

Alzheimer Disease Assessment for Adults with Intellectual Disability

Geunyeong Pyo, Ph.D.
Illinois Department of Human Services
Division of Developmental Disabilities

Dr. Alois Alzheimer (1864 – 1915)



History of Alzheimer's Disease

- In 1901, Alois Alzheimer began studying a 51-year-old woman names Auguste who had symptoms of profound memory loss, confusion and irritability.
- In 1906, he published “a peculiar disease” of the case of Augueste. He did autopsy of her brain and described dramatic shrinkage and abnormal deposits in and around nerve cells.
- in 1910, Emil Kraepelin, a German psychiatrist, names “Alzheimer's Disease” in the 8th edition of his book Psychiatrie.
- In 1976, Robert Katzman, a neurologist, brought the disease to the public's eye. He was the first to circulate the idea that Alzheimer's Disease is not a normal part of aging.

Neurocognitive disorder (DSM-V)

- The primary clinical deficits is in cognitive function (vs. cognitive deficits due to mental illness).
- Impaired cognition has not been present since birth or very early life; it represents a decline from a previously attained level of functioning (vs. neurodevelopmental disorders)
- Some NCD conditions affect younger individuals (e.g., TBI, HIV)
- Some NCD conditions affect a single domain of cognitive functioning (e.g., stroke).
- Dementia usually affect older adults and cause a broader range of cognitive functioning

Causes of NCD

➤ Degenerative Disorders

Alzheimer's Disease, Diffuse Lewy Body Disease, Lewy Body Variant of Alzheimer's disease, Frontal lobe dementia, Frontal-Temporal dementia, ALS, Pick's disease, Creutzfeld-Jakob disease, Primary Progressive Aphasia, Parkinson's Disease, Huntington's Disease

➤ Vascular Diseases

Stroke, multi-infarct dementia, heart disease producing emboli or reduced perfusion, Binswanger's disease, subarachnoid hemorrhage, chronic subdural hematoma, small vessel disease

➤ Toxic or Metabolic disease

Alcoholism, Vit-B12 deficiency, folate deficiency

Causes of NCD

- **Immunologic disease or infection**
Multiple sclerosis, chronic fatigue syndrome, immunoglobulin deficiencies, infections, AIDS, meningitis, chronic encephalitis, neurosyphilis
- **Systemic diseases**
Liver disease, kidney disease, lung disease, diabetes, Wilson's disease
- **Trauma:** head trauma, Dementia Pugilistica—boxer's syndrome
- **Cancer:** brain tumors, metastatic tumors
- **Ventricular disorders:** normal pressure hydrocephalus, obstructive hydrocephalus, non-obstructive hydrocephalus
- **Convulsive disorders**
- **White matter diseases:** leukodystrophies

NCD due to degenerative disorders

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

Diagnostic criteria of Neurocognitive Disorder due to Alzheimer Disease (DSM-V)

- Clear evidence of decline in memory and learning and at least one other cognitive domain (based on detailed history or serial neuropsychological testing).
- Steadily progressive, gradual decline in cognition, without extended plateaus.
- No evidence of mixed etiology (i.e. absence of other neurodegenerative or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline).
- Probable AD/possible AD: probable if there is evidence of a causative AD genetic mutation from either genetic testing or family history

NCD due to degenerative disorders

Mixed dementia

- Characterized by the hallmark abnormalities of more than one cause of dementia—most commonly AD combined with vascular dementia, followed by AD combined with DLB, and AD with vascular dementia and DLB.
- Recent studies suggest that mixed dementia is more common than previously thought, with about half of older people with dementia have more than one cause of dementia.
- The likelihood of having mixed dementia increases with age and is highest in the people age 85 or older.

Diagnostic criteria of Alzheimer Disease for individuals with ID

Currently, there is no consensus within the ID field regarding methods to assess dementia or objective criteria for diagnosis (Krinsky-McHale & Silverman, 2013).

Epidemiology of AD

(Alzheimer Facts and Figures, 2016)

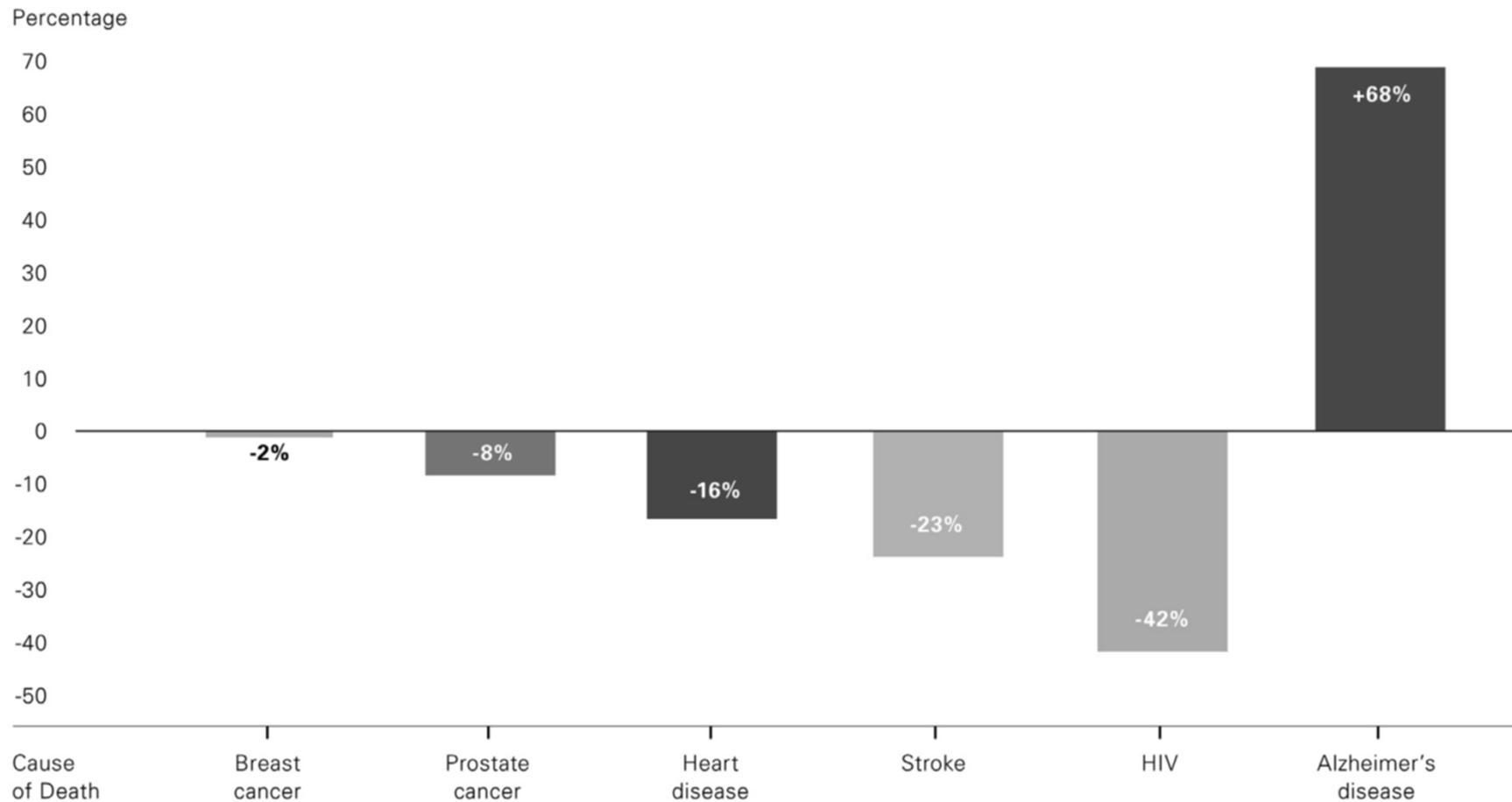
- 5.4 million Americans of all ages have AD.
- 5.2 million people with AD are age 65 years or older.
- About 200,000 individuals with AD are younger than 65.
- Because AD is underdiagnosed and underreported, a large portion of Americans with AD may not know they have it.

Mortality

(Alzheimer Facts and Figures, 2016)

- The 6th leading cause of death in the US.
- The 5th leading cause of death for people age 65 or older.
- While other major causes of death have decreased, Alzheimer deaths have increased
- AD is the only disease among the top 10 causes of death in US that cannot be prevented, cured or even slowed.

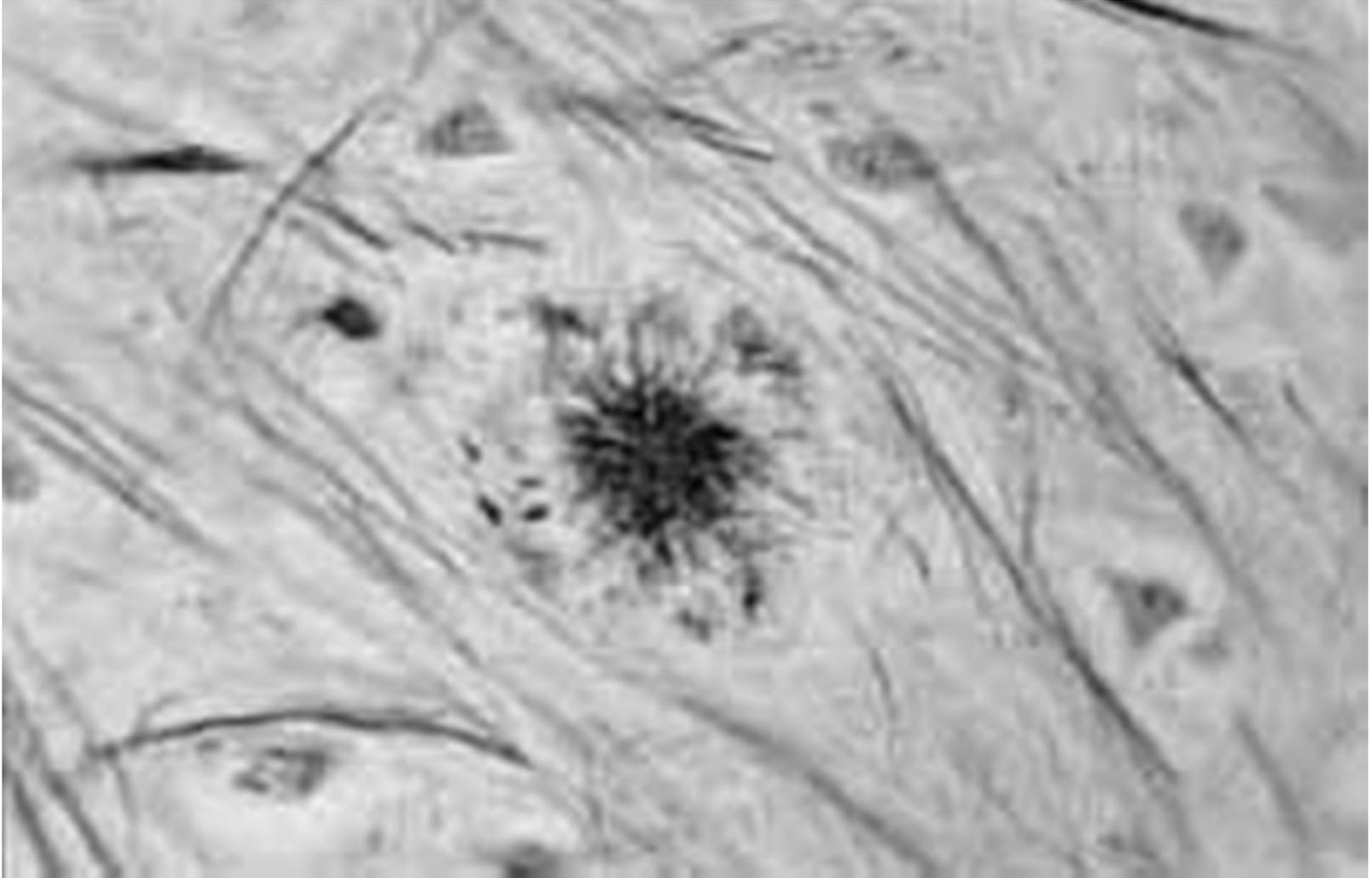
Percentage changes in causes of death (all ages) between 2000-2010



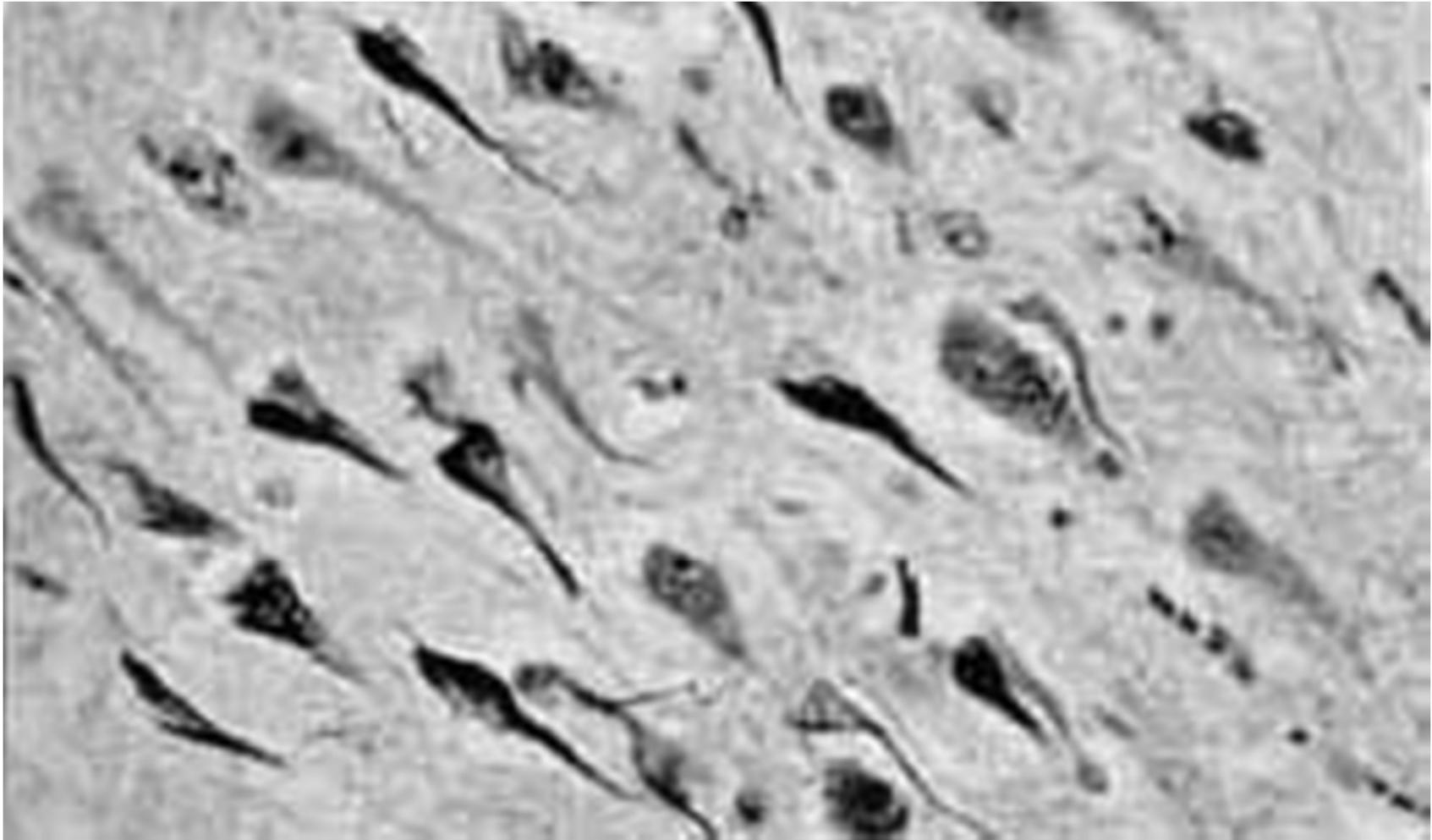
Changes in the AD brain

- A healthy adult brain has about 100 billion neurons with 100 trillion synapses.
- The brain changes of AD may begin 20 or more years before symptoms appear.
- In AD, the accumulation of β -amyloid is believed to interfere with the neuron-to-neuron communication at synapses and to contribute to cell death.
- Tau tangles block the transport of nutrients and other essential molecules in the neuron and to contribute to cell death.

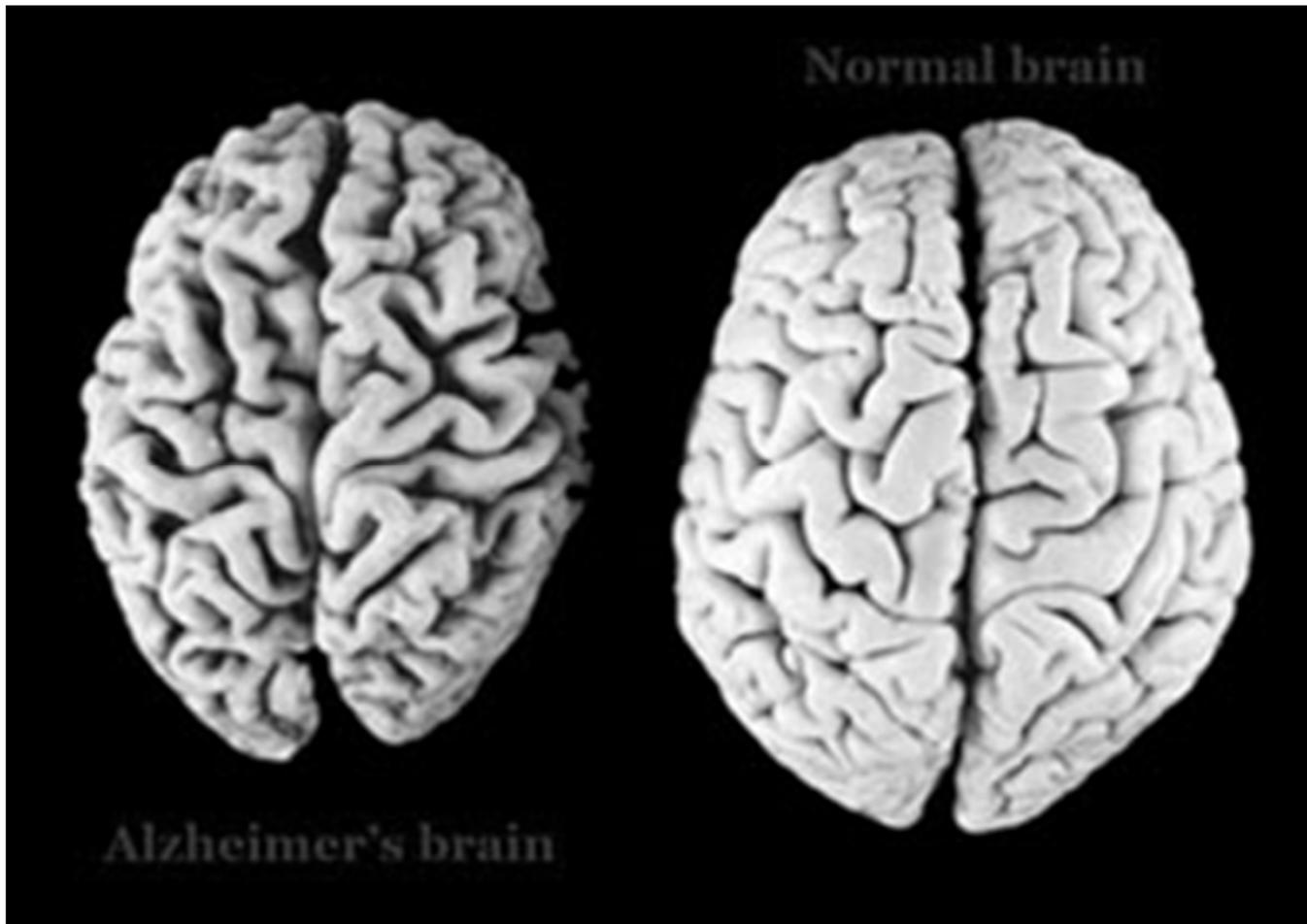
Senile Plaque



Neurofibrillary Tangles

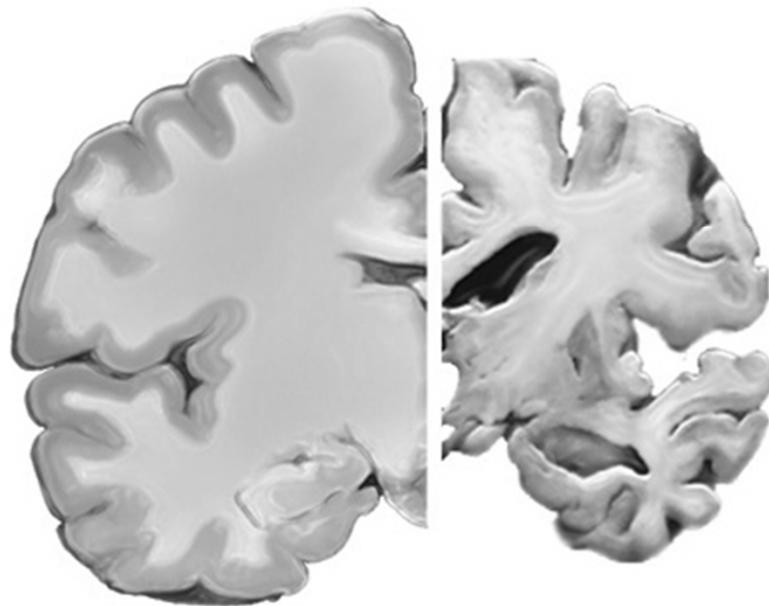


1,100-1,400g → below 1,000g

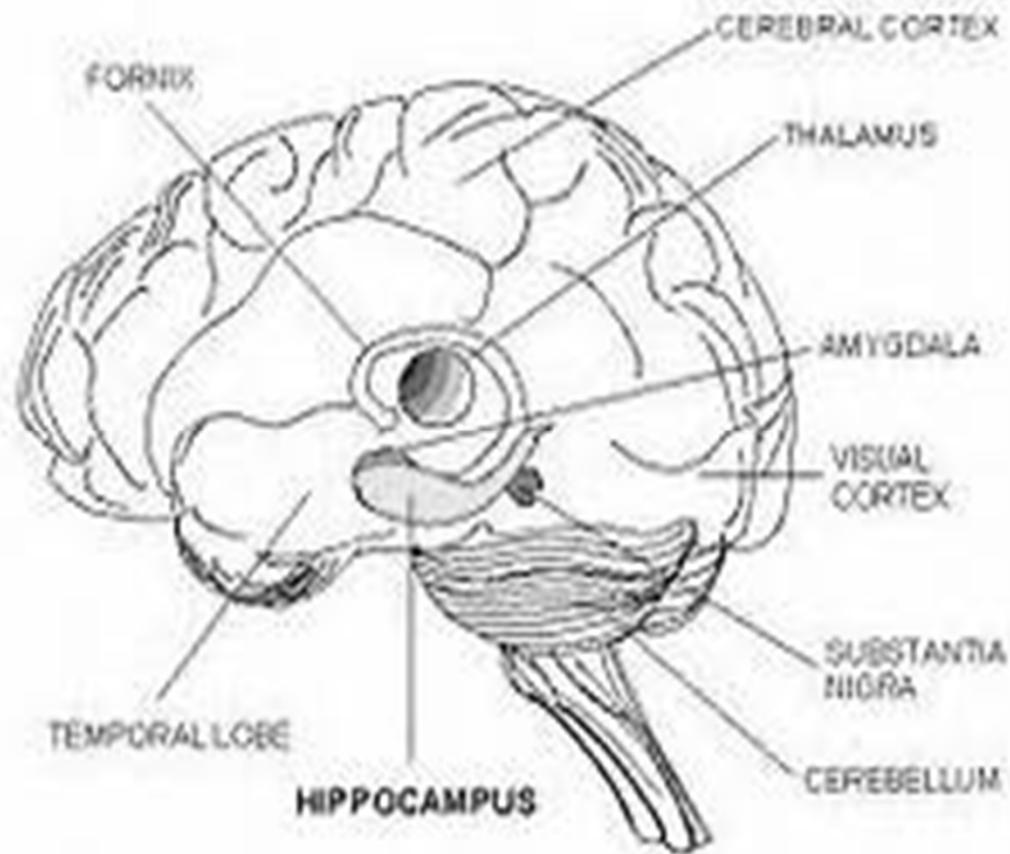


Healthy
Brain

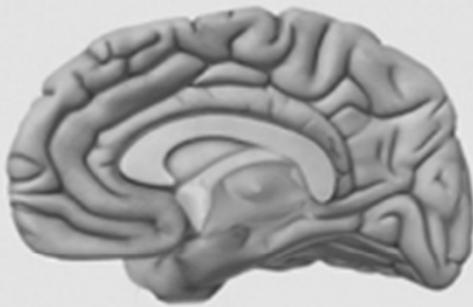
Severe
Alzheimer's



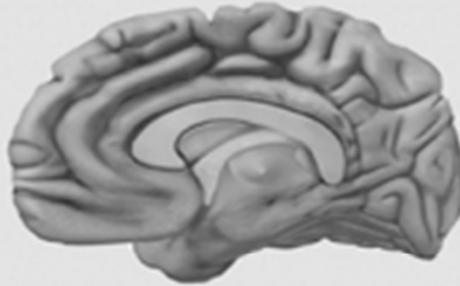
Hippocampus



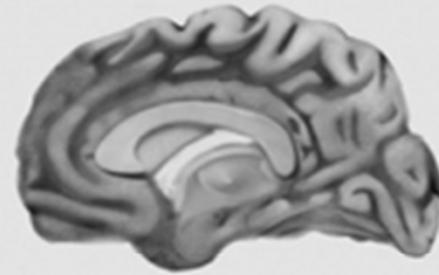
Progression of AD



Preclinical
Alzheimer's Disease



Mild to moderate
Alzheimer's Disease



Severe
Alzheimer's Disease

Stages of AD

- Preclinical AD (research purpose)
- Mild cognitive impairment
- Early stage of AD
- Middle stage of AD
- Late stage of AD

Preclinical AD

- Proposed as a “potential” stage of AD in 2011
- Individuals may have measurable changes in the brain, CSF and/or biomarkers that indicate the earliest signs of AD.
- No noticeable symptoms such as memory loss
- This proposal reflects current thinking that AD may begin 20 years or more before symptoms occur.

Mild Cognitive Impairment

- Noticeable declines in cognition but not of sufficient severity to meet diagnostic criteria for dementia
- Originally thought that functional abilities are largely unaffected
- However, subsequent research has shown that declines in instrumental activities of ADLs can be affected (Winblad et al, 2004).
- People with MCI, especially MCI involving memory problems, are more likely to develop AD and other dementias than people without MCI.

Mild Cognitive Impairment

- An average of 32% of individuals with MCI developed AD in 5 years.
- In some cases of MCI is actually an early stage of AD or another form of dementia.
- However, MCI can develop for reasons other than AD, and MCI does not always lead to dementia.
- It is important that people experiencing cognitive impairment seek help as soon as possible for diagnosis and possible treatment.

Early stage of AD

- Problems coming up with the right word or name
- Trouble remembering names when introduced to new people
- Having greater difficulty performing tasks in social or work settings
- Forgetting material that one has just read
- Losing or misplacing a valuable object
- Increasing trouble with planning or organizing

Middle stage of AD

- Forgetfulness of events or about one's own personal history
- Being unable to recall their own address or telephone number or the high school or college from which they graduated
- Confusion about where they are or what day it is
- The need for help choosing proper clothing for the season or the occasion
- Trouble controlling bladder and bowels in some individuals
- Changes in sleep patterns, such as sleeping during the day and becoming restless at night
- An increased risk of wandering and becoming lost
- Feeling moody or withdrawn, especially in socially or mentally challenging situations
- Personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand-wringing or tissue shredding

Late stage of AD

- Require full-time, around-the-clock assistance with daily personal care
- Lose awareness of recent experiences as well as of their surroundings
- Require high levels of assistance with daily activities and personal care
- Experience changes in physical abilities, including the ability to walk, sit and, eventually, swallow
- Have increasing difficulty communicating
- Become vulnerable to infections, especially pneumonia

Risk factors

Autosomal-dominant AD

- Genetic mutations involve the gene for the amyloid precursor protein, or presenilin-1 or 2 proteins (<1% of cases of AD) guarantees of developing AD (95% chance).
- In such individuals, symptoms tend to develop before the age of 65 years, sometimes as early as age 30 years.

Down syndrome

- Free trisomy 21--three full copies of the 21st chromosome (95% of DS cases)
- The amyloid precursor protein (*APP*) gene is present on chromosome 21.
- The overexpression of the *APP* is related to the deposition of amyloid in the brain of individuals with DS.
- By age 40, most people with DS have significant levels of beta-amyloid plaques and tau tangles in their brains.
- However, elevated $A\beta$ alone is insufficient to explain the high incidence of AD in people with DS (Jones et al, 2009).

Genetic factors in late-onset AD (sporadic AD)

- Most cases of AD are sporadic type, in which environmental and genetic differences may act as risk factors.
- Most recent genome-wide association studies (GWAS) have found 19 genes that appear to affect the risk.

Apolipoprotein- ϵ 4 genes

It involves with the transport of cholesterol and phospholipids in the brain

Genotype		% of those with AD	
➤ ϵ 2/2	% of Population	1	0.1
➤ ϵ 2/3		12	4
➤ ϵ 3/3		60	35
➤ ϵ 3/4		21	42
➤ ϵ 4/4		2	16

ApoE and AD

- 65-80% of all AD patients have at least one $\epsilon 4$ allele.
- $\epsilon 3/4$ 2-3 fold increased risk of AD
- $\epsilon 4/4$ 8-12 fold increased risk of AD
- Inheriting the $\epsilon 4$ gene increases risks of AD, but does not guarantee of developing.

Apolipoprotein- ϵ 4 genes and DS

For individuals with ID from DS—the risk associated with APO ϵ 4 in DS appears to be lower than what is associated with AD (Rohn et al. 2014).

Family history

- Individuals with a first-degree relative with AD are more likely to develop AD.
- When AD runs in family, heredity (genetics), shared environmental and life style factors, or both may play a role.

Age

(Alzheimer Disease Facts and Figures 2016)

Prevalence of AD in the US

- 85+ years: 37%
- 75-84 years: 44%
- 65-74 years: 15%
- <65 years: 4%
- AD is not a normal part of ageing.
- Older age alone is not sufficient to cause AD.

The oldest of the old

- People who make it through their nineties without developing AD are actually at a lower risk than people in their eighties (Perls, 1998).
- Half of the people who died between 95 and 99 have brain-infarcts, whereas only 22% of the people who died over 100 have infarcts.

Gender and Racial risk for AD

- Almost 2/3 of individuals with AD are woman
- African-Americans and Hispanics (primarily Caribbean-Am) are more likely to have AD than whites; primarily they have a higher risk for HBP and diabetes
- Genetic factors do not appear to account for the large prevalence differences among races.
- Health conditions, education level, life style, socioeconomic status may be more important.

Risk Factors (modifiable)

Up to half of AD and dementia cases may be attributable to potentially modifiable risk factors (Barnes and Yaffe, 2011).

Risk Factors (modifiable)

Vascular dementia:

- It is very common on older individuals with dementia, with about 50% having pathological evidence of vascular dementia (infarcts). In most cases, the infarcts coexist with AD pathology.
- In the past, evidence of vascular dementia was used to exclude a diagnosis of AD. That practice is no longer considered consistent with the pathologic evidence, which shows that the brain changes of AD and vascular dementia commonly coexist (mixed dementia).

Risk Factors (modifiable)

- Cardiovascular risk factors (smoking, HBP, diabetes, obesity, high cholesterol) are associated with a higher risk of developing AD and other dementias.
- Factors that protect the heart may also protect the brain and reduce the risk of developing AD and other dementias (e.g., Mediterranean diet, exercise).

Risk Factors (modifiable)

AD brain vs. AD symptoms

Nun Study (Snowdon et al, 1997)

- AD brain + small infarcts: 93% dementia
- AD brain + no infarcts: 57% dementia

Bennett et al. (2006)

- 1/3 of individuals ages 82-85 who met neuropathological criteria for AD did not have clinical symptoms of dementia

Risk Factors (modifiable)

Type II diabetes Mellitus (T2DM)

- Risk for AD doubles after developing T2DM
 - Ott *et al.*, Neurology, 1999;
 - Arvanitakis *et al.*, Archives of Neurology, 2004
- T2DM is present in 80% of AD patients
 - Janson *et al.*, Diabetes, 2004

Risk Factors (modifiable)

Traumatic Brain Injury

- Moderate TBI is associated with twice the risk of developing AD and severe TBI is associated with 4.5 times the risk.
- Repeated mild TBI (e.g., boxers, football players, hockey players) might increase the risk of neurodegenerative diseases.

Risk Factors (modifiable)

Education

- People with fewer years of formal education are at higher risk for AD than those with more years of formal education.
- People with lower education attainment may have a higher risk for AD by factors common to people in lower socioeconomic groups (increased risk for disease, less access to medical care).

Social and cognitive engagement

- Remaining socially and cognitively active may help build cognitive reserve capacity.

Risk Factors (modifiable)

Cognitive reserve hypothesis

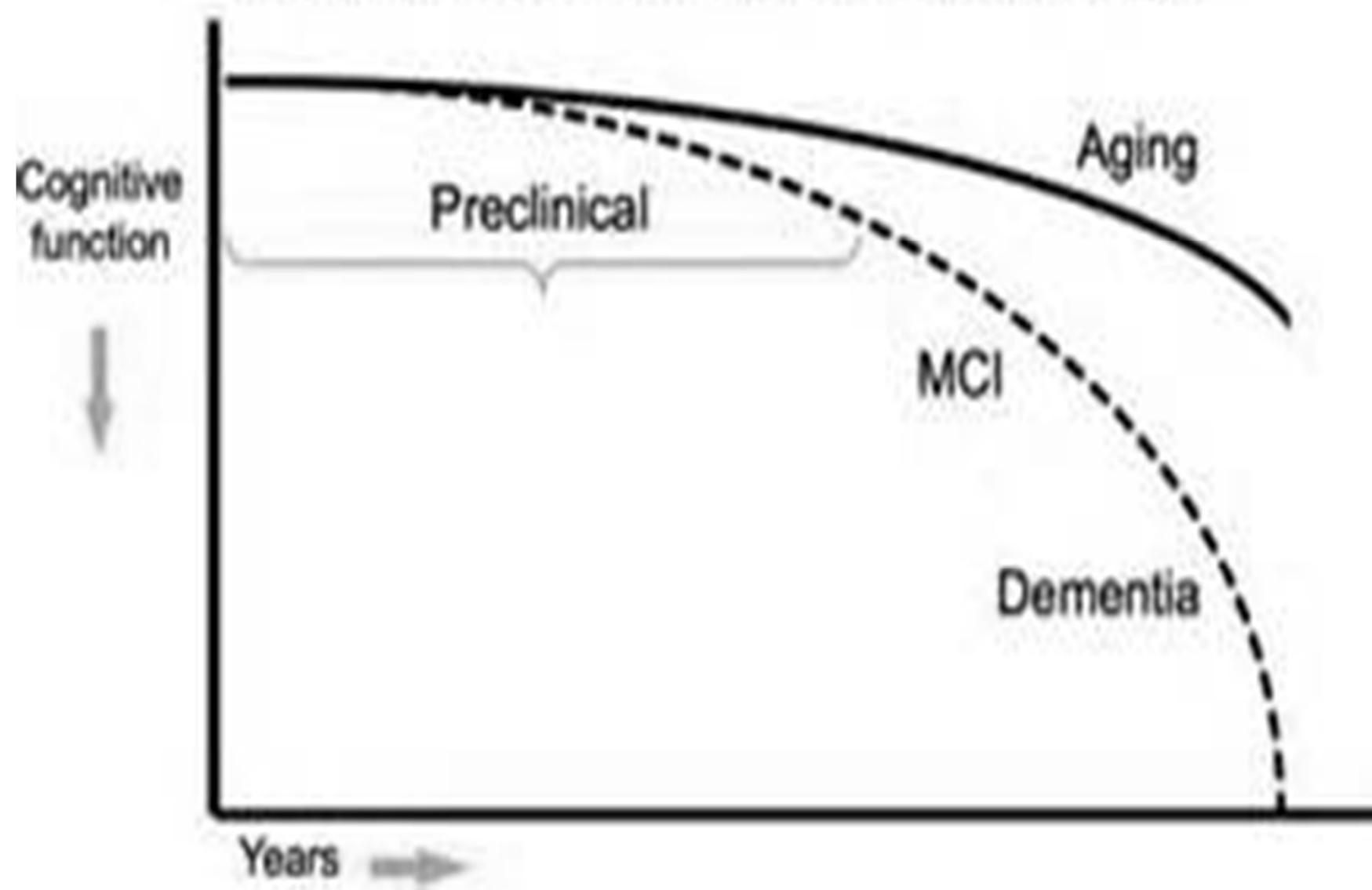
- Having more years education and cognitively active life increases the connection between neurons in the brain and enables the brain to compensate for the early brain changes of AD.

What is normal ...

What is NOT



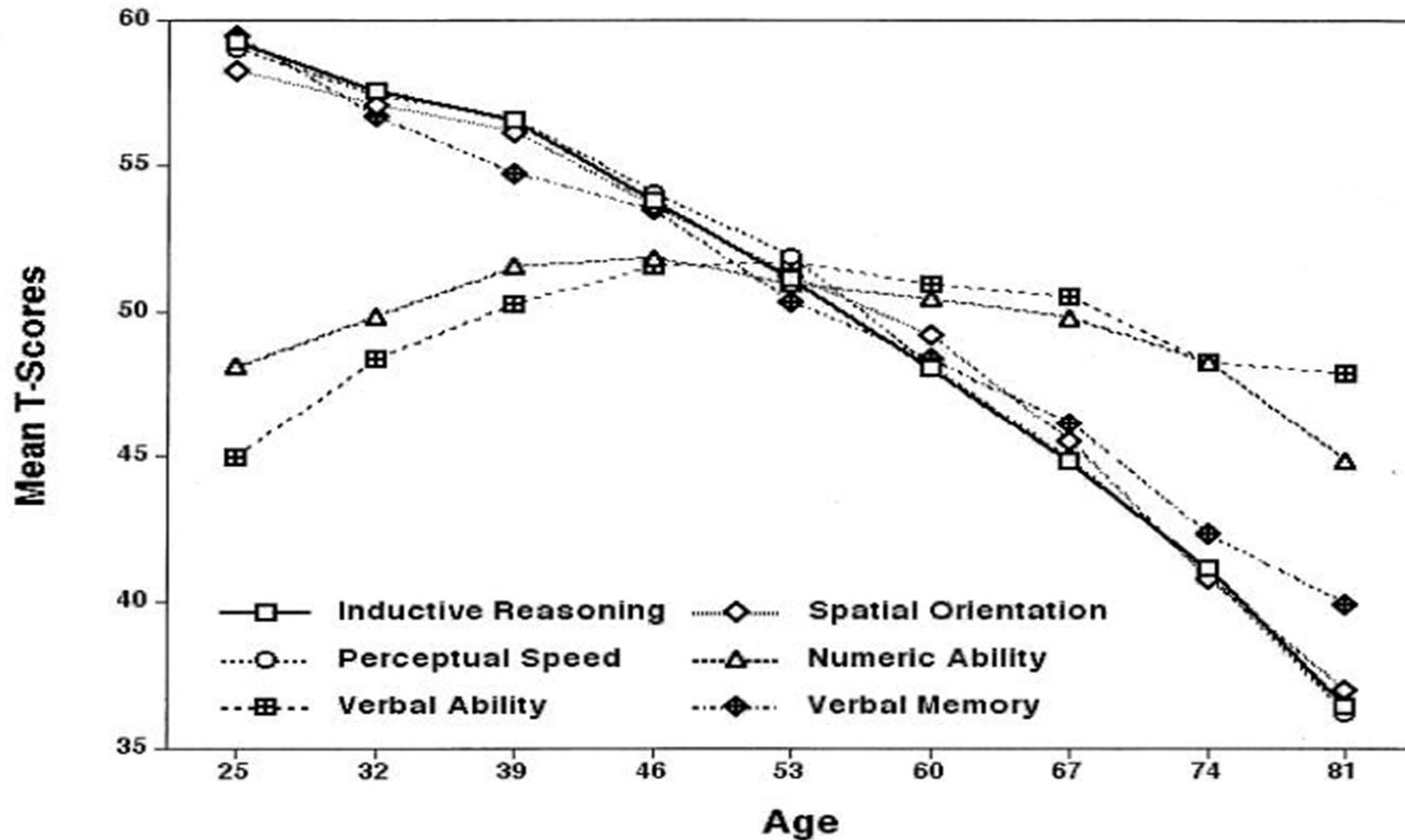
The continuum of Alzheimer's disease



Study methods of aging

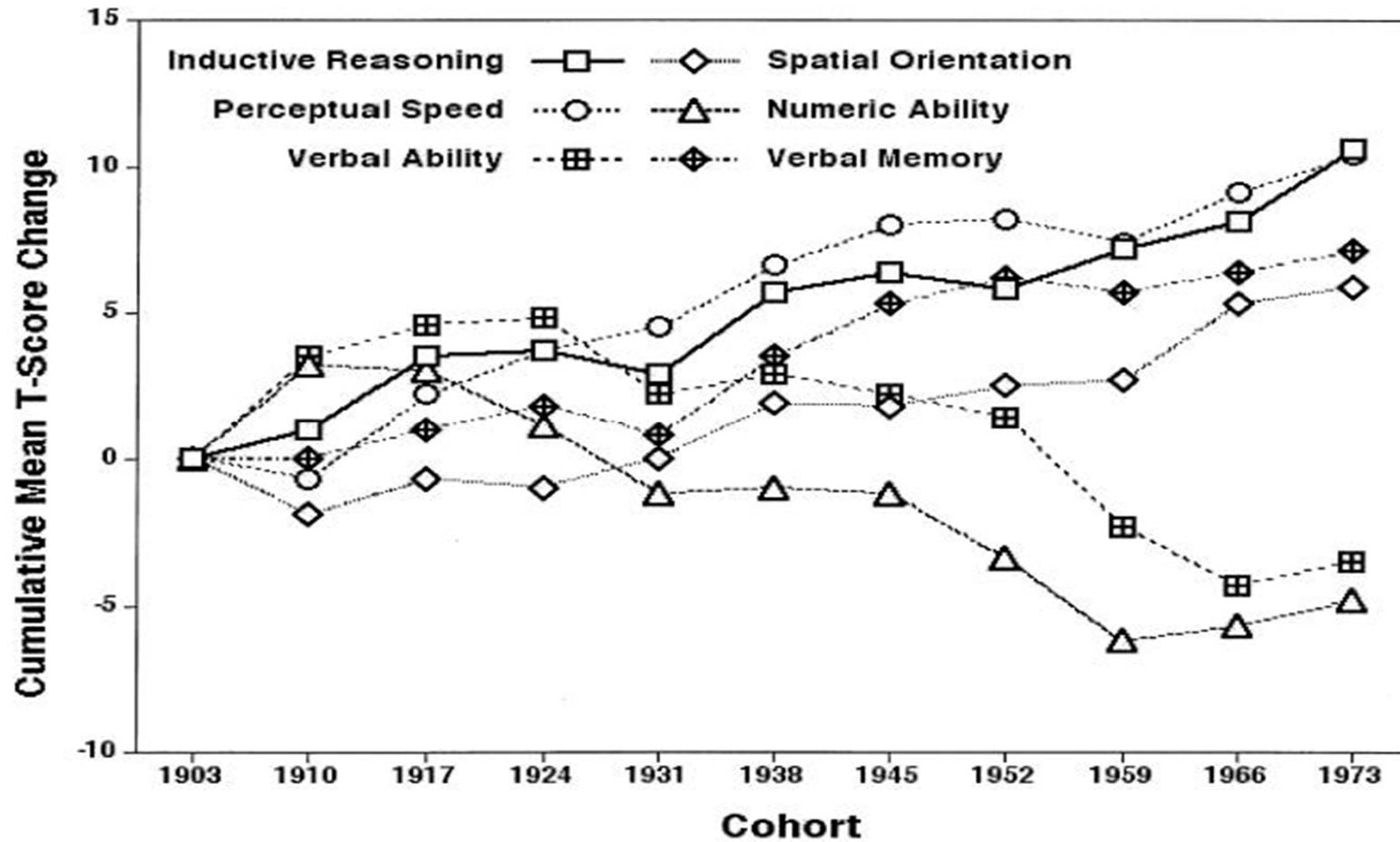
- Cross-sectional studies compare different study participants of different ages to study aging effects.
- Longitudinal studies compare same study participants at different ages to study aging effects.

Cross-sectional studies of aging (Schaie, 2006)



Cohort effect of cross-sectional study

(Schaie, 2006)

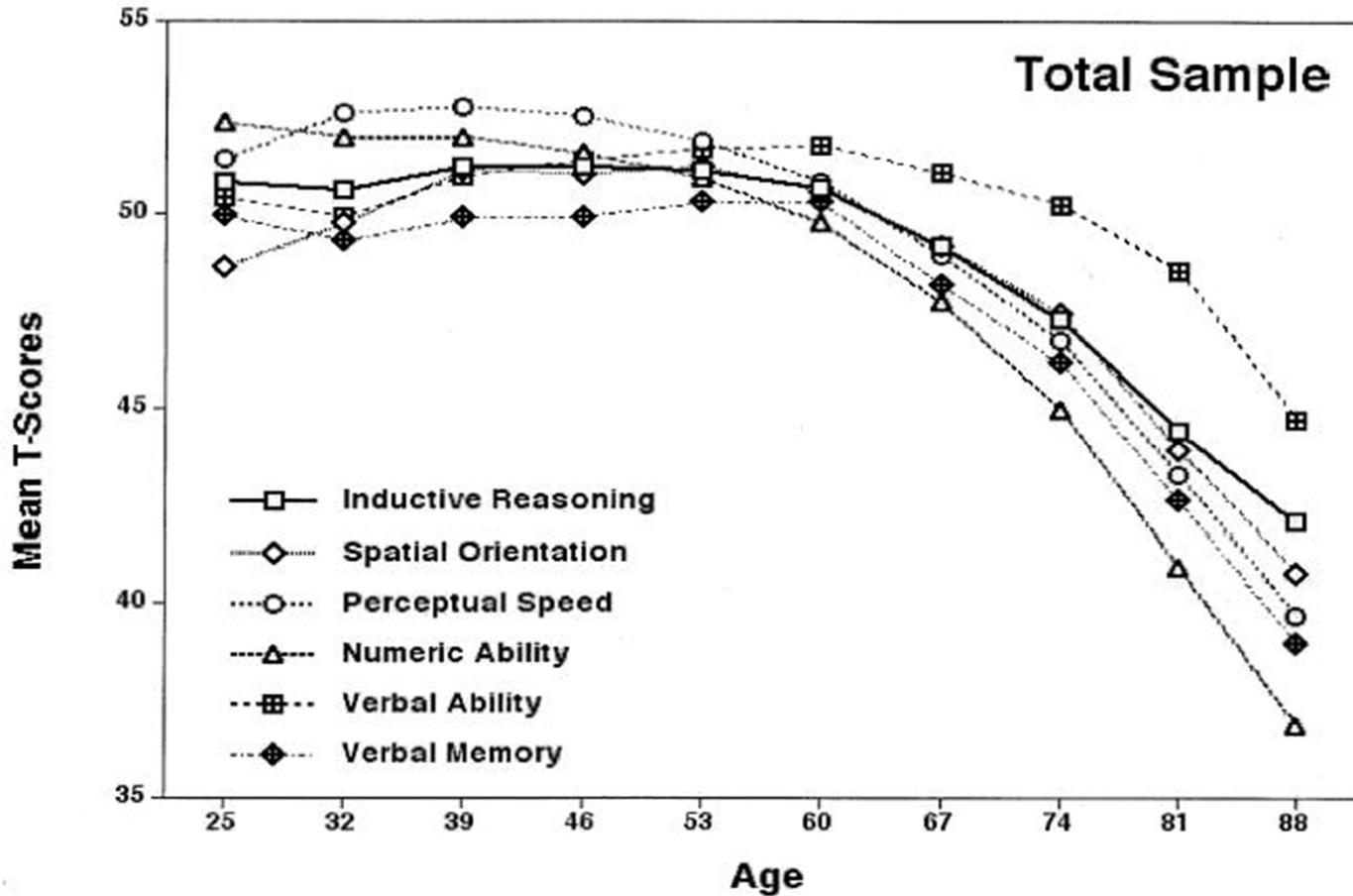


Seattle Longitudinal Study (Schaie, 2006)

Began in 1956 with the age range from 20 to 70 years and followed more than 5000 people for well over four decades.

Longitudinal studies of aging

(Schaie, 2006)



Seattle Longitudinal Study (Schaie, 2006)

- No uniform pattern of age-related change across all intellectual abilities
- Abilities acquired through schooling or experience tend to be stable
- Perceptual speed decline begins in young adulthood but more steeply after late 70s
- Cohort effects account for more of the variance in different ages.
- Individual differences in what skills decline as well as the extent of such decline are substantial.

Seattle Longitudinal Study (Schaie, 2006)

The following variables may reduce the risk of cognitive decline in old age:

- Absence of chronic diseases
- A complex and intellectually stimulating environment
- A flexible personality style at midlife
- High intellectual status of spouse
- Maintenance of high levels of perceptual processing speed

Longitudinal study for individuals with ID

(Devenny, et al, 1996)

- Annual evaluations of a group of 91 adults with DS (31-63 years of age) and 64 adults with other forms of ID (31-76 years of age) over a period of up to 6 years (mean IQ 50s)
- Normal ageing would include small, incremental declines in performance on tests of short term memory; slight decline in short term memory **(less than 1% per year)** was associated with increasing age in adults with DS, but not with their peers.
- Selective reduction of psychomotor speed, with the preservation of other cognitive abilities
- Declines in functioning were not characteristic of the participants
- Adults with DS may be experiencing premature but otherwise normal ageing.

Alzheimer Disease in persons with DS

- Adults with DS have higher risk of developing AD compared to adults with ID from other etiologies. They tend to develop AD at younger ages than adults with ID from other etiology.
- Nearly all adults with DS over 35 years of age exhibit some of the key neuropathological changes characteristic of AD
- The non-fibrilized types of amyloid plaques which have been shown to be so pervasive in even relatively young adults with DS appear to be unrelated to the disruption of neural systems (Wisniewski & Silverman, 1996).
- It was speculated that the brain mechanisms of AD among individuals with DS may be different from that of general population.

Alzheimer Disease in persons with DS

- Dementia occurs in people with DS in 9.4 % in the age group 30-39 which increases to 54.5 % in the age group 60-69 (Prasher et al. 2015).
- The risk of developing AD among adults with DS is much lower than previously thought.
- For people with ID of non-DS causes aged 65 or older, the incidence of dementia is up to five times higher than in the general population, peaks at age 70-74 (Strydom et al, 2013).
- The average age of onset for clinical manifestations of AD in individuals with DS is between 51 and 54 years of age, and in individuals with ID from other causes tends to be over 65.

Alzheimer Disease in persons with DS

- Prevalence rates of AD did not differ among different levels of ID.
- Age was a strongest risk factors and was not influenced by gender or severity of ID (Strydom et al, 2009).
- The evidence for gender and the level of ID as potential risk factors is inconclusive (Bush et al. 2004)
- In DS patients the early, selective accumulation of Abeta peptides is independent of the ApoE genotype, but the APO ϵ 4 predisposes to various causes of premature death (Folin et al, 2003).

Memory impairment of AD in persons with DS

- Memory loss is a predominant symptom in individuals showing decline.
- The memory decline occurs before other areas of cognitive impairment (Devenny, et al, 1996).
- The presence of AD would represent a distinct departure from the course of normal ageing in these individuals (Haxby & Shapiro, 1992).
- **20% or more** below an individual's highest previous total recall score during two consecutive test sessions (Krinsky-McHale et al.1997)

Memory impairment of AD in persons with DS

- Declines in memory may occur earlier than more global behaviors, such as those identified by informant-based scales.
- Higher functioning individuals with ID have been known to display a relatively long pre-clinical period in which the memory decline occurred several years prior to a diagnosis (Devenny et al. 2000).
- There is a relatively long pre-clinical period in which this memory decline occurs that can be detected by testing (Devenny, et al, 2002).
- Any decline on cognitive tests must be accompanied by documentation of changes in everyday functioning before the declines can be considered diagnostic (Cooper & Prasher, 1998).



Non-memory cognitive impairment of AD in persons with DS

- Impaired orientation and visuospatial memory at the beginning of the study, and praxis and language function deteriorates later (Oliver et al, 1998) .
- All individuals with possible AD declined on questions of orientation to time and on object naming (Devenny, et al, 1996).

Maladaptive behaviors of AD in persons with DS

- Changes in vegetative function (urinary incontinence, sleep disturbance, becoming tired easily, eating too much or little)
- Gait disturbance
- Confusion (wandering, difficulty finding their way around, lack of boundaries)
- Mood changes (irritability, agitation, restlessness, aggression)
- Deterioration of self-care skills (difficulty with dressing and washing)
- Difficulty with communication

Maladaptive behaviors of AD in persons with DS

- Obnoxious behaviors (e.g., lying, reacting poorly to frustration or criticism, demanding excessive attention, impudent attitude towards authority)
- lack of boundaries (e.g., takes others' property, disrespecting others' personal space)
- overestimating own abilities
- Maladaptive behaviors were significantly elevated prior to the occurrence of subsequent adaptive decline. (Urv, et al, 2003).

Maladaptive behaviors of AD in persons with DS

- Holland et al.(1998) hypothesized that the presentation and course of dementia in people with DS may be modified by the effects of the pre-existing abnormalities of brain development, frontal lobes in particular. For this reason, the earliest features of dementia in people with DS may give rise to a clinical picture similar to that found in frontal lobe dementia.

Maladaptive behaviors of AD in persons with DS

- Decreased mood, restlessness and disturbed sleep were found to be more common in the DS group, whereas aggression was more common in the group without DS (Cooper & Prasher, 1998).
- Dementia status did not influence any of the measures of aggression except for the self-abusive behavior (Cosgrave et al., 1999)

Maladaptive behaviors of AD in persons with DS

- Cosgrave and colleagues (1999) found no relationship between AD and the prevalence of behavior disturbances
- Zigman and colleagues (2002) reported that only 16% of individuals with DS who displayed functional decline had a formal diagnosis of AD: age-related medical concerns unrelated to AD, like arthritis, Parkinson's disease, or cardiovascular problems may play an important role in the decline in adaptive behaviors.
- Disability level and comorbidity can explain 10% of the ADL score variation, whereas dementia conditions can only explain 3% of the ADL score variation based on the caregiver's report (Lin et al, 2014)

Maladaptive behaviors of AD (cont)

- A diagnosis of dementia should be discouraged if observable behavioral changes are not accompanied by evidence of cognitive decline, and it will require consideration of all possible causes of functional decline, including those that are treatable (Working Group, 1996).

Guidelines for Dementia-related Health
Advocacy for Adults with Intellectual
Disabilities and Dementia of the National
Task Group on Intellectual Disabilities and
Dementia Practices (Dec 2014)

NTG's guidelines

- Provide caregivers with information on risk factors and signs associated with dementia in adults with ID.
- Increased caregivers' awareness of symptoms (raise the index of suspicion) associated with dementia.
- Ensure that life history and functioning information is retrieved, reconstructed, or developed when possible.
- Initiate cooperative continuing education programs in aging and ID for local health care practitioners and ancillary personnel.
- Increase practitioners' understanding of the likely symptoms and presentation of dementia by adults with ID.

NTG's guidelines

- Establish a regional directory of practitioners who are experienced with examining adults patients with ID.
- Assist caregivers through organizational support with finding health care providers who are knowledgeable and experienced with assessing adults with ID.
- Establish a 'dementia specialist' or 'dementia team' on an agency or regional basis who/which can assist caregivers with gathering information and obtaining a referral for a dementia assessment (as well as consult within follow-ups).

NTG's guidelines

- Improve communication between caregivers and practitioners by training and instituting a process for dementia-related health advocacy amongst caregivers.
- Establish follow-up processes with assigned clinicians or advocates so that families have access to personnel who can help advise them.
- Provide training or education materials to caregivers on communication with health personnel.
- Implement innovative approaches to health assessment as part of the planning and organizing of local dementia capable services.

The Working Group for the Establishment of
Criteria for the Diagnosis of Alzheimer Disease
(AD) in Individuals with Intellectual Disability
under the auspices of the International
Association for the Scientific Study of
Intellectual Disability (IASSID) and the
American Association on Mental Retardation
(AAMR) 1996

The Working Group's guidelines

- While some age-associated changes are normal (e.g., changes in stamina and sensory abilities), gross mental deterioration is not
- Some behavioral changes may look like AD, but may be the result of other causes and may be reversible
- The differential diagnostic process should be essentially the same as that used in the general population, except for modifications made to accommodate differing cognitive skills
- The individual's own abilities and level of functioning (i.e. his or her baseline of performance) should be the basis for evaluating subsequent changes

The Working Group's guidelines

- All adults with ID should be evaluated using standardized procedures at least once before 40 years of age to all adults with DS and before 50 years of age to adults with ID from other causes in order to establish baseline levels of performance when healthy.
- Longitudinal administration of tests is an absolute necessity to make a diagnosis of dementia (every 1-5 years depending on age and risk for dementia), and as soon as possible when dementia is suspected.

The Working Group's guidelines

- It is imperative to obtain information from informants who are familiar with the individual's current everyday behavior, and preferably, with past behaviors.
- A diagnosis of dementia should be discouraged if observable behavioral changes are NOT accompanied by evidence of cognitive decline.

The Working Group's guidelines: Dementia evaluation

- Interview with the patient and informants
- Behavior rating scales
- Cognitive tests
- Physical assessment (pulse rate, respiration rate, blood pressure, body temperature, and level of alertness etc)
- Neurological examination
- Laboratory tests (CBC, CMP, thyroid stimulating hormone, free T4, Vitamin B12 Level, folate, urinalysis, sedimentation rate, and CT of brain)

The Working Group's Dementia Battery (Informants' rating scales)

- Dementia Questionnaire for Mentally Retarded Persons
- Dementia Scale for Down Syndrome
- Reiss Screen for Maladaptive Behavior
- Scales of Independent Behavior-Revised
- AAMR Adaptive Behavior Scale-Residential and Community
- Stress Index

The Working Group's Dementia Battery (Informants' rating scales)

- The Dementia Questionnaire for Mentally Retarded (DMR) and the Dementia Scale for Down Syndrome (DSDS) have widely been used to evaluate dementia in individuals with ID
- It appears that the DMR may be slightly more effective.
- The DMR Sum of Social Scores subscale is the variable that best predicted AD.

The Working Group's Dementia Battery: Direct assessment

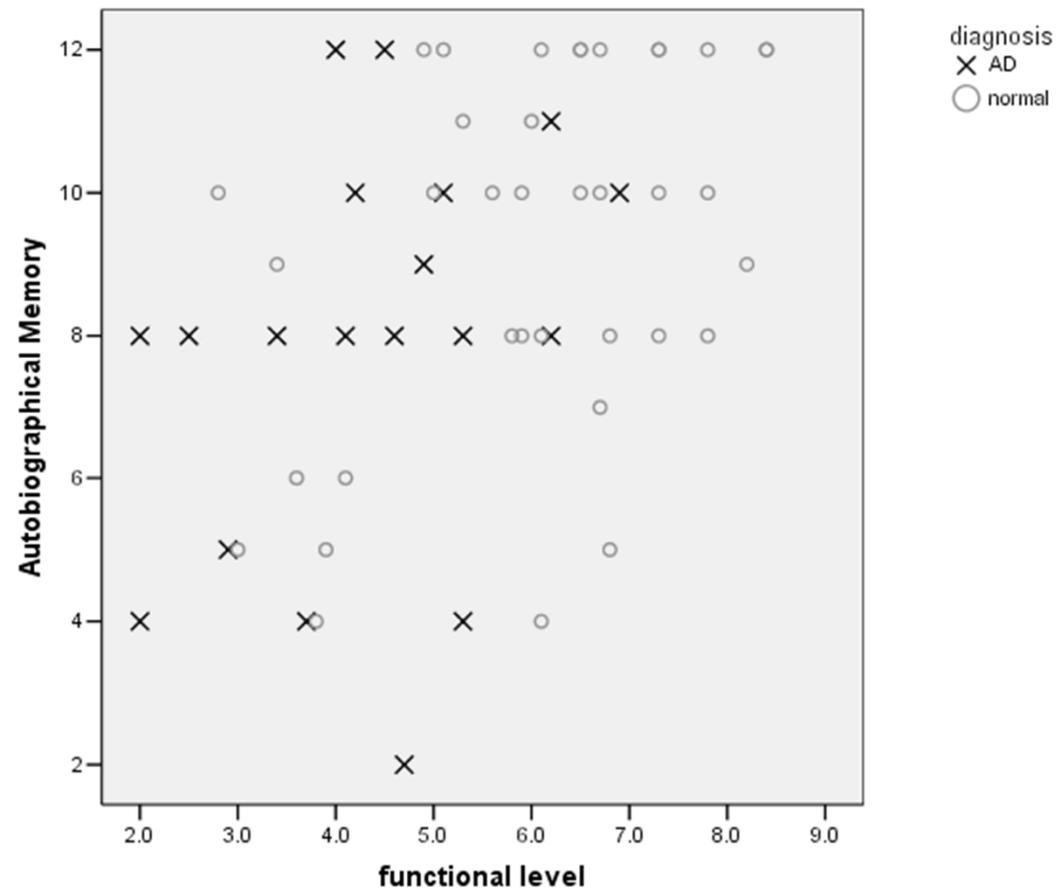
- Test for Severe Impairment
- Stanford Binet Sentences
- Fuld (modified) test
- Spatial Recognition Span
- Autobiographical Memory
- Orientation
- Boston Naming Test
- McCarthy Verbal Fluency
- Simple Commands
- Purdue Pegboard test
- Developmental Test of Visual Motor Integration

Performances on the memory tests recommended by the “Working Group”

Variables	Controls (n=31)	Patients with AD (n=13)
Autobiographical memory *	9.74±2.24	8.38±2.57
Orientation *	9.74±4.15	7.08±3.20
TSI-total	20.83±1.84	19.85±3.18
TSI immediate memory	2.55±0.62	2.38±0.87
TSI-delayed memory	0.55±0.51	0.77±0.44
OMT immediate recall	4.43±2.49 (n=25)	4.14±2.48 (n=6)
OMT-immediate recognition	18.54±2.06 (n=25)	16.67±3.20 (n=6)
OMT-delayed recognition	18.63±2.24 (n=25)	18.00±2.53 (n=6)

* p <0.05

Score distribution of Autobiographical Memory test (Pyo GY et al. 2010)

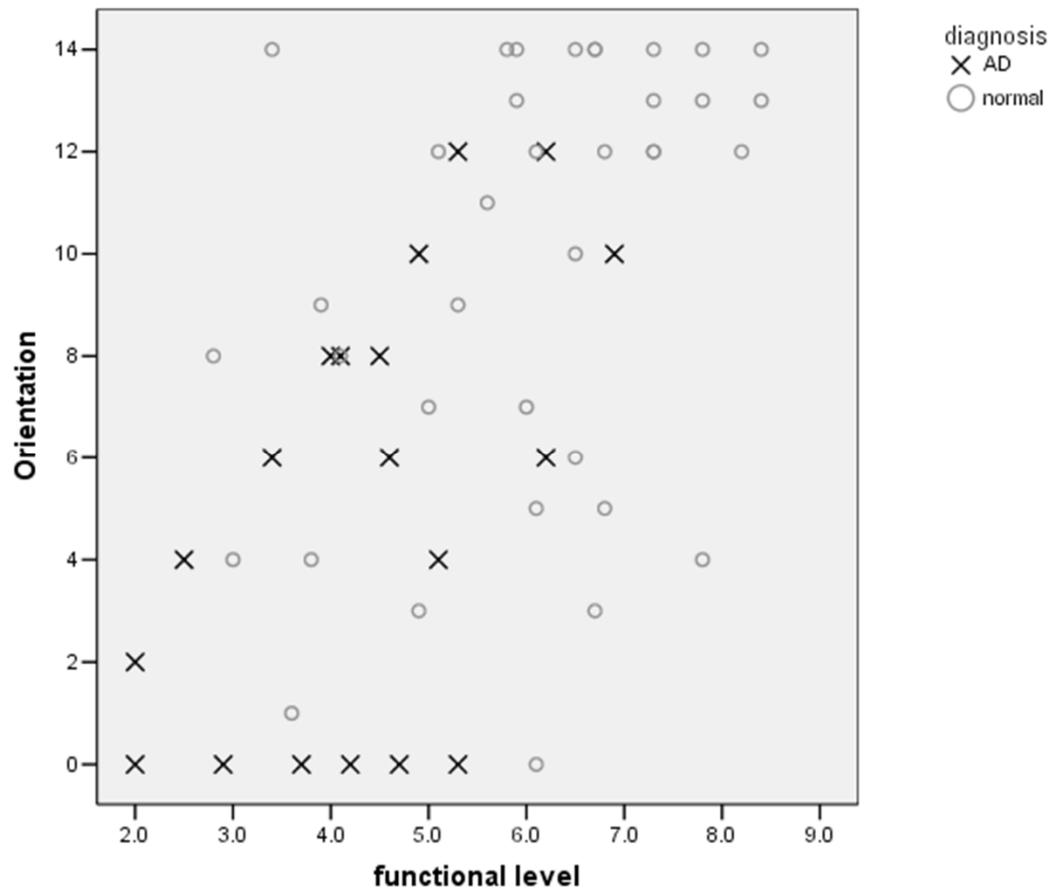


Item analysis of the Autobiographical Memory test

Items	Controls (n=35)	Patients with AD (n=16)	p-value
First name	100.0	100.0	0.322
Last name	100.0	94.7	0.322
Birthday-month	70.0	78.9	0.347
Birthday-date	70.0	63.2	0.406
Birthday-year	47.5	26.3	0.102
Age	32.5	15.8	0.301

Score distribution of Orientation test

(Pyo GY et al. 2009)



ORIENTATION TEST

- What is today's date?
- What day of the week is this?
- What month is this?
- What year is this?
- What is the name of the place you live at?
- What city do you live?
- What state do you live?

Item analysis of the Orientation test

	Controls (n=35)	Patients with AD (n=16)	p-value
Month	80.0	50.0	0.013
Week	65.0	33.3	0.016
Date	37.5	16.7	0.080
Year	50.0	16.7	0.011
The current location	77.5	27.8	0.000
City	77.5	50.0	0.023
State	65.0	38.9	0.040

Picture Recognition Memory Test



Picture Recognition Memory Test



Construct validity of the Picture Recognition Memory Test (Pyo et al. 2007)

Variables (score range)	Controls	Patients with AD	d†
PRMT-Immediate (0-15)**	11.25±3.89 (n=20)	5.40±2.76 (n=10)	1.64
PRMT-Delayed (0-15)**	11.20±4.12 (n=20)	5.10±2.89 (n=10)	1.62
TSI-Total (0-24)	20.21±2.37 (n=19)	18.80±5.79 (n=10)	0.37
TSI-Memory (0-4)	3.29±0.77 (n=19)	2.67±1.03 (n=10)	0.72
OMT-Recall (0-10)	5.20±2.30 (n=10)	3.67±0.58 (n=3)	0.73
OMT-Immediate Recognition (0-20)	17.70±2.50 (n=10)	14.33±1.53 (n=3)	1.43
OMT-Delayed Recognition (0-20)	18.00±2.63 (n=10)	17.67±1.53 (n=3)	0.13

** p < 0.001

Demographic characteristics of the participants

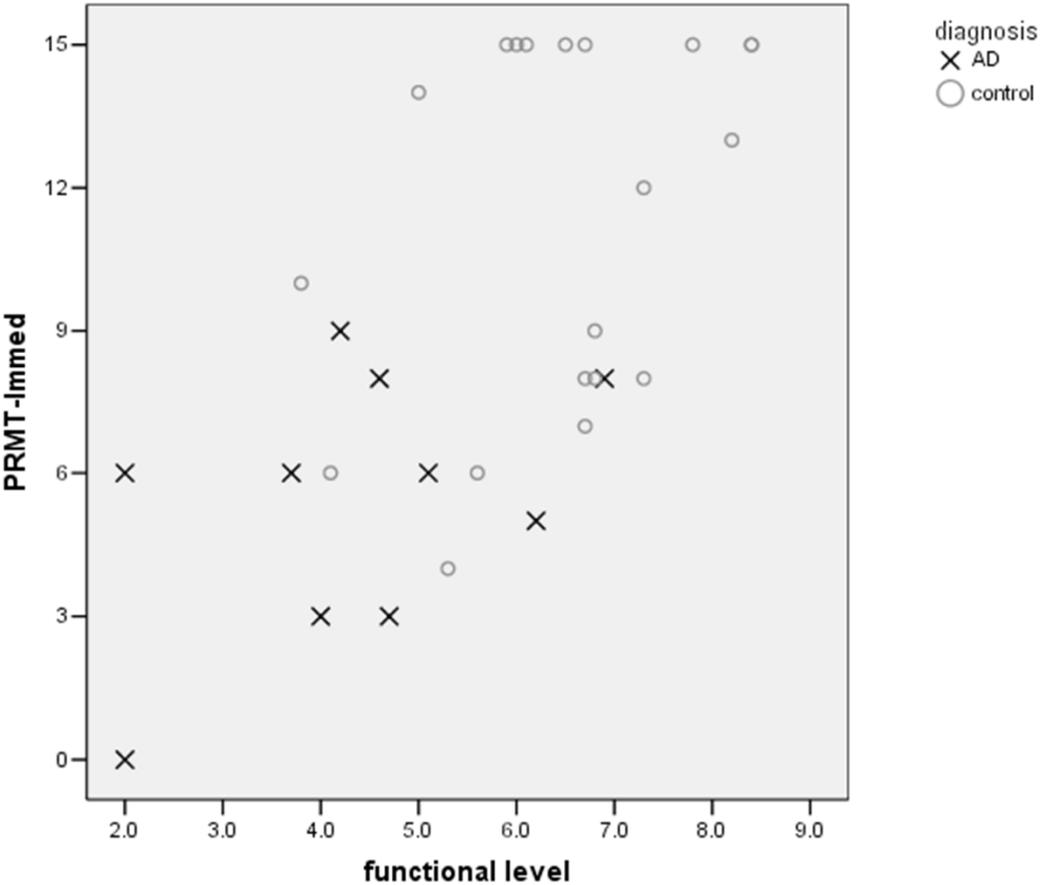
	Normal controls (n=38)	AD patients (n=19)
IQ	35.03±12.23	30.32±10.13
Functional level*	6.06 ±1.46	4.34 ±1.38
Age	51.58 ±6.01	54.06 ±9.85
Moderate/Severe	19/20	7/12
Men/women	36/2	12/7
DS/other causes	12/26	9/10

*p=0.001

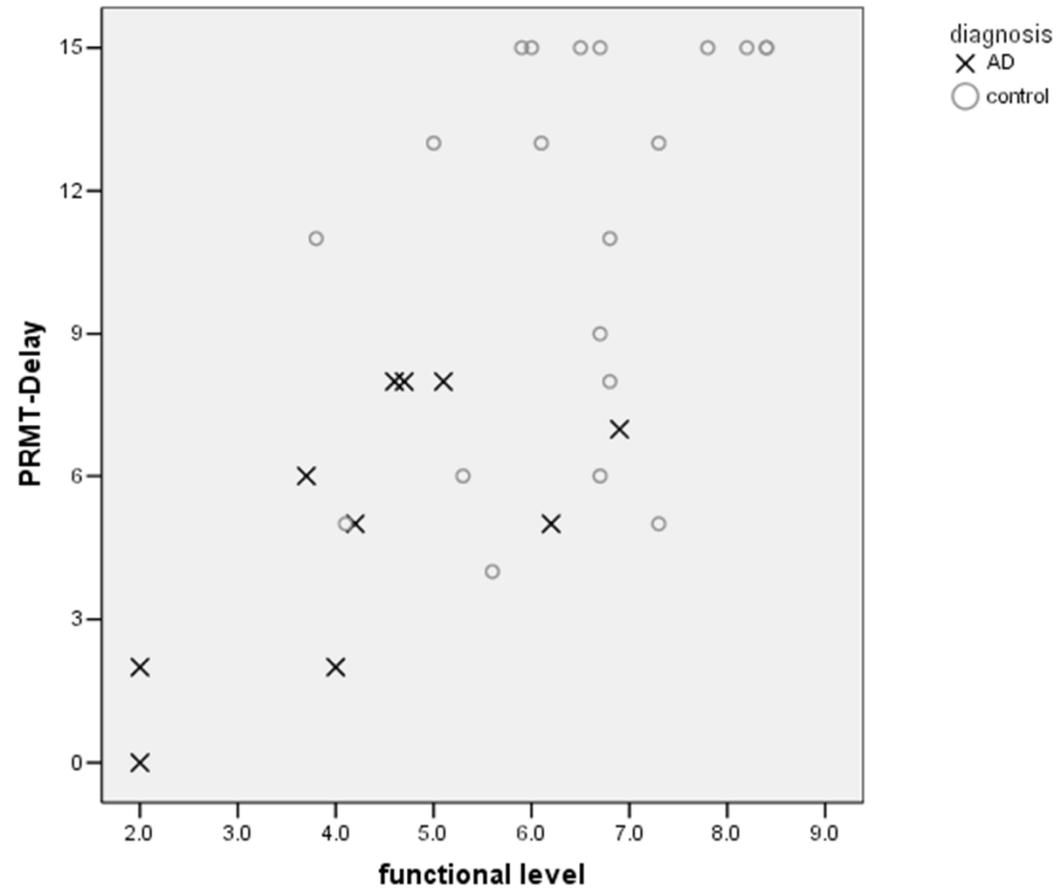
Comparison of the PRMT scores by the diagnostic groups and the etiologies of ID (Pyo et al, 2010)

Variables	Etiology of ID	Controls	Patients with AD
PRMT-Immediate	DS	14.83±0.41 (n=6)	4.17±2.79 (n=6)
	Other etiologies	9.71±3.69 (n=14)	7.25±1.50 (n=4)
PRMT-Delayed	DS	14.67±0.82 (n=6)	4.67±3.08 (n=6)
	Other etiologies	9.71±4.08 (n=14)	5.75±2.87 (n=4)

Score distribution of PRMT-Immediate



Score distribution of PRMT-Delayed



Case 1. 53-year old man with moderate ID from Down Syndrome

	2006	2008
Picture Recognition Test-Immediate	12	8
Picture Recognition Test-Delayed	14	7

Case 2. 47-year old man with moderate ID from Down Syndrome

	2005	2006	2007	2008
Picture Recognition Test-Immediate	12	11	8	3
Picture Recognition Test-Delayed	13	9	7	5

Case 3. 48-year old man with severe ID from Down Syndrome.

	2004	2006	2008
Picture Recognition Test-Immediate	8	9	3
Picture Recognition Test-Delayed	7	2	3

*adaptive Behavior Index Scores

These scores are based upon the problem behaviors listed above. Large negative scores indicate more serious problem behaviors. A score near 0 is average.

Internalized	-11	(± 3)	marginal problems
Asocial	-29	(± 4)	moderate problems
Externalized	-25	(± 3)	moderate problems
General	-29	(± 2)	moderate problems

ICAP Service Score/Level

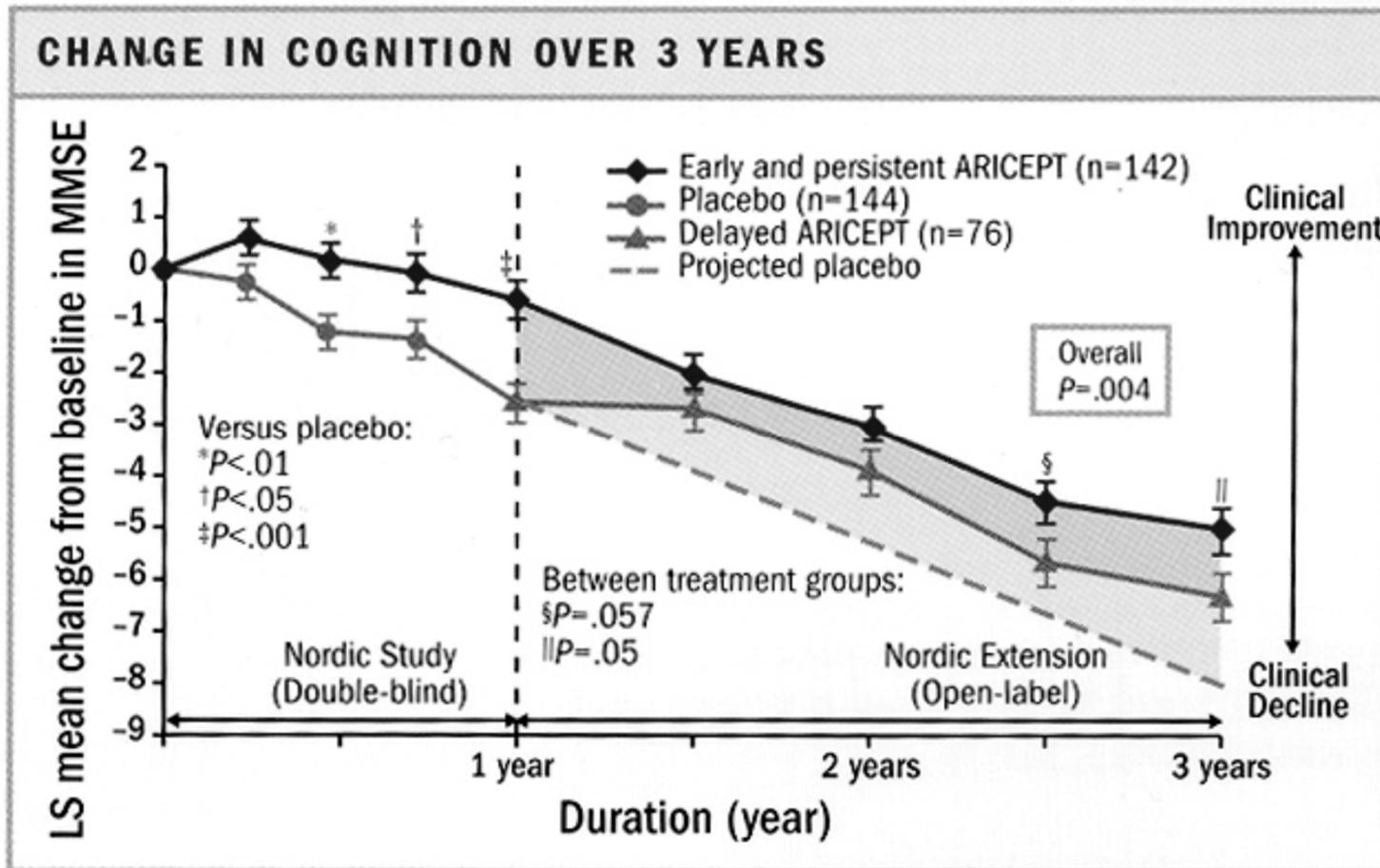
These scores are based on both adaptive behavior and problem behavior. They range from less than 20 (level 1, total care and intense supervision) to 90 or greater (level 9, infrequent or no assistance for daily living).

Score	31	
Level	3	extensive personal care and/or constant supervision

Historical Summary

Evaluation Date	10/2000	11/1999	11/1998	03/1991
Motor domain	393	411	414	402
Social/Communication	451	479	465	448
Personal Living	440	467	452	449
Community Living	453	431	450	428
Broad Independence	434	447	445	432
Age equivalent in months	34	47	44	32
Maladaptive Behavior				
Internalized	-11	-10	-10	-11
Asocial	-29	-10	-31	-30
Externalized	-25	-18	-23	-23
General	-29	-18	-28	-29
Service Score	31	47	37	30

Treatment



Disease-Modifying Treatment

- None of the pharmacologic treatments available today for AD slows or stops the damage and destruction of neurons that cause AD and make the disease fatal (Alzheimer Disease Facts and Figures 2016).

Treatment of AD

- Cholinesterase inhibitors: Inhibit the breakdown of acetylcholine
 - donepezil (mild-mod-severe AD)
 - rivastigmine (mild-mod AD)
 - galantamine (mild-mod AD)

Treatment of AD

- Memantine (Namenda[®])
 - An NMDA-receptor antagonist
 - Approved for moderate-to-severe AD
 - Approved for use with or without a cholinesterase inhibitor

Donepezil

- Only one double blind, placebo randomized controlled study has reported (Prasher, 2002).
- 16 DS participants in the donepezil 10mg group and 14 DS participants in the placebo group for 24 weeks
- 37% (6/16) of treatment group and 14% (2/14) of placebo group reported improvement.
- 50% of Donepezil group and 20% of placebo group reported adverse events; two participants left because of severe diarrhea and acute cholecystitis.
- Major adverse effects of treatment group: fatigue (44 %), diarrhea (38%), insomnia (25%), nausea (25%), anorexia (19%), agitation (19%), vomiting (13%), muscle cramps (13%)

Donepezil

- In the first six weeks of the study, the treatment group deteriorated in psychiatric behaviors before recovering to a level just over baseline at the end of the study period.
- people with DS have an increased incidence of cardiovascular disease including slow heart rates.
- Donepezil has a tendency of reducing the heart rate and is contraindicated for those with cardiac and respiratory problems.
- The optimum dose in patients with DS may be lower than the recommended regular dose (Kondon, 2005).

Rivastigmine, Memantine, Galantamine

- Rivastigmine (Exelon)
- Memantine (Namenda)
- Galantamine (Razadyne)
- No randomized controlled trials with a placebo group

If you still remember...Questions?

