

# Is Dementia Inevitable?

Professor Martin Rossor  
UCL Institute of Neurology

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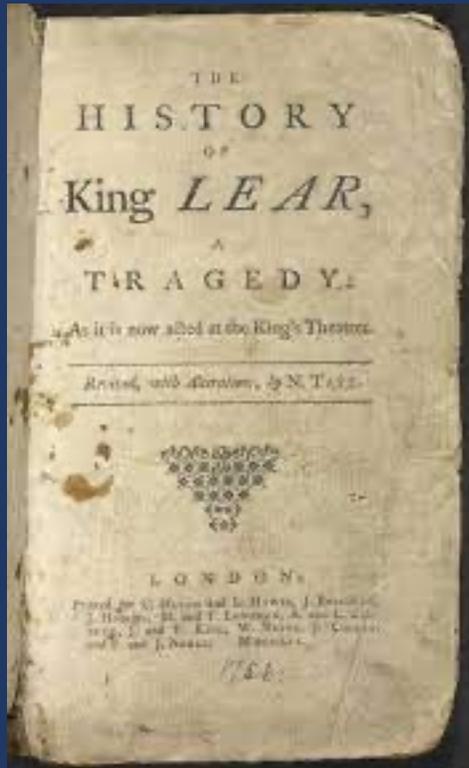
Gresham lecture  
5 April 2022



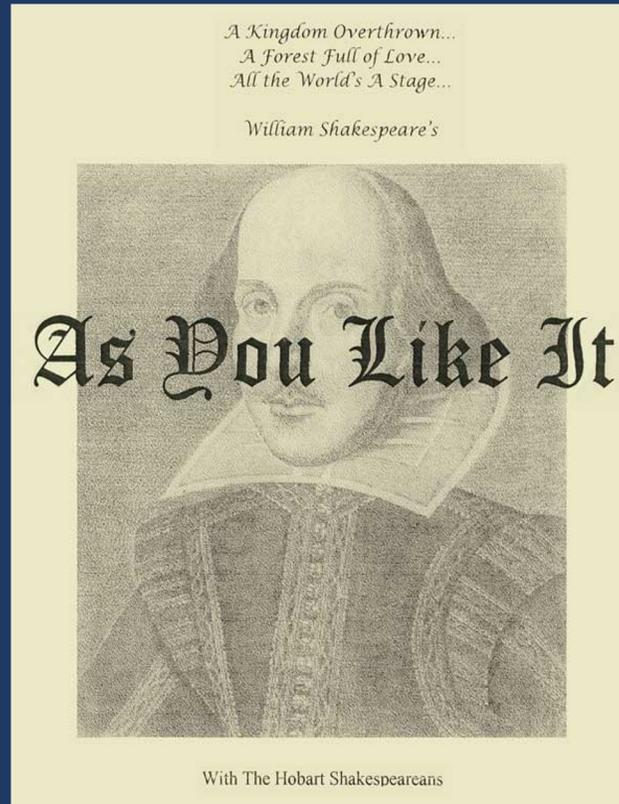




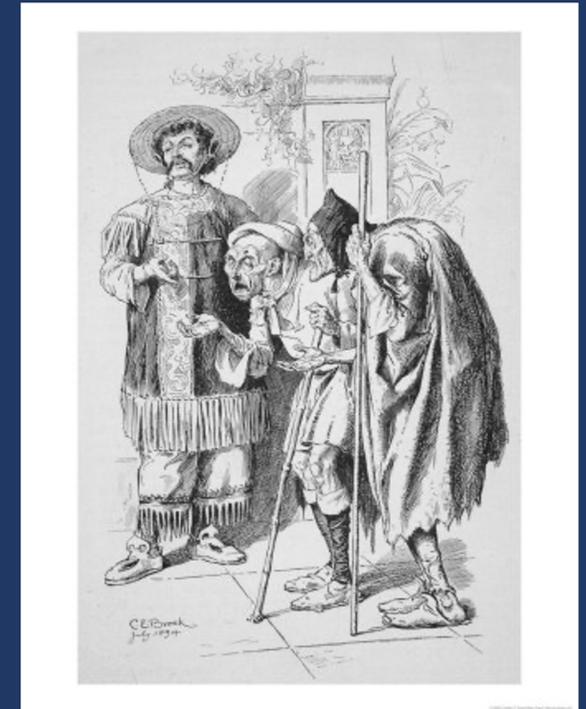
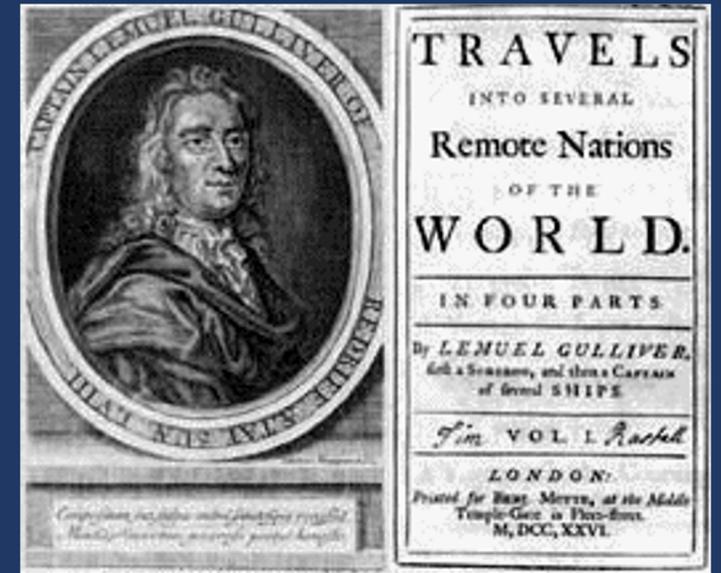
Ptah-hotep Egyptian 5<sup>th</sup> Dynasty



Pray, do not mock me.  
I am a very foolish fond old man,  
Fourscore and upward,  
not an hour more nor less.  
And to deal plainly  
I fear I am not in my perfect mind.



Last scene of all, that ends this  
strange eventful history, is second  
childishness and mere oblivion, sans  
teeth, sans eyes, sans taste, sans  
everything.



# Senior Dementia in Cats



OUR PETS HEALTH

## Complete Guide to Dementia in Dogs (senility signs + treatment)



because they're family

# Exciting Causes of Dementia – Table of Causes

<i>Physical Causes</i>		<i>Moral Causes</i>	
Menstrual disorders	15	Disappointed affection	5
Critical Period	35	Frights	7
Consequences of confinement	8	Political Shocks	8
Falls upon the head	3	Disappointed ambition	3
Progress of age	49	Want	5
Ataxic fever	3	Domestic trials	12
Suppression of hemorrhoids	2	Unknown causes	14
Mania	18		
Monomania	15		
Paralysis	5		
Apoplexy	2		
Syphilis and abuse of mercury	3		
Errors of regimen	6		
Abuse of wine	11		
		<b>TOTAL</b>	<b>235</b>

A Treatise on Insanity - Esquirol, 1845



Städt. Irren-Anstalt Frankfurt a. M.

No.

# Aerztliche Acten

über

Auguste *D*

geb: *SD*

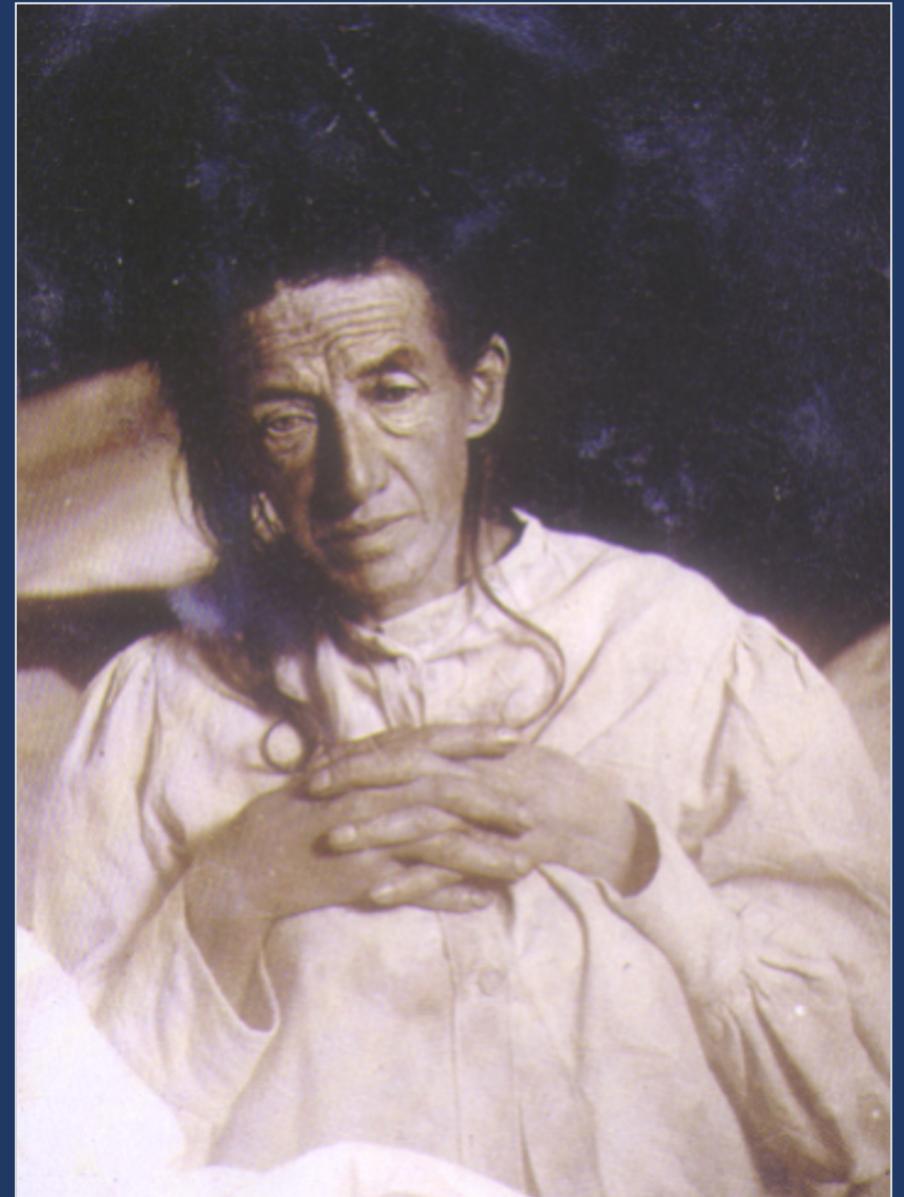
Alter: *31* Jahre.

Religion: *evangelisch*

Lfd. No.	Aufgenommen	Entlassen
1.	am 25. November 1901	am
2.	"	"
3.	"	"
4.	"	"
5.	"	"
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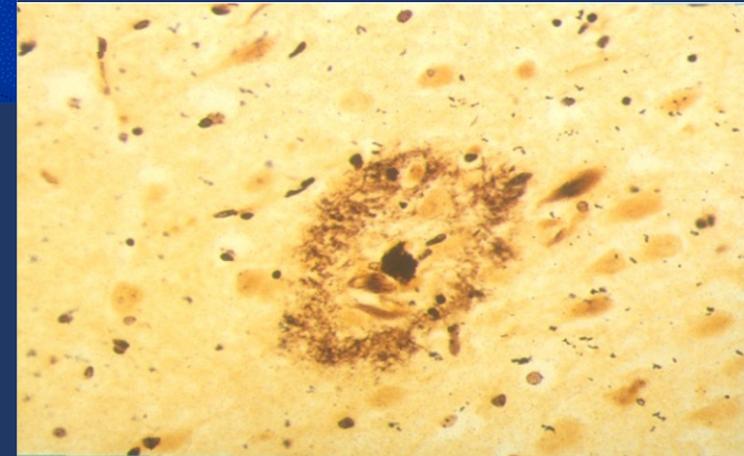
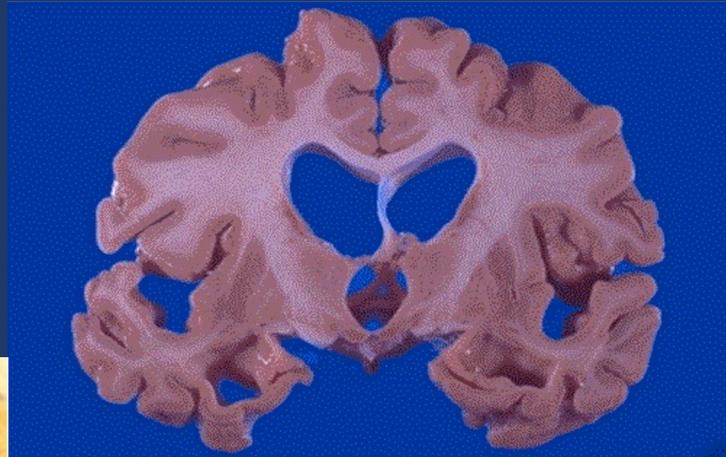
Gestorben am 8. April 1906.

*26. II San. Anstalt d. Irrenanstalt/Main*  
*L. C.*  
*L. C.*  
*Auguste D*  
*L. C.*  
*L. C.*  
*L. C.*  
*L. C.*  
*Frankfurt*



# Alzheimer's Disease

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Neurofibrillary tangles and neuritic amyloid plaques

Dementia is a syndrome  
NOT a disease diagnosis

Dementia means  
severe and multiple cognitive impairments

Dementia is not the same as Alzheimer's Disease

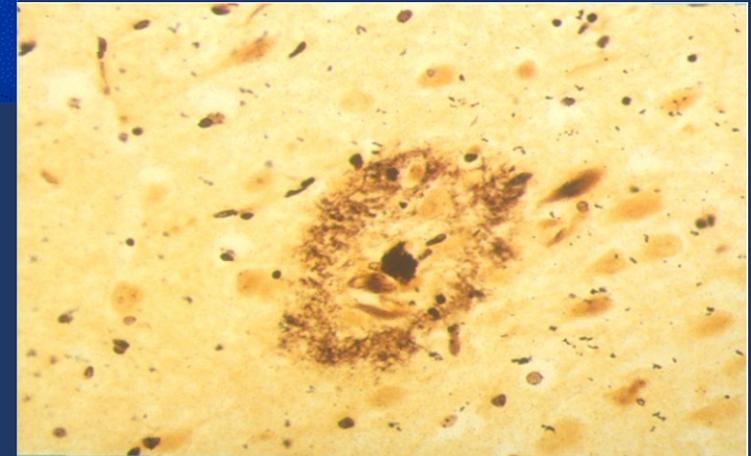
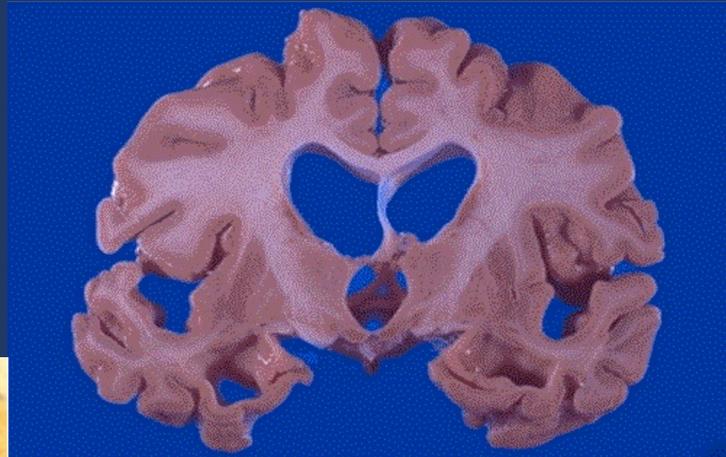
# Definition of Dementia

Dementia is a global impairment of higher cortical function, including memory, the capacity to solve the problems of day-to-day living, the performance of learned perceptuomotor skills, the correct use of social skills and control of emotional reactions, in the absence of gross clouding of consciousness. The condition is often irreversible and progressive.

Royal College of Physicians 1981

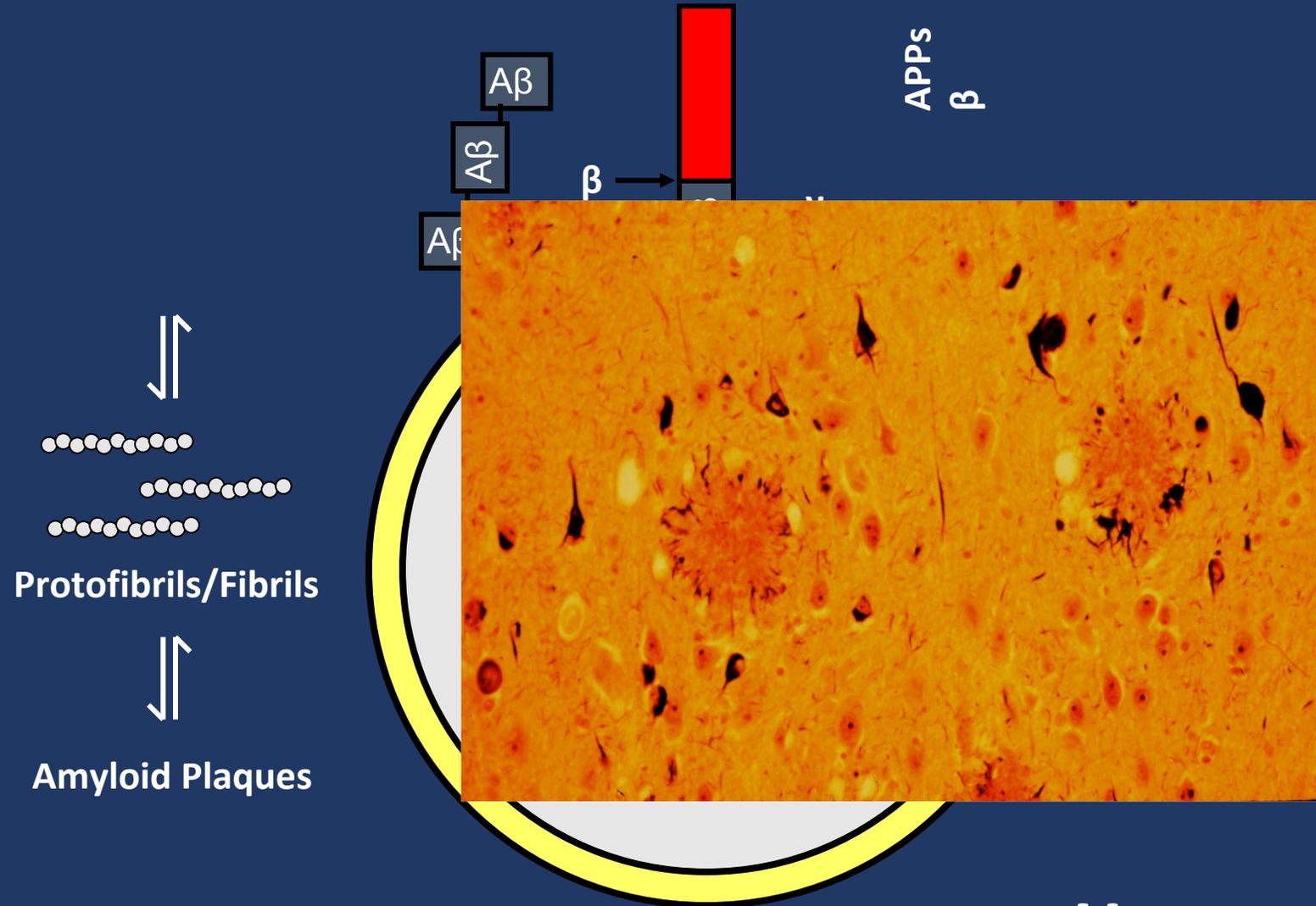
# Alzheimer's Disease

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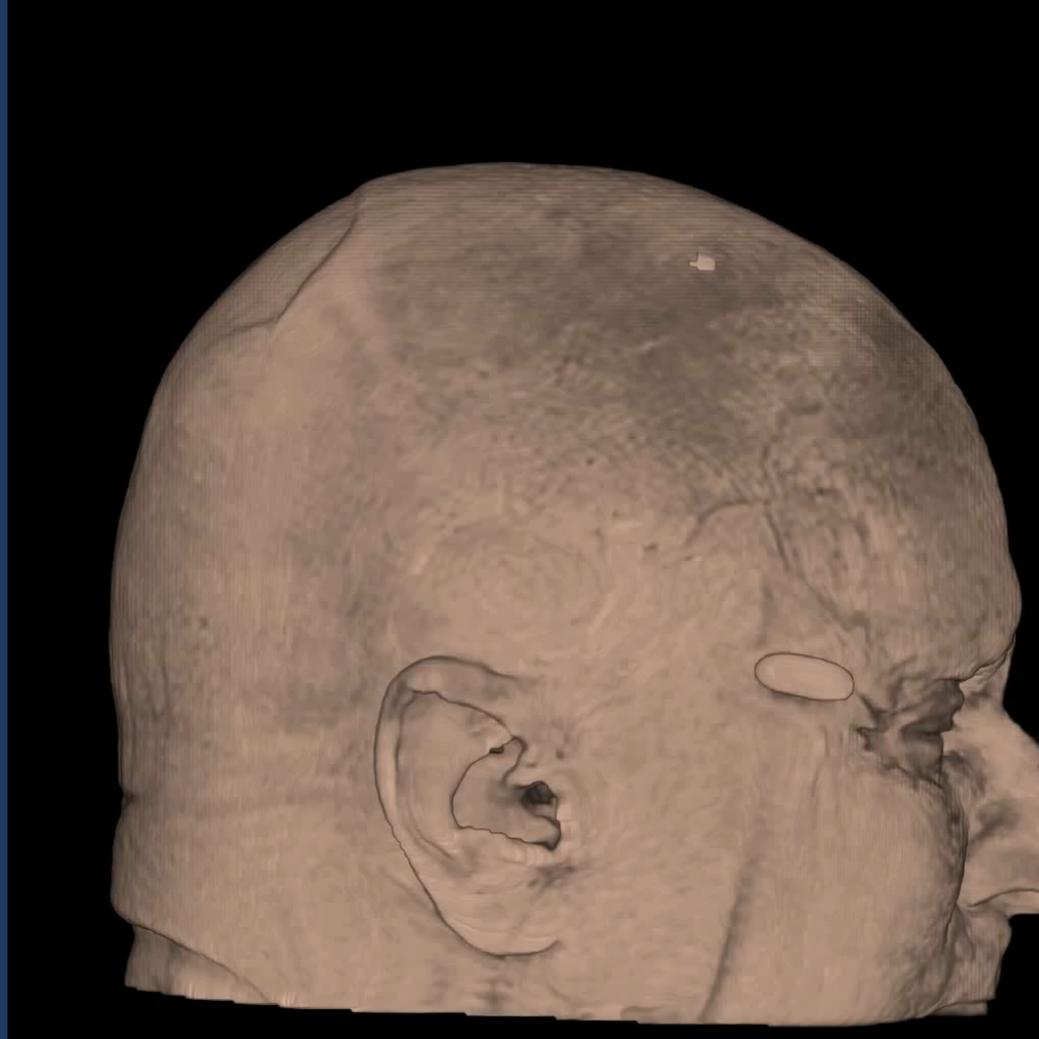
Neurofibrillary tangles and neuritic amyloid plaques

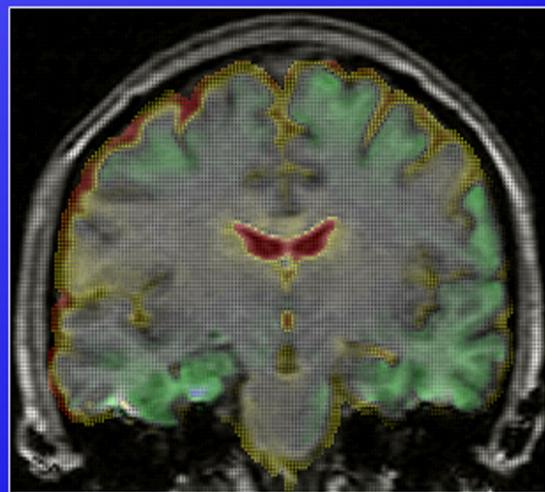
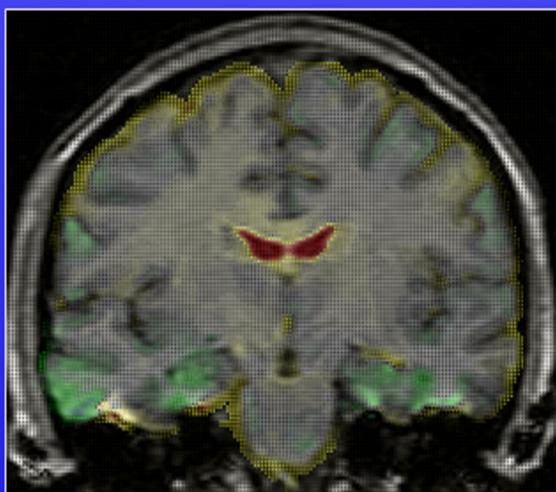
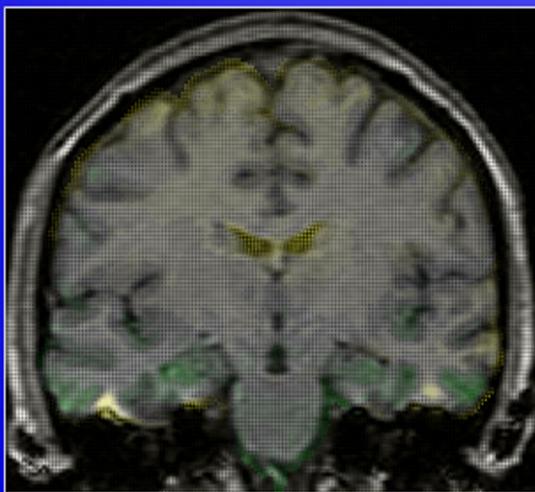
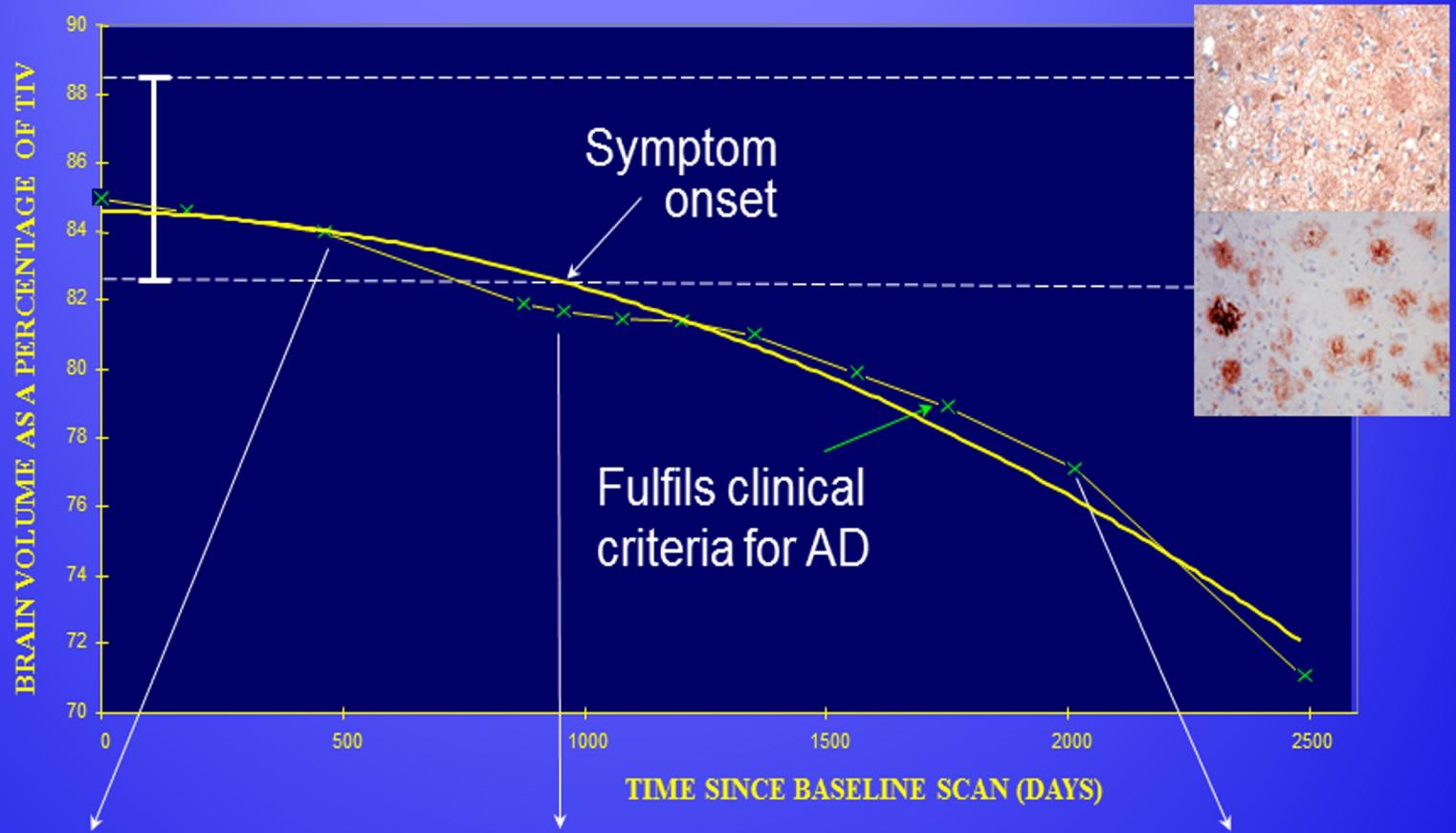
# APP processing, A $\beta$ aggregation, and amyloid pathology



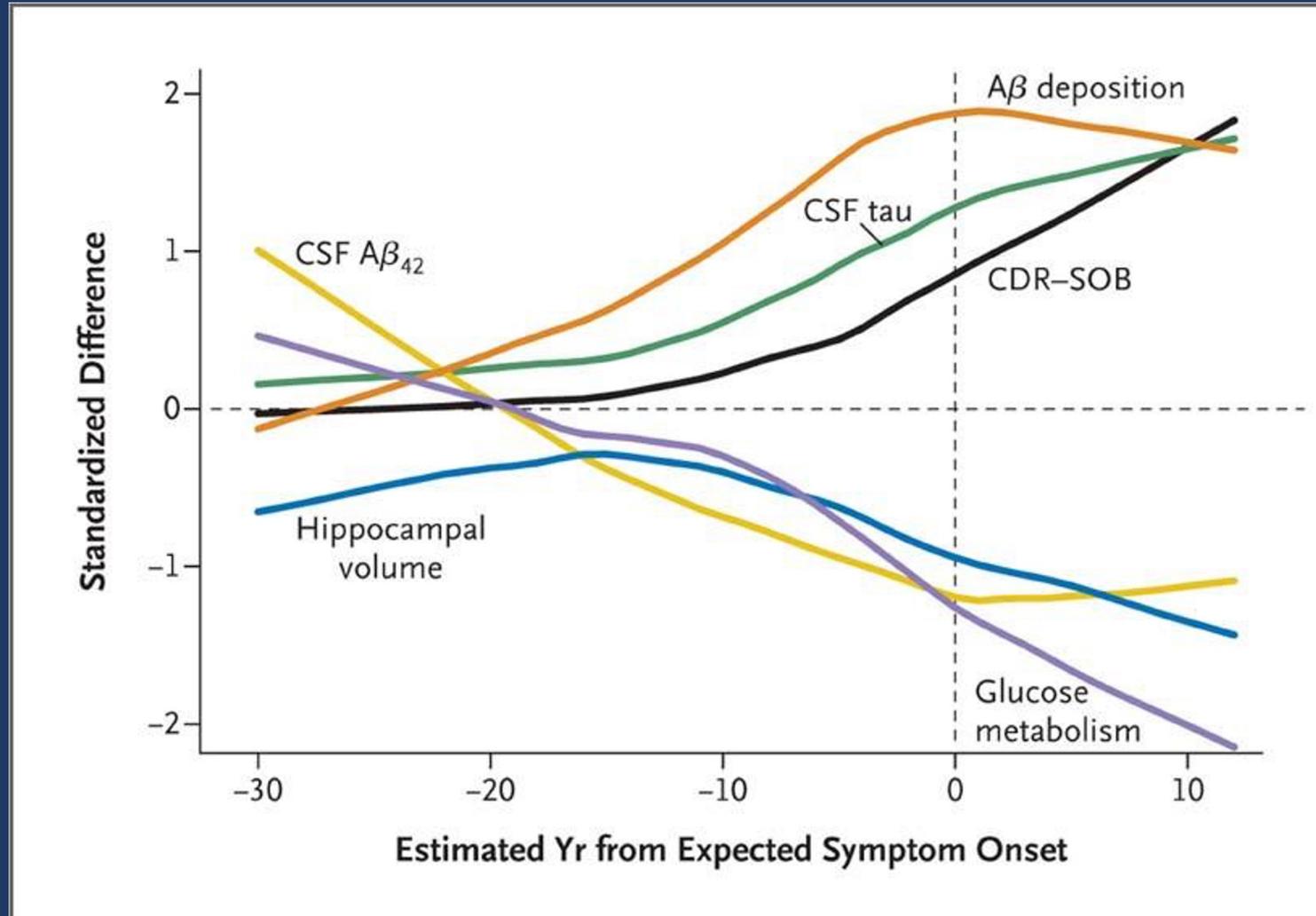
Haass et al

# Alzheimer's Disease – progressive atrophy MR imaging from ADNI data





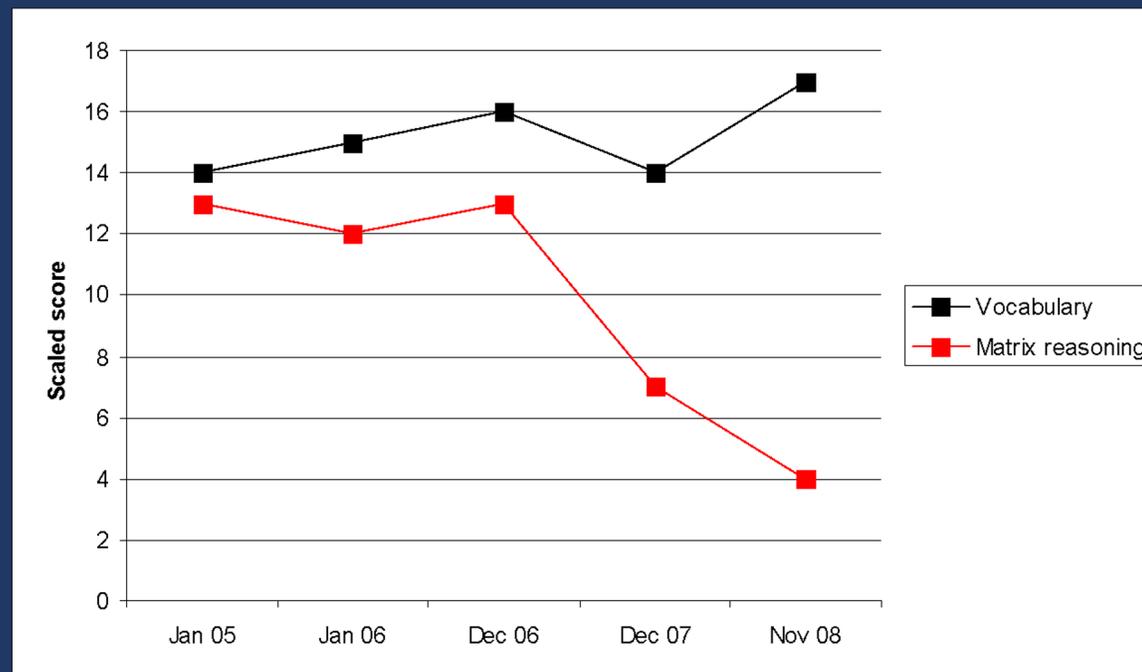
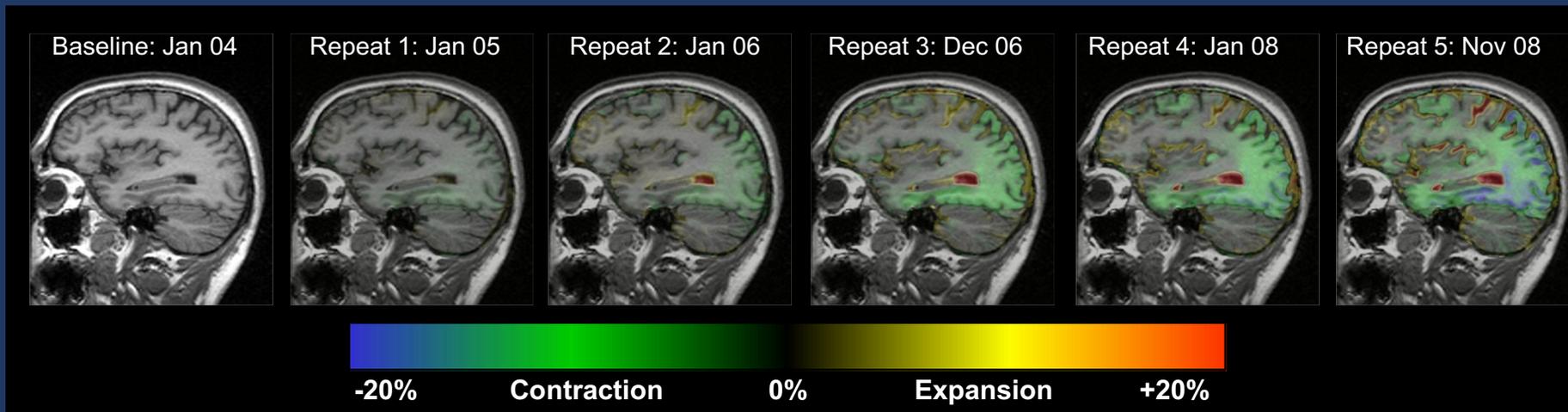
# Comparison of Clinical, Cognitive, Structural, Metabolic, and Biochemical Changes as a Function of Estimated Years from Expected Symptom Onset



Bateman RJ et al. N Engl J Med 2012;367:795-804

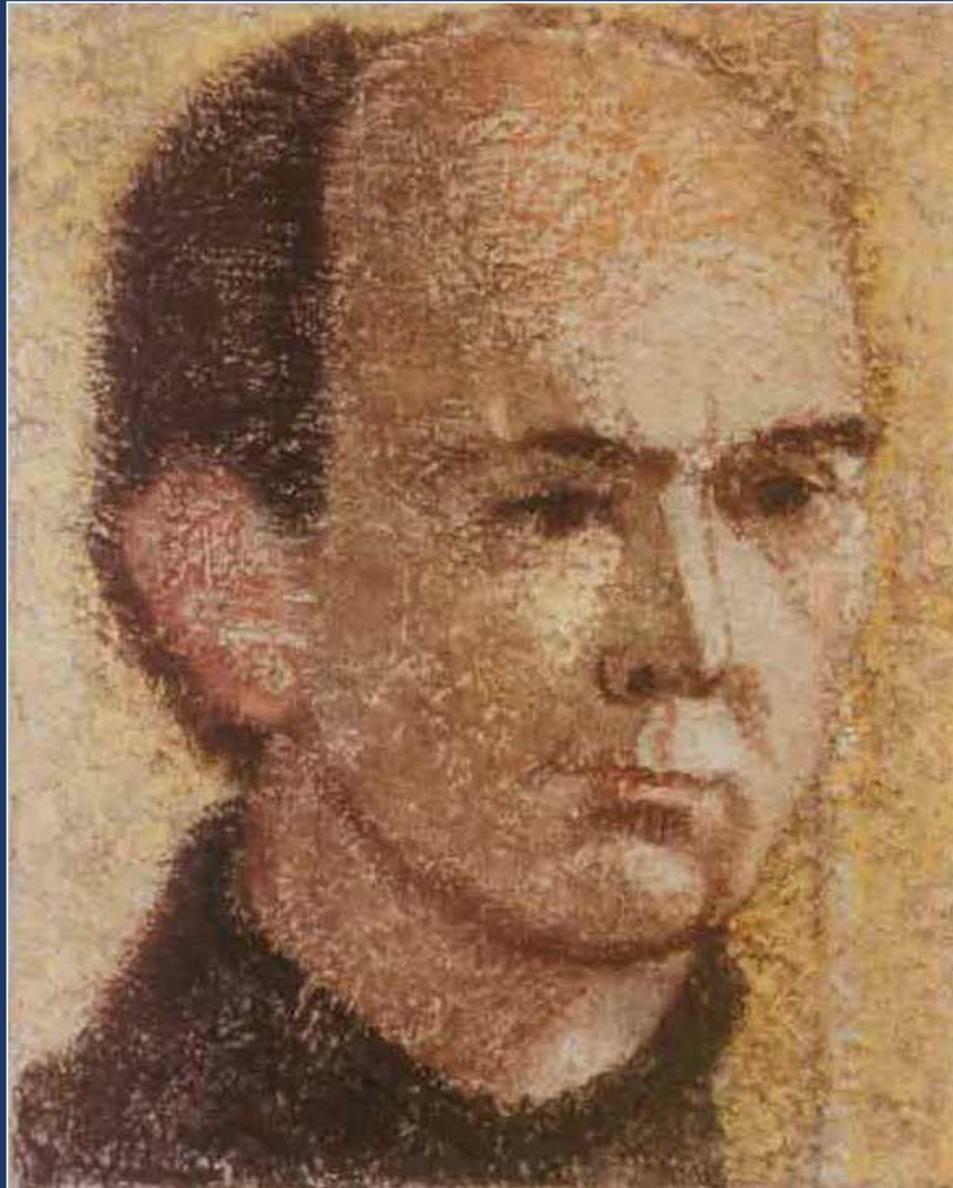


The NEW ENGLAND  
JOURNAL of MEDICINE



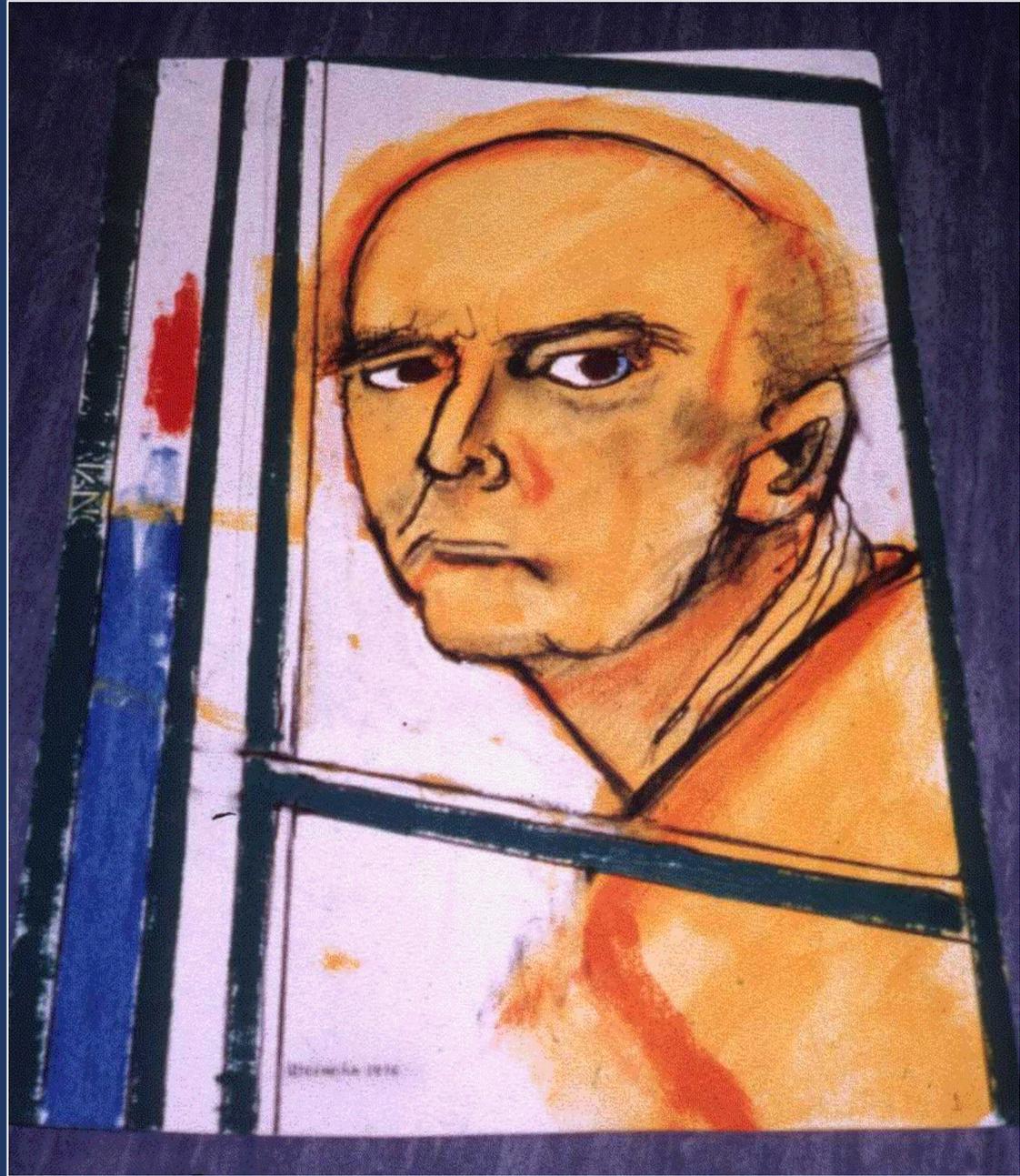


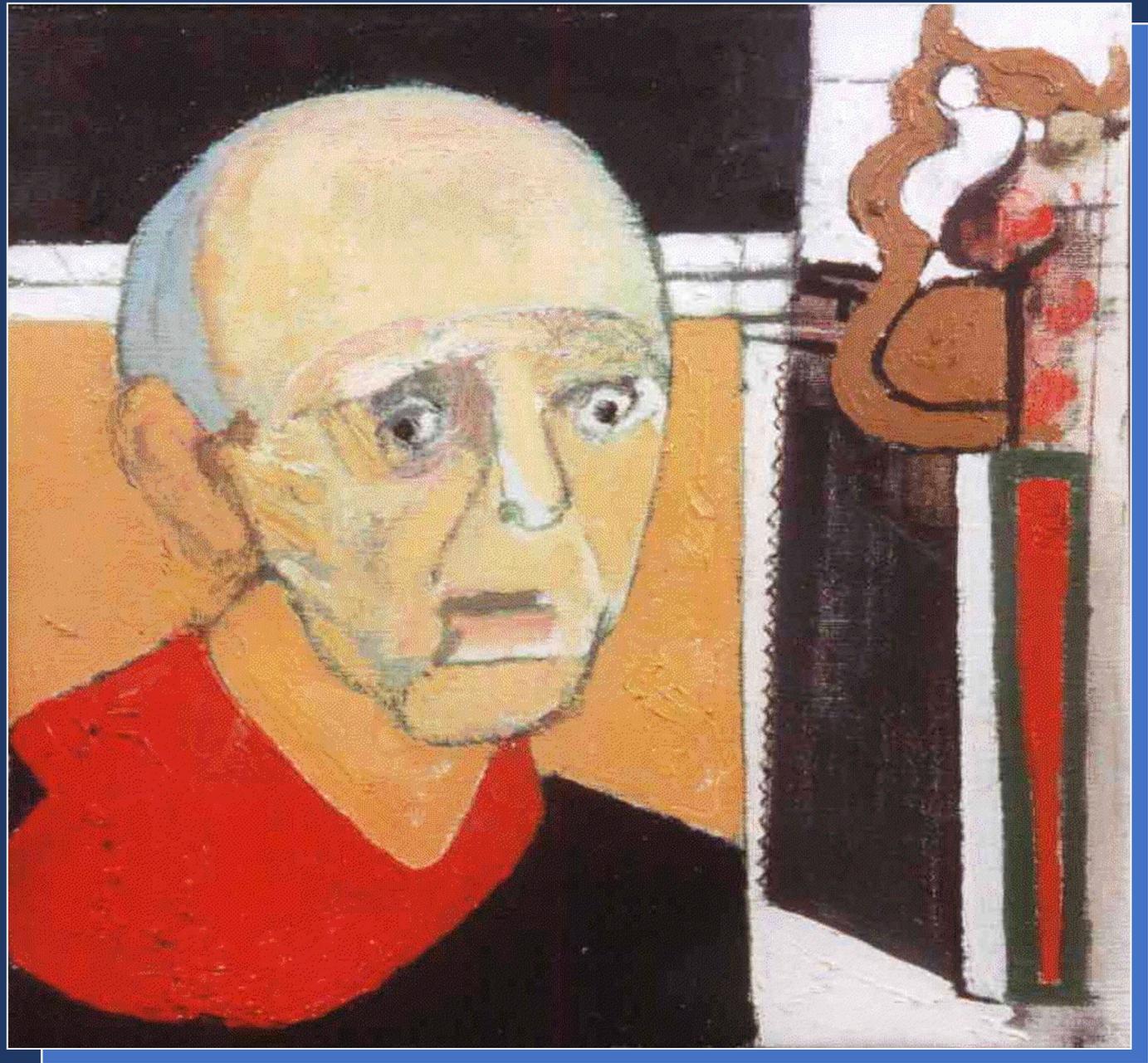


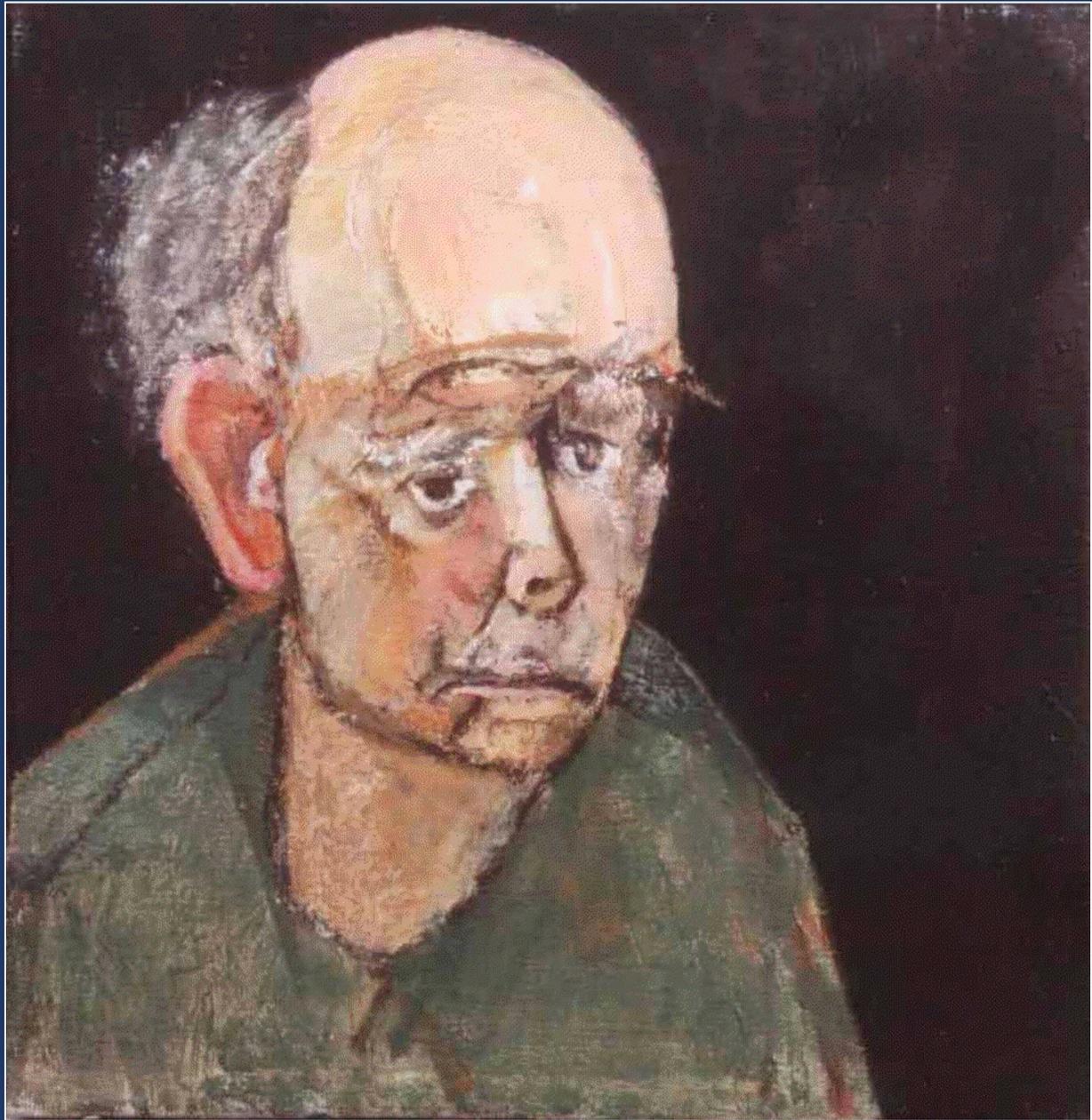


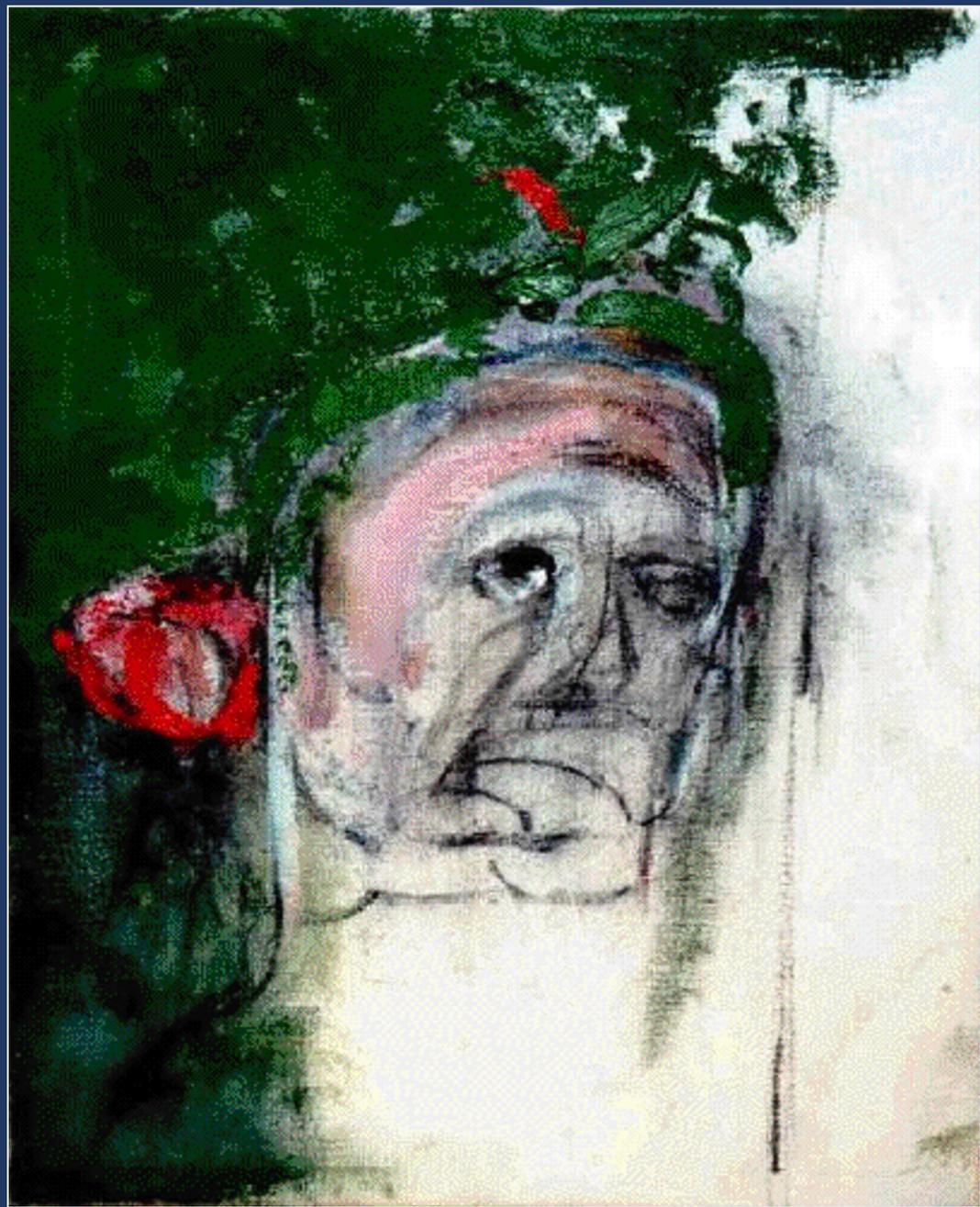
William  
Utermohlen  
1933-2007

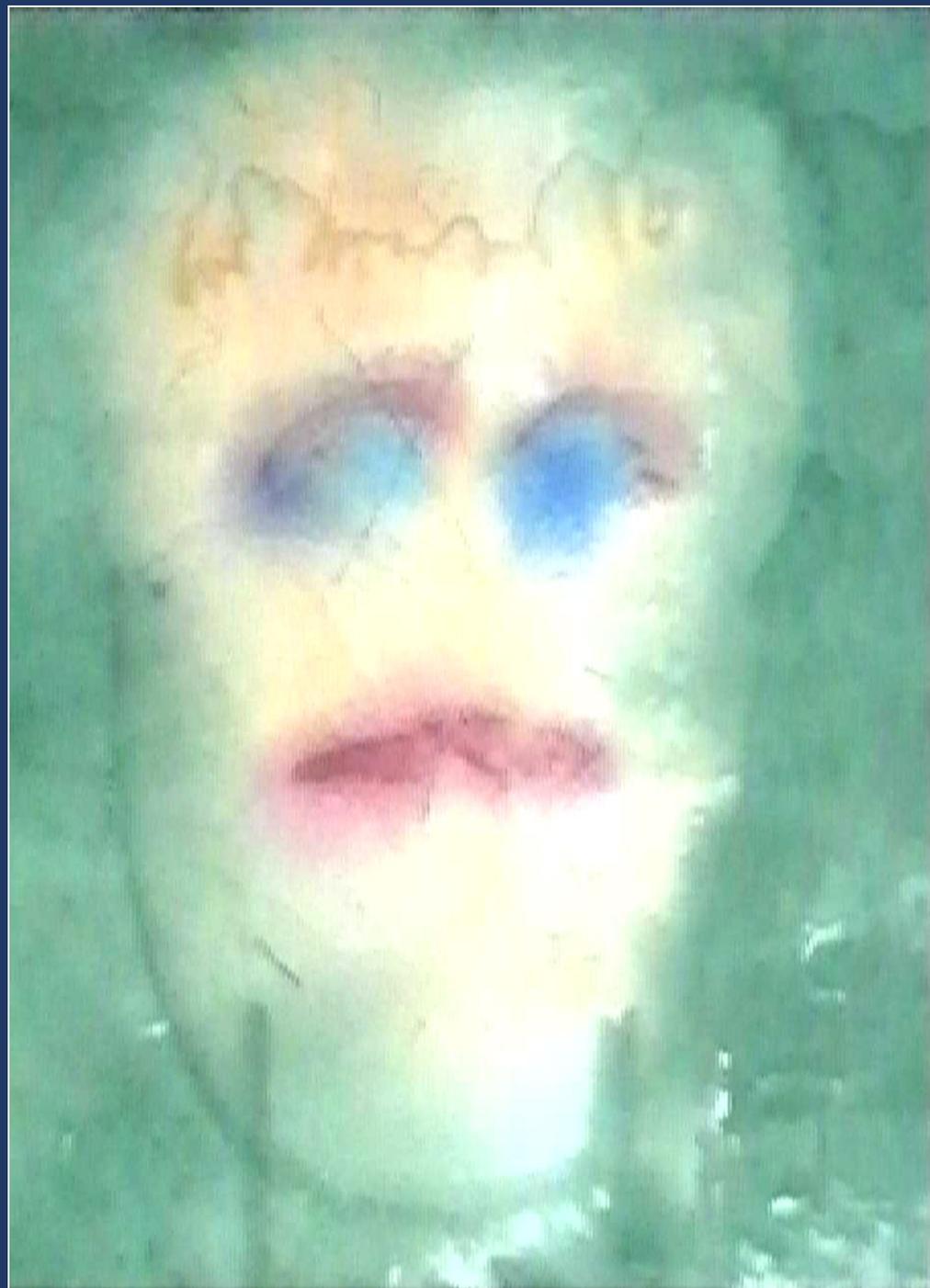
Crutch, Isaacs and Rossor  
Lancet 2001









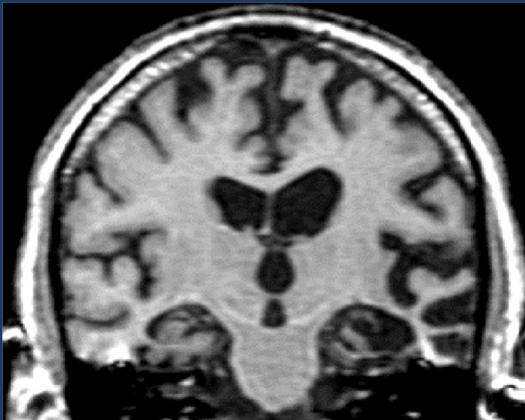
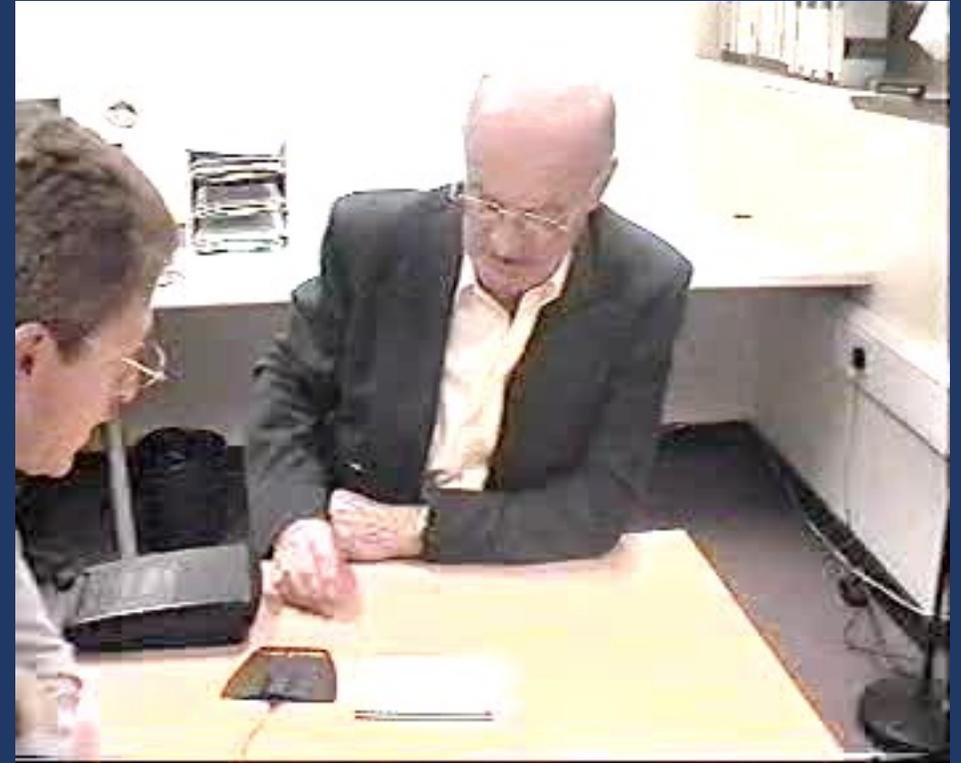


Dementia is a syndrome  
NOT a disease diagnosis

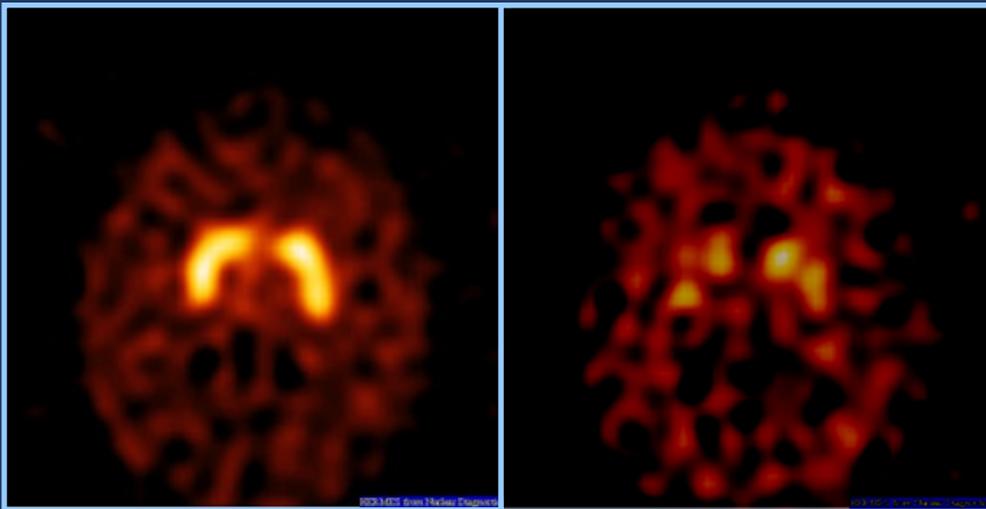
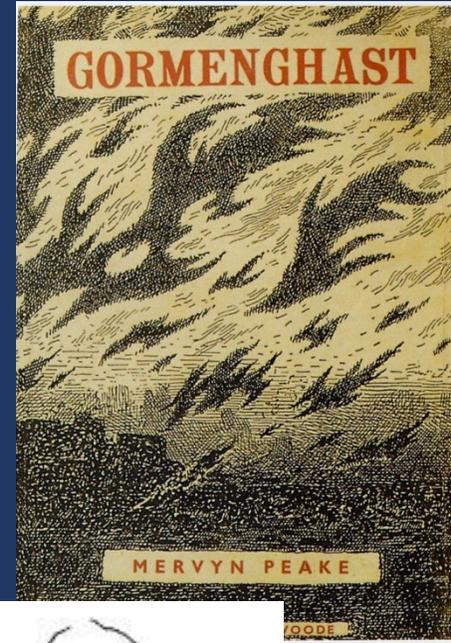
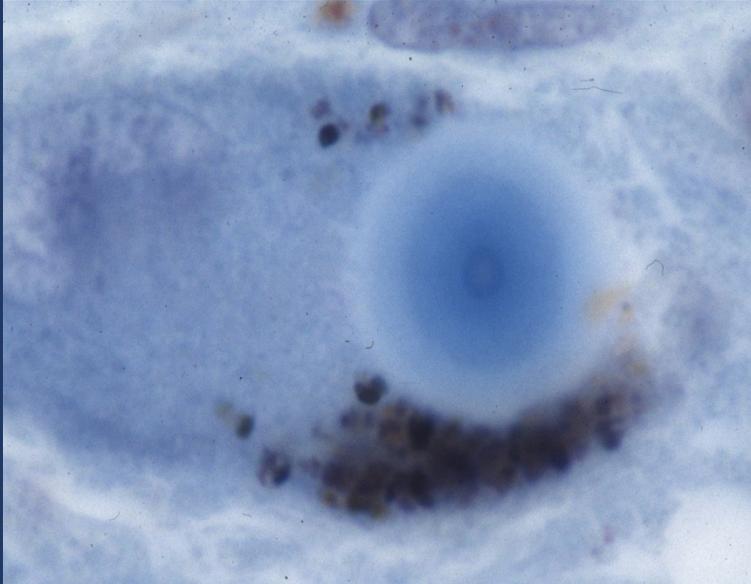
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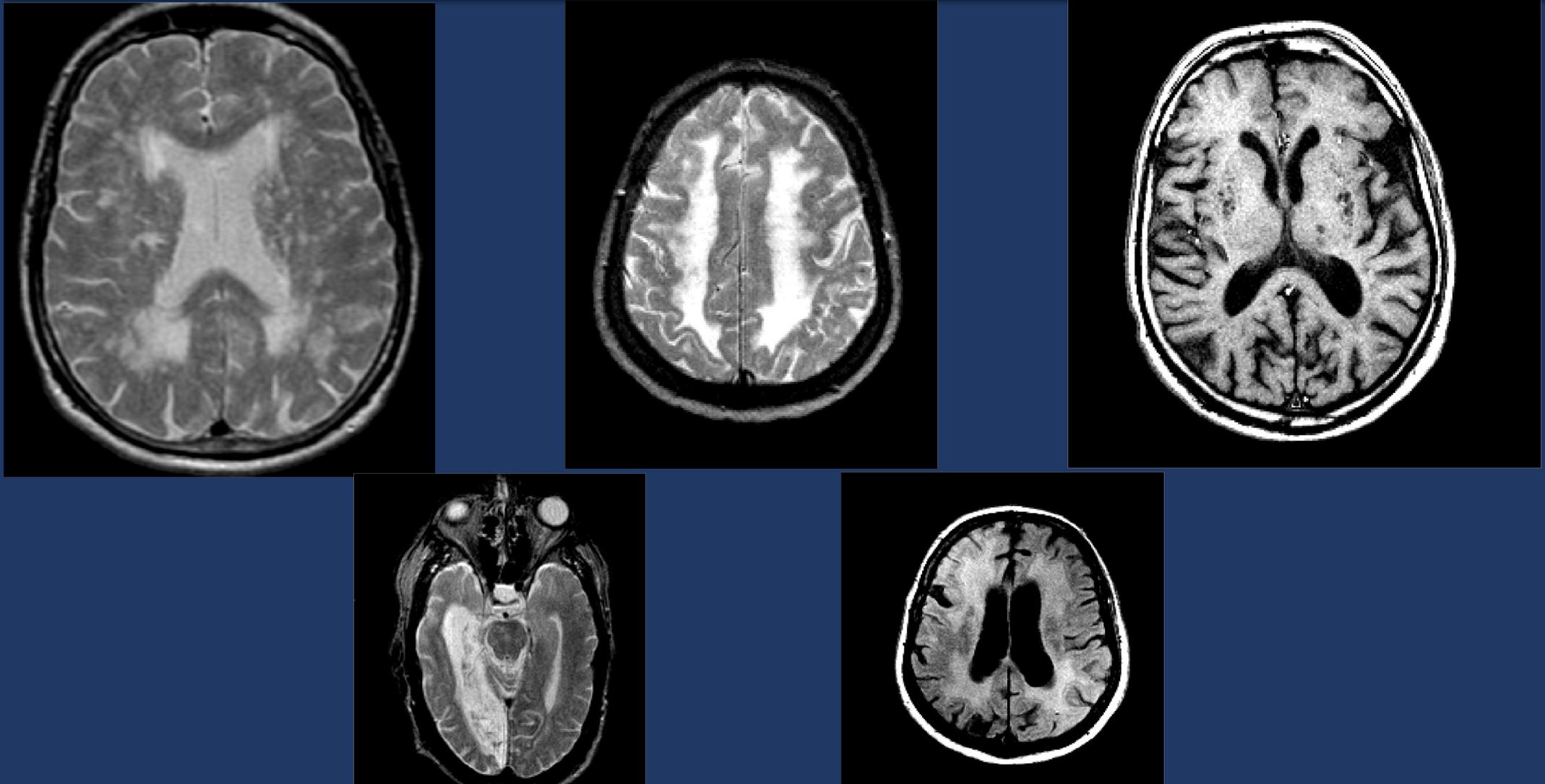
# Semantic Dementia



# Dementia with Lewy Bodies



# Vascular Dementia



## Ockham's Razor



## Hickam's dictum



*Everyone complains of their memory*

*....but none of their judgment*

Duc de La Rochefoucauld

# Forgetting as a form of adaptive engram cell plasticity

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Tomás J. Ryan  and Paul W. Frankland 

**Abstract** | One leading hypothesis suggests that memories are stored in ensembles of neurons (or ‘engram cells’) and that successful recall involves reactivation of these ensembles. A logical extension of this idea is that forgetting occurs when engram cells cannot be reactivated. Forms of ‘natural forgetting’ vary considerably in terms of their underlying mechanisms, time course and reversibility. However, we suggest that all forms of forgetting involve circuit remodelling that switches engram cells from an accessible state (where they can be reactivated by natural recall cues) to an inaccessible state (where they cannot). In many cases, forgetting rates are modulated by environmental conditions and we therefore propose that forgetting is a form of neuroplasticity that alters engram cell accessibility in a manner that is sensitive to mismatches between expectations and the environment. Moreover, we hypothesize that disease states associated with forgetting may hijack natural forgetting mechanisms, resulting in reduced engram cell accessibility and memory loss.

Nature Reviews  
Neuroscience  
Volume 23  
March 2022

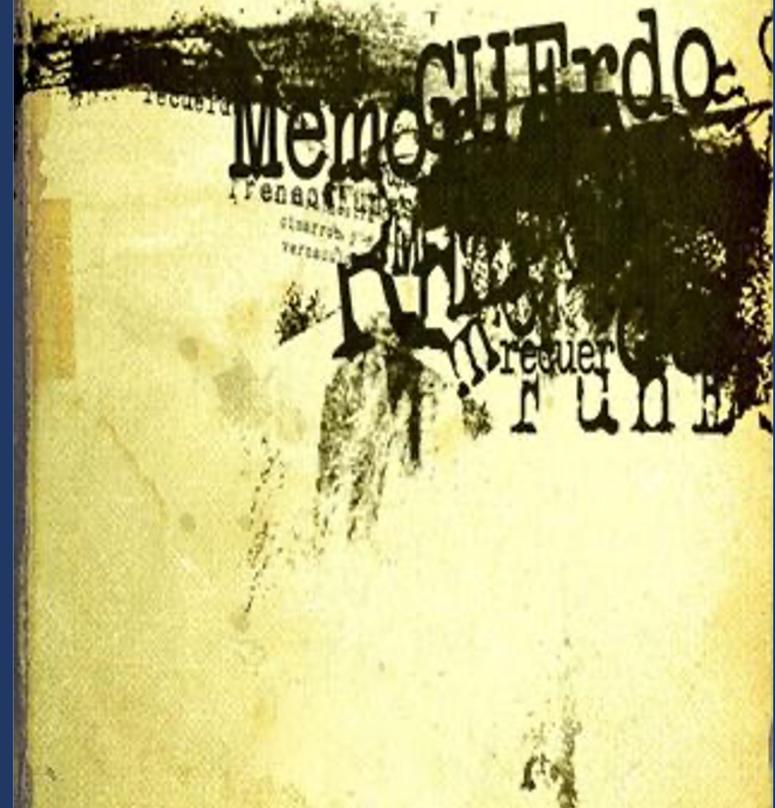


Penguin Modern Classics

**Jorge Luis Borges**  
**Labyrinths**

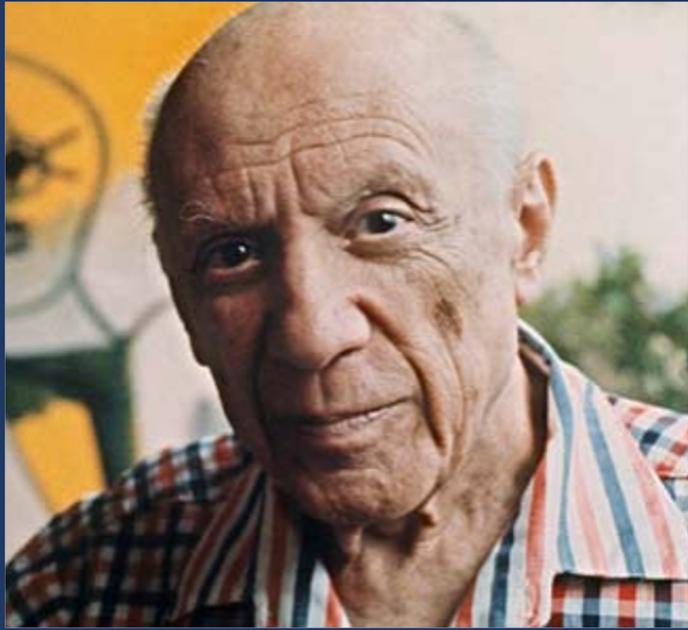


Jorge Luis Borges  
Funes el memorioso



Jeanne Calment 1875-1997





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**HEALTHY HEADING IS KEY TO FIGHTING DEMENTIA**

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# THE LANCET

July 2017

www.thelancet.com

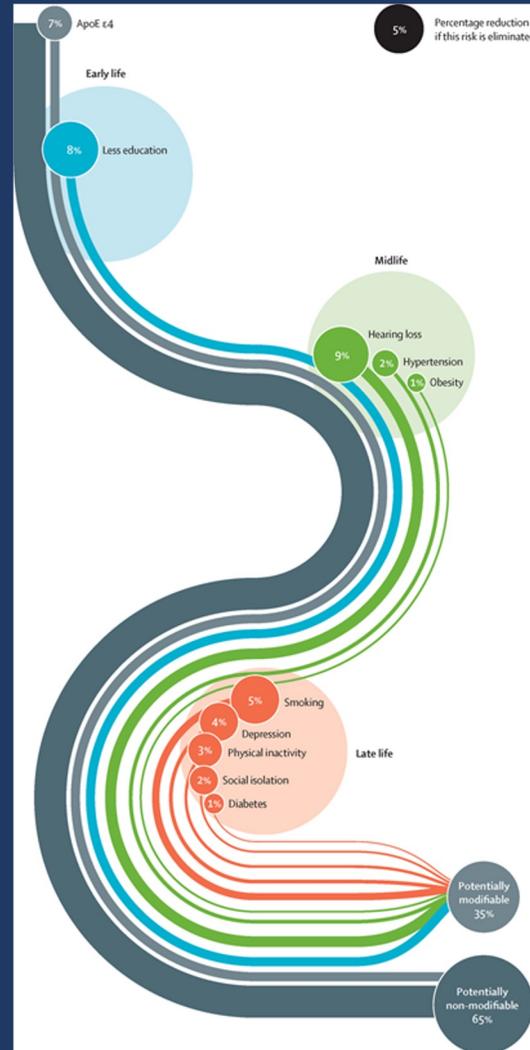
## The Lancet Commission on dementia



“Effective dementia prevention, intervention, and care could transform the future for society and vastly improve living and dying for individuals with dementia and their families. Acting now on what we already know can make this difference happen.”

A Commission by The Lancet

Lancet. 2017 Jul 19. doi: 10.1016/S0140-6736(17)31363-6



## The Lancet Commission: Potentially modifiable risk factors

### Dementia prevention, intervention, and care

	Relative risk for dementia (95% CI)	Prevalence	Community	PAF	Weighted PAF*
<b>Early life (age &lt;18 years)</b>					
Less education (none or primary school only)	1.6 (1.26–2.01)	40.0%	64.6%	19.1%	7.5%
<b>Midlife (age 45–65 years)</b>					
Hypertension	1.6 (1.16–2.24)	8.9%	57.3%	5.1%	2.0%
Obesity	1.6 (1.34–1.92)	3.4%	60.4%	2.0%	0.8%
Hearing loss	1.9 (1.38–2.73)	31.7%	46.1%	23.0%	9.1%
<b>Later life (age &gt;65 years)</b>					
Smoking	1.6 (1.15–2.20)	27.4%	51.1%	13.9%	5.5%
Depression	1.9 (1.55–2.33)	13.2%	58.6%	10.1%	4.0%
Physical inactivity	1.4 (1.16–1.67)	17.7%	26.6%	6.5%	2.6%
Social isolation	1.6 (1.32–1.85)	11.0%	45.9%	5.9%	2.3%
Diabetes	1.5 (1.33–1.79)	6.4%	70.3%	3.2%	1.2%

Data are relative risk (95% CI) or %. Total weighted PAF and population attributable fraction. \*Weighted PAF is the relative contribution of each risk factor.

Population Attributable Fraction = 35%

Table 1: Potentially modifiable risk factors for dementia

# Age-specific incidence rates been falling in some countries

## A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II

*Fiona E Matthews, Antony Arthur, Linda E Barnes, John Bond, Carol Jagger, Louise Robinson, Carol Brayne, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration*

Lancet 2013; 382: 1405–12

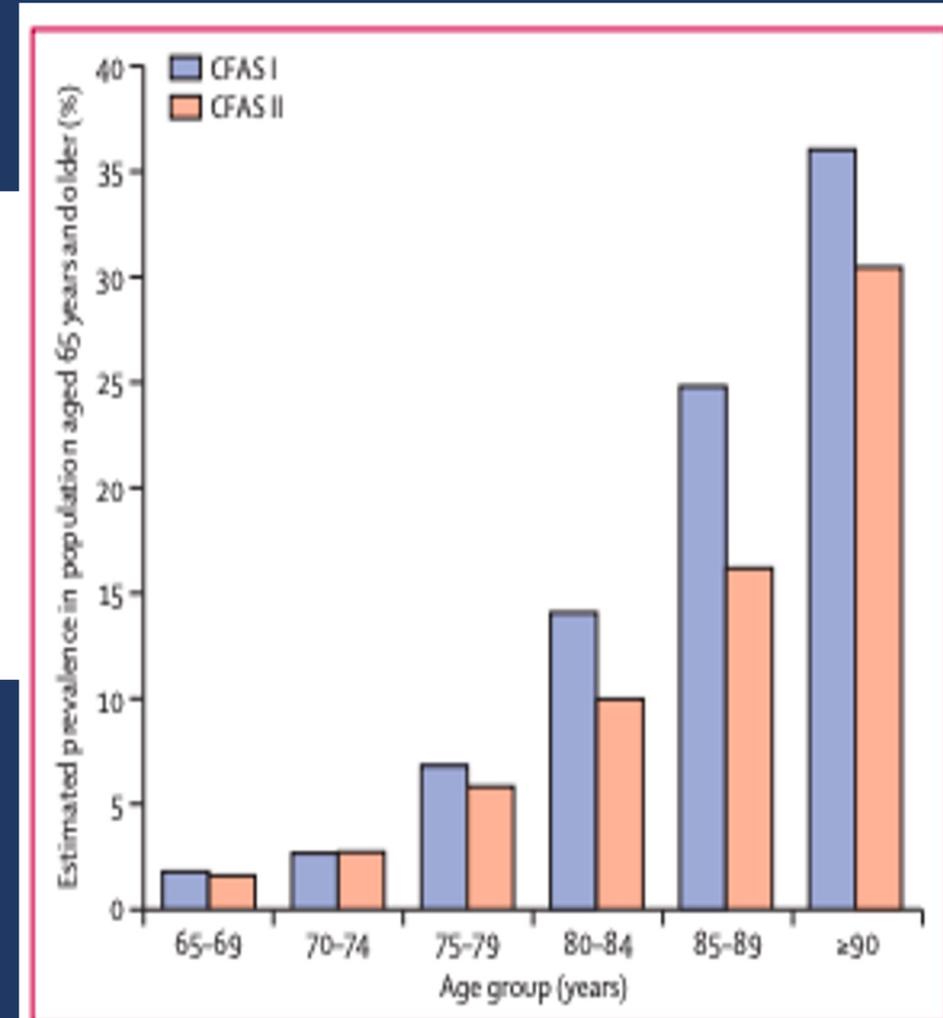
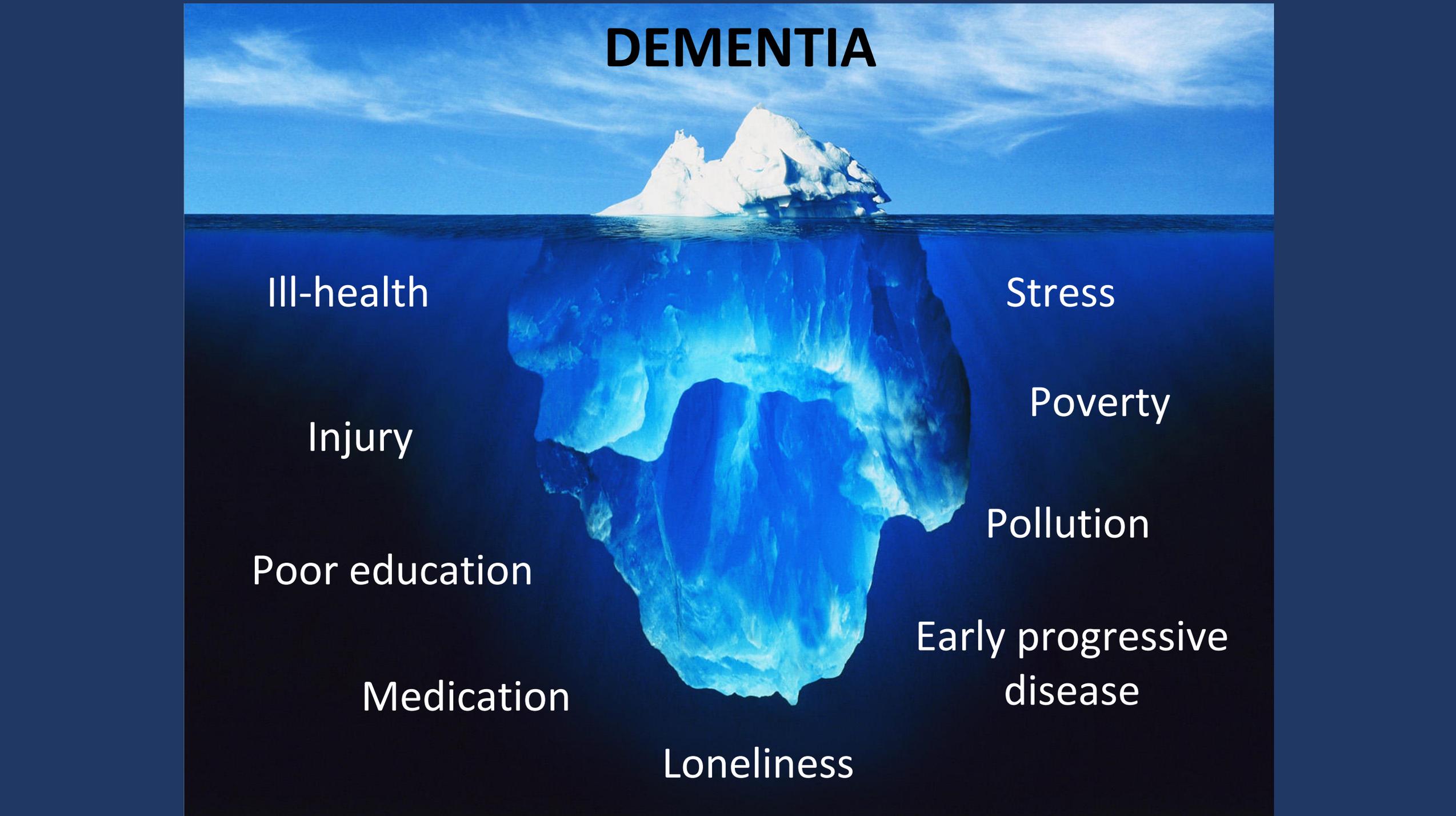


Figure 1: CFAS I and CFAS II age-specific dementia prevalence  
CFAS=Cognitive Function and Ageing Study.

# DEMENTIA

An iceberg floating in a blue ocean under a blue sky with light clouds. The tip of the iceberg is above the water line, while the much larger, submerged part is below. The submerged part is labeled with various risk factors for dementia. The water is a deep blue, and the sky is a lighter blue with wispy clouds.

Ill-health

Stress

Injury

Poverty

Poor education

Pollution

Medication

Early progressive  
disease

Loneliness

# Cognitive Health

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- Protect Head
- Do not smoke
- Diet
- Wine
- Sleep
- Meditation/relaxation
- Exercise: physical and mental
- Curiosity

# Is Dementia Inevitable?

Professor Martin Rossor  
UCL Institute of Neurology

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Gresham lecture  
5 April 2022

