging





Stages of Dementia

Knowing the stage can help inform plans for treatment.

TABLE 1
Cognitive enhancers approved for Alzheimer disease

Drug	Proprietary name (date approved)	Indications	Formulations
Cholinesterase inhibitors			
Donepezil	Aricept (1996), generics available	Mild to moderate disease (5–10 mg), moderate to severe disease (10–23 mg)	Tablets, disintegrating tablets
Rivastigmine	Exelon (2000), generics available	Mild to moderate disease	Tablets, oral solution, transdermal patch
Galantamine	Razadyne (2001), generics available	Mild to moderate disease	Immediate-release tablets, oral solution, extended-release tablets
N-methyl-D-aspartate receptor antagonist			
Memantine	Namenda (2003), generics available	Moderate to severe disease	Tablets, oral solution
Combination drug			
Donepezil + memantine	Namzaric (2014), generics available	Moderate to severe disease	Extended-release capsules



Stages of Dementia

Knowing the stage can help inform plans for care.

CAREPLANNING

1 2 3



Stages of Dementia

- To define the Goal of Care.



Fig :Model of changing care goals and priorities throughout the course of dementia (European Association of Palliative Care, 2015)



Stages of Dementia

An understanding of the disease stages and what to expect along the way should provide some clarity to help family members and caregivers navigate through this difficult journey.





How Fast Does Dementia Progress?

Dementia moves at different speeds for everyone. While some stages may take years for some patients, others may go through the stage months to develop to the next stage.



How does the disease progress?

- There is no uniform disease **trajectory**...
- **different individuals will have unique experiences in each stage.**
- The symptoms in each stage can vary from person to person and stages can also overlap considerably which makes it difficult to place a person with Alzheimer's in a specific stage.



How does the disease progress?

- Men having a relatively shorter life expectancy than women.
- An older age of onset of AD (>80 years) may be associated with a slower rate of decline compared with younger patients.
- early neuropsychiatric symptoms including psychosis, agitation, and aggression have been associated with more rapid decline.



How does the disease progress?

- The average life expectancy after a diagnosis of AD has been reported to be between 8 and 10 years but may range from

3 to 20 years.

- it depends heavily on how impaired the person is at the time of diagnosis.



How does the disease progress?

- It is a terminal disease ...
- The two most common causes of death were pneumonia (38.4%) and ischemic heart disease (23.1%).

Cause of death in patients with dementia disorders.H. R. Brunnström E. M. Englund
: 19 March 2009, European Journal of Neurology

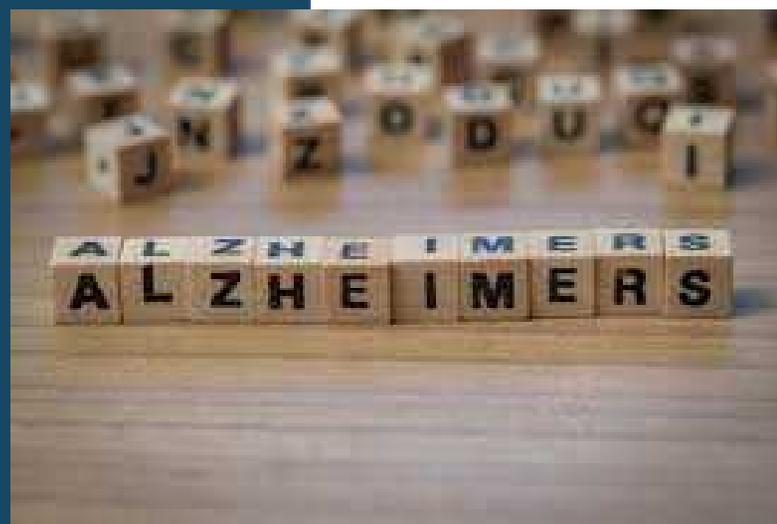
Alzheimer's **Stages**





Stages of Dementia

**Cognitive Decline
and
Functional Decline**





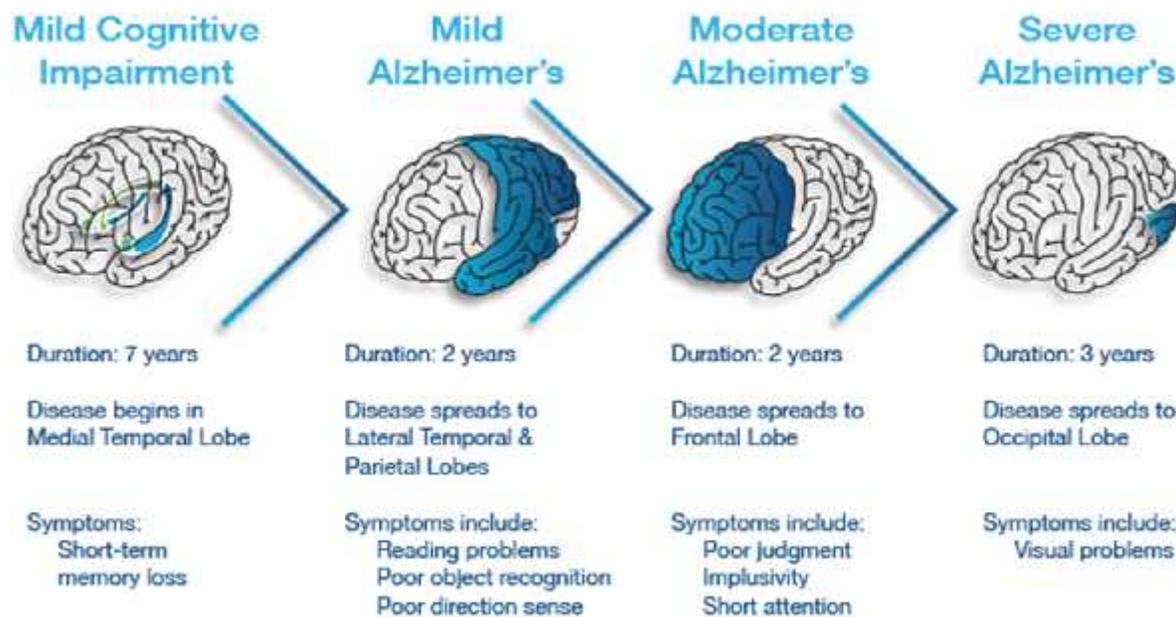
Stages of Dementia

- **3-stage scale.**
- **Global Deterioration Scale / Reisberg Scale(GDS).**
- **Functional Assessment Staging Test (FAST).**
- **Clinical Dementia Rating (CDR).**



3 stages:

- **Mild (early-stage)**
- **Moderate (middle-stage)**
- **Severe (late-stage)**





Mild Dementia (early)

- an individual can still function rather independently.
- Other difficulties may include issues with planning, organizing, concentrating on tasks, or accomplishing parts of employment, if the individual is still in the workforce.
- This early stage on average, lasts between 2 and 4 years.



Moderate Dementia

- **In most cases is the longest stage of the disease.**
- **brain damage is extensive enough that a person has mood and behavior changes, such as aggressiveness, difficulty sleeping, depression, paranoia, repeating actions and / or words, hoarding, anger, wandering, incontinence, and frustration may be seen.**
- **This moderate stage of dementia, on average, lasts between 2 and 10 years.**



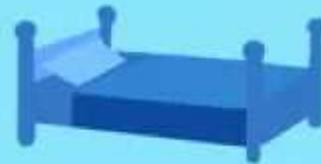
Severe dementia (Advanced)

- **According to the Alzheimer's Association (2018), for individuals with dementia, approximately 40% of their time is spent in this last stage of dementia.**
- **will require extensive assistance with daily living activities, such as personal hygiene and eating.**
- **At the very end of this stage, the individual will most likely be bedridden.**
- **This severe stage of dementia lasts approximately 1 to 3 years.**

What to Expect in Late-Stage Dementia



Loss of facial expression



Bedbound, requires
around-the-clock care



Unable to speak



Problems with everyday
activities like bathing,
dressing, eating



Unable to walk or sit up
without assistance



Global Deterioration Scale / Reisberg Scale

- divides the disease into seven stages based on the amount of cognitive decline:
 - stages 1-3 do not typically exhibit enough symptoms for a dementia diagnosis.
 - Stage 4 is considered “early dementia,” usually at the time a diagnosis has been made.
 - stages 5 and 6 are considered “middle dementia”.
 - stage 7 is considered “late dementia”.
-
- Reisberg, B., Ferris, S. H., de Leon, M. J., and Crook, T. (1982). Modified from Global Deterioration Scale. American Journal of Psychiatry, 139:1136–1139.



Global Deterioration Scale / Reisberg Scale

This model consists of the following 7 stages:

Stage	Deficit in cognition and function	Usual Care
Stage 1	No Impairment – No memory loss	Independent
Stage 2	Very Mild Cognitive Decline – Normal memory loss associated with aging	Independent
Stage 3	Mild Cognitive Decline – Friends and family members begin to notice cognitive problems	Independent
Stage 4	Moderate Cognitive Decline – Neurologists can confidently diagnose Alzheimer's; poor short-term memory, may forget personal details, difficulty with simple arithmetic	Dependent \slightly
Stage 5	Moderately Severe Cognitive Decline – Begins to need help with daily activities, significant confusion, disorientation, may no longer be possible to live alone	Dependent
Stage 6	Severe Cognitive Decline – Worsened memory loss, difficulty recognizing family members, some personality changes	Dependent
Stage 7	Very Severe Cognitive Decline – Final stage; communication is limited, physical systems also decline	Dependent

TABLE 2

Alzheimer disease: Severity, associated symptoms, and recommended treatment

Dementia category	Global Deterioration Scale (stages 1–7)	Medications
Not demented	<p>1 No cognitive impairment</p> <p>2 Very mild decline: age-associated cognitive impairment</p> <p>3 Mild cognitive impairment, minor neurocognitive decline</p>	No indication for cognitive enhancers
Mild dementia	<p>4 Decreased knowledge of current and recent events</p> <p>Decreased ability to travel, handle finances, and manage basic activities of daily living</p>	Cholinesterase inhibitors
Moderate dementia	<p>5 Unable to recall a major relevant aspect of their current life, an address or telephone number of many years, or the names of close family members</p> <p>Basic activities of daily living begin to be impaired</p>	Cholinesterase inhibitors with or without an NMDA receptor antagonist
Severe dementia	<p>6 Occasionally forgets the name of the spouse or caregiver on whom he or she is entirely dependent</p> <p>Unaware of all recent events and experiences in their lives</p> <p>Most basic activities of daily living impaired</p>	Cholinesterase inhibitor (donepezil) with or without an NMDA receptor antagonist
Advanced dementia	<p>7 Cannot speak or walk, has incontinence and difficulty swallowing</p>	No randomized controlled trials in stage 7

NMDA = *N*-methyl-D-aspartate

Based on information in references 11 and 12.



Functional Assessment Staging Test (FAST)

- **FAST also employs a seven-stage system based on one's level of functioning and ability to perform daily living activities.**
- **A person may be at a different stage cognitively (GDS stage) than functionally (FAST stage).**



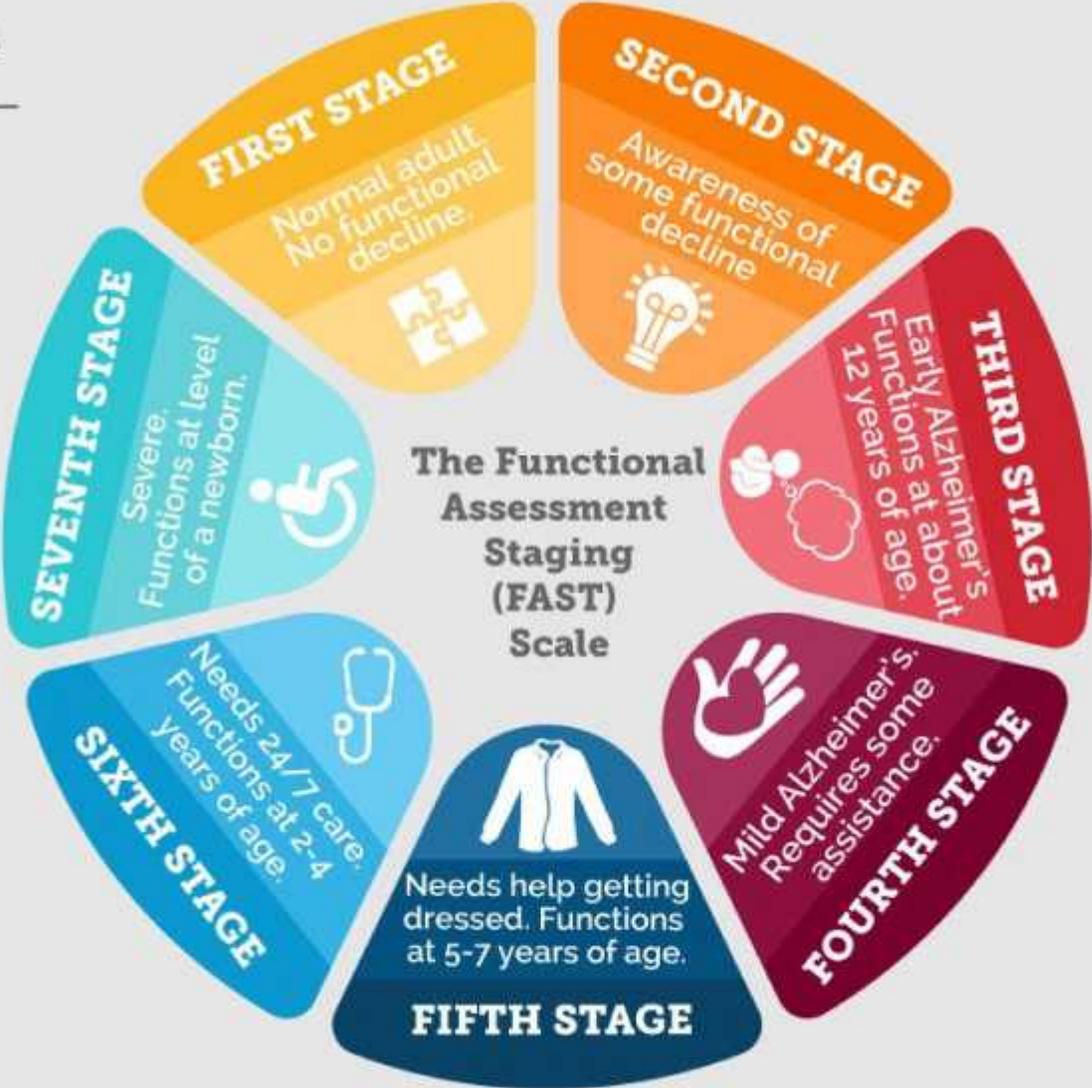
Functional Assessment Staging Test (FAST)

Stage	Patient Condition	Level of Functional Decline	Expected Duration of Stage
Stage 1	Normal adult	No functional decline.	N/A
Stage 2	Normal older adult	Personal awareness of some functional decline.	Unknown
Stage 3	Early Alzheimer's disease	Noticeable deficits in demanding job situations.	Average duration of this stage is 7 years.
Stage 4	Mild Alzheimer's	Requires assistance in complicated tasks such as handling finances, traveling, planning parties, etc.	Average duration of this stage is 2 years.
Stage 5	Moderate Alzheimer's	Requires assistance in choosing proper clothing.	Average duration of this stage is 1.5 years.
Stage 6	Moderately severe Alzheimer's	Requires assistance with dressing, bathing, and toileting. Experiences urinary and fecal incontinence.	Average duration of this stage is 3.5 months to 9.5 months.
Stage 7	Severe Alzheimer's	Speech ability declines to about a half-dozen intelligible words. Progressive loss of ability to walk, to sit up, to smile, and to hold head up.	Average duration of this stage is 1 year to 1.5 years.

The Stages of Alzheimer's Disease

To better understand how Alzheimer's disease affects the Hypothalamus and other regions of the brain, it's helpful to first have an understanding of the seven primary stages of this progressive disease.

The FAST scale was developed at the New York University Medical Center's Aging and Dementia Research Center.





Clinical Dementia Rating (CDR)

- **The Clinical Dementia Rating (CDR) scale uses a five-point system .**
- **Based on cognitive abilities and the individual's ability to function.**
- **This is the most widely used staging system in dementia research.**



Clinical Dementia Rating (CDR)

- **six areas: Memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care.**
- **Based on semi-structured interviews with the potential dementia patient and others, such as a family member.**

The CDR scoring table and rules were published in the journal NEUROLOGY, 1993; 43:2412-2414 (author Morris, JC).

Table 1 - Classification of the categories evaluated by the Clinical Dementia Rating.

Impairment level	None (0)	Questionable (0.5)	Mild (1)	Moderate (2)	Severe (3)
Memory	No memory loss or slight inconsistent forgetfulness	Consistent forgetfulness, partial recollection of events.	Moderate memory loss; more marked for recent events; defect interferes with daily activities.	Severe memory loss; only highly learned material retained.	Severe memory loss; only fragments remain.
Orientation	Fully oriented.	Fully oriented except with slight difficulties with time relationships.	Moderate difficulty with time relationships, oriented in familiar areas.	Severe difficulty with time relationships, almost always disoriented to place.	Oriented to person only.
Judgement & Problem Solving	Solves everyday problems, such as financial affairs; judgement preserved.	Slight difficulty in solving problems, similarities and differences.	Moderate difficulty on handling problems, similarities and differences, social judgement maintained.	Severely impaired in handling problems, similarities and differences; social judgment impaired.	Unable to make judgements or solve problems.
Community Affairs	Independent function in job, shopping, social groups.	Slight impairment in these activities.	Is not independent in these activities, appears normal to casual inspection.	Is not independent outside home, appears well enough to be taken to events outside the home.	Is not independent outside the home, appears to be too ill to be taken to events outside the home.
Home and Hobbies	Daily life at home, hobbies and intellectual interests well maintained.	Daily life at home, hobbies and intellectual interests slightly impaired.	Slight impairment of tasks at home, more difficult chores, hobbies and interests are abandoned.	Only simple chores are maintained, restricted interests, poorly maintained.	No significant function at home.
Personal Care	Fully capable of self-care.	Fully capable of self-care.	Needs assistance.	Requires assistance in dressing and hygiene.	Requires much help with personal care; frequent incontinence.



Stages of Dementia

- **Cognitive tools.(MMSE)**
- **Brain imaging.(CT, functional MRI, PET)**
- **Biomarkers.**



Cognitive testing:

the Mini-Mental State Examination (MMSE),
a number of studies have found that patients decline 3 to 3.5 points on average on the MMSE each year

	Area of Functional Impairment			
MMSE Scores	30-25 maybe	24-21	21-10	9-0
Stage	Normal	mild/early	moderate	severe
ADI		problems with driving, finances, shopping	assistance with dressing, grooming, toileting	Problems with eating, walking
Communication		word-finding, repeating, goes off topic, loses track	sentence fragments, "empty" speech, vague terms (i.e. this, that)	speech disturbances (i.e. during, stuttering)
Memory	subjective problems with names or misplacing objects	three item recall, orientation (time then place)	WORD spelling, language and 3 step command	all areas show obvious deficits
	Years	2-4 years	2-3 year	2-3 years

These are general guidelines to the progression of the disease. There is much individual variability.

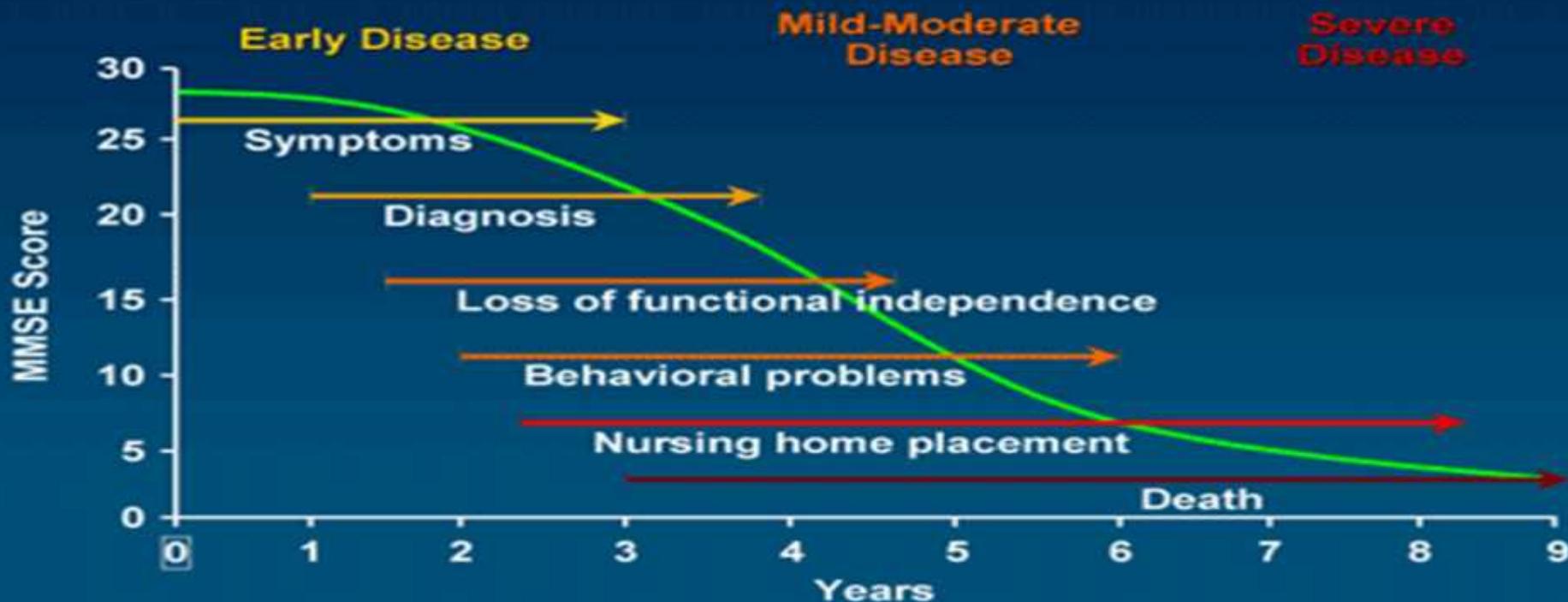


How does the disease progress?

Medscape®

www.medscape.com

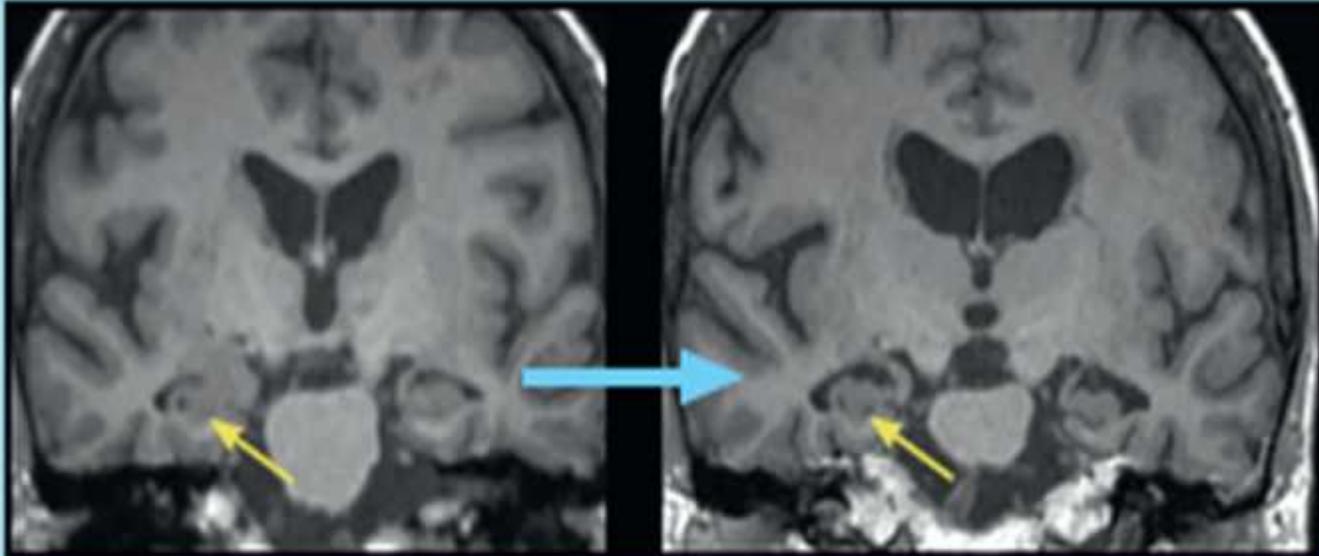
Alzheimer's Disease: Natural History



Adapted from Feldman H, Gracon S. Alzheimer's disease: symptomatic drugs under development. In: Gauthier S (ed). Clinical Diagnosis and Management of Alzheimer's Disease. Martin Dunitz: London, 1996:239_259.



Brain Imaging :



Serial coronal MRI scans (T1) demonstrating five-month progression in bilateral hippocampal atrophy characteristic of early Alzheimer's disease. Right hippocampus highlighted.

Case courtesy of Dr Bruno Di Muzio, Radiopaedia.org, rID: 37720

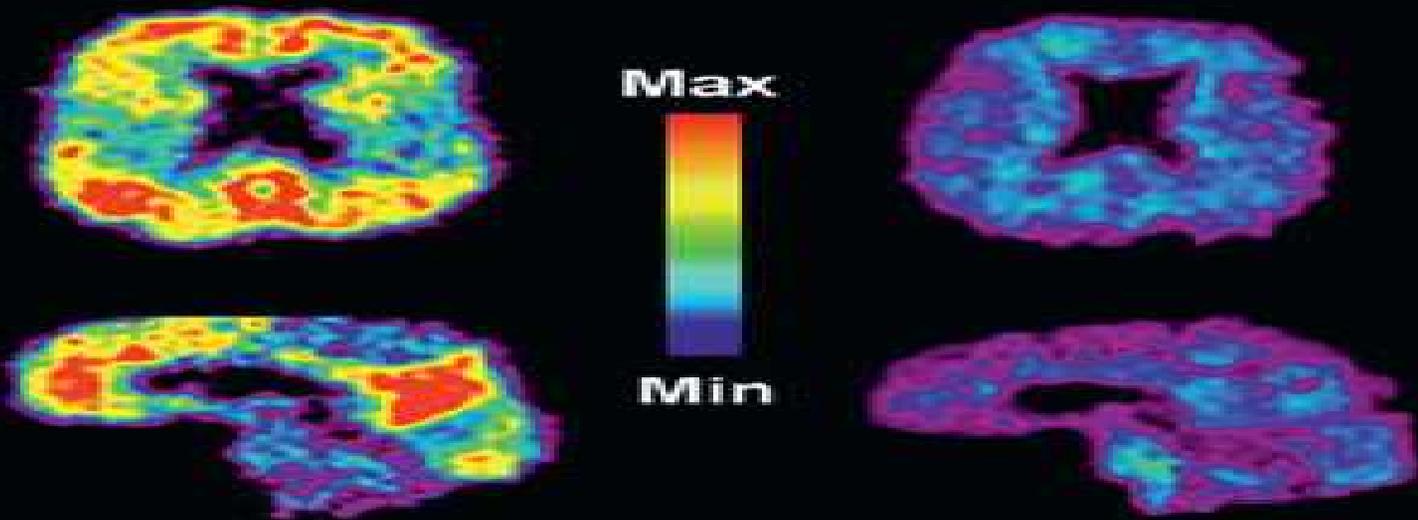


Coronal CT demonstrating more advanced hippocampal atrophy and ventricular enlargement as a result of later stage Alzheimer's disease. Note the grainier image quality.

Case courtesy of Dr Frank Gaillard, Radiopaedia.org, rID: 33753

AD

Control



PiB PET SCANS



University of Pittsburgh
PET Amyloid Imaging Group

Axial and sagittal PET brain images demonstrating difference in amyloid content of cerebral tissue between a patient with Alzheimer's disease (AD) and control.
From http://commons.wikimedia.org/wiki/File:PiB_PET_Images_AD.jpg by KLUNKWE.

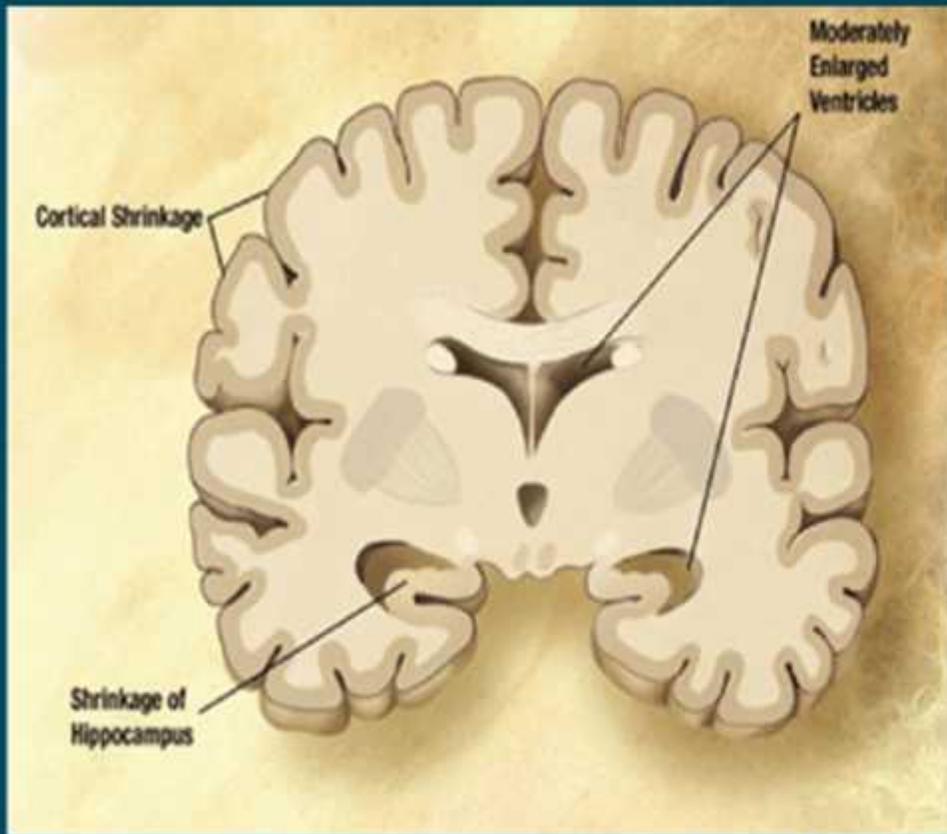


Figure 3: Physiological Structure of the Brain of a Person Diagnosed with Mild Alzheimer's Disease⁶ Image Courtesy NIH

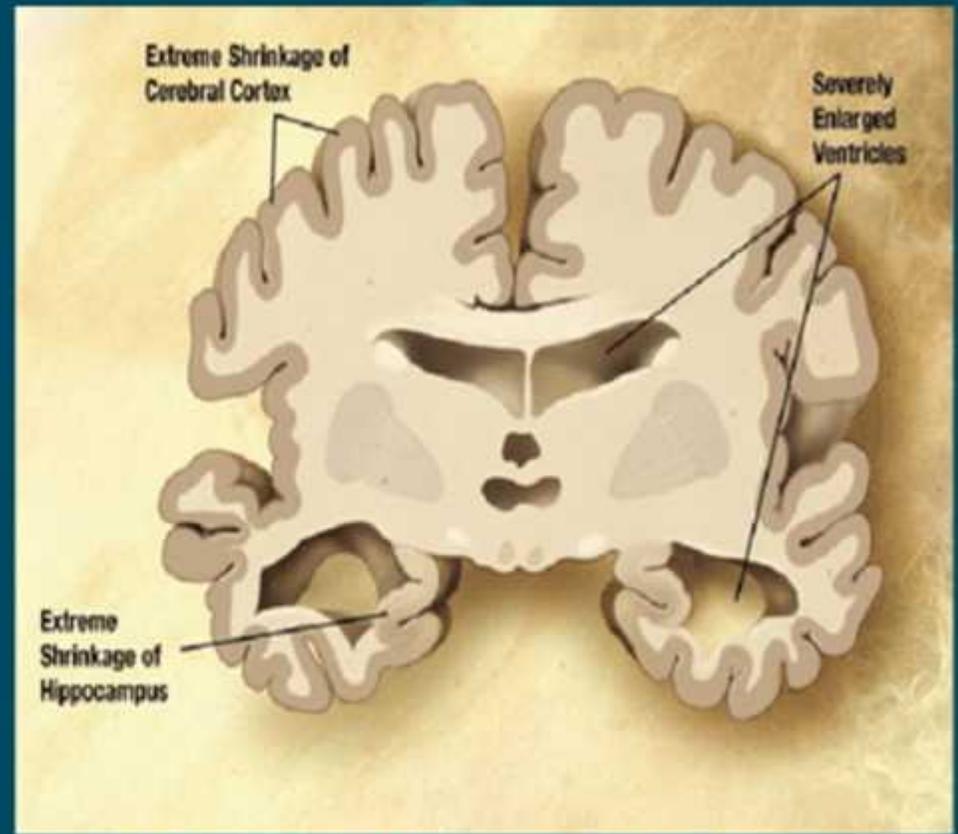
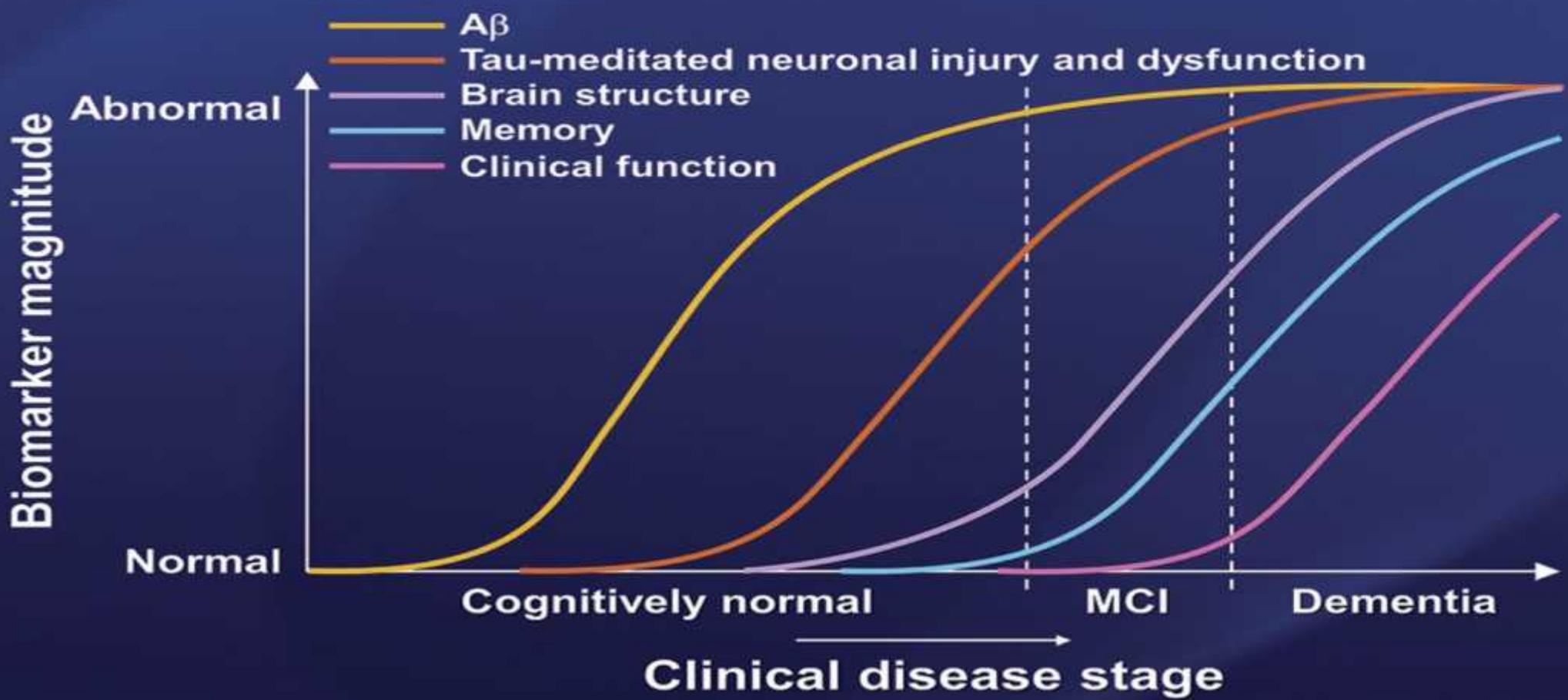


Figure 4: Physiological Structure of the Brain of a Person Diagnosed with Severe Alzheimer's Disease⁶ Image Courtesy NIH

Hypothetical Model of Dynamic Biomarkers of the Alzheimer's Pathological Cascade



Thank you

