

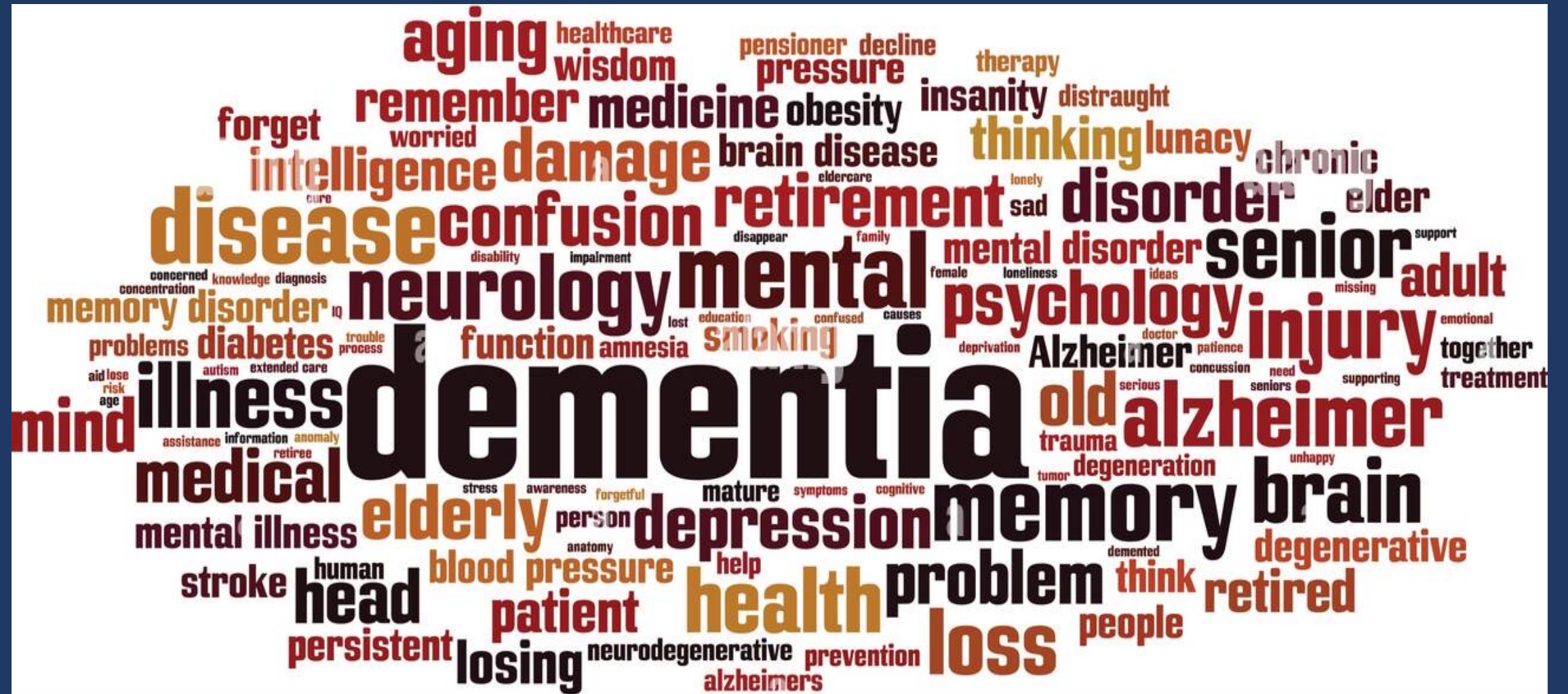
Is Dementia Inevitable?

Professor Martin Rossor

UCL Institute of Neurology

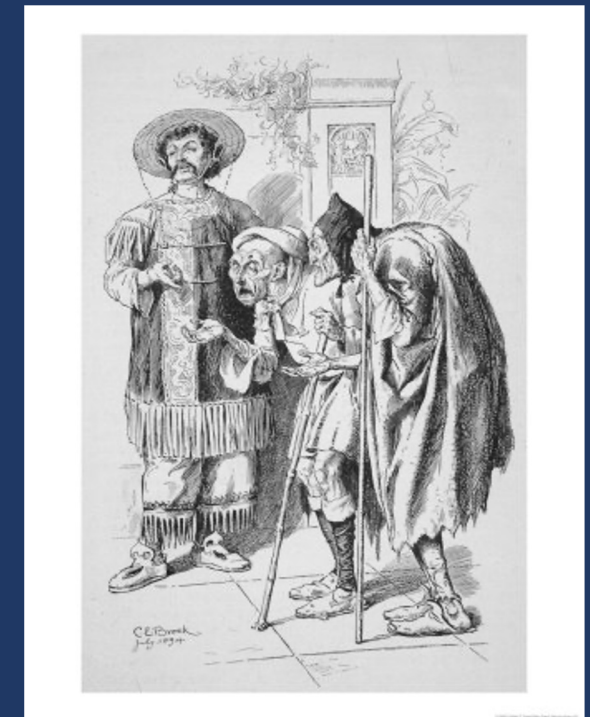
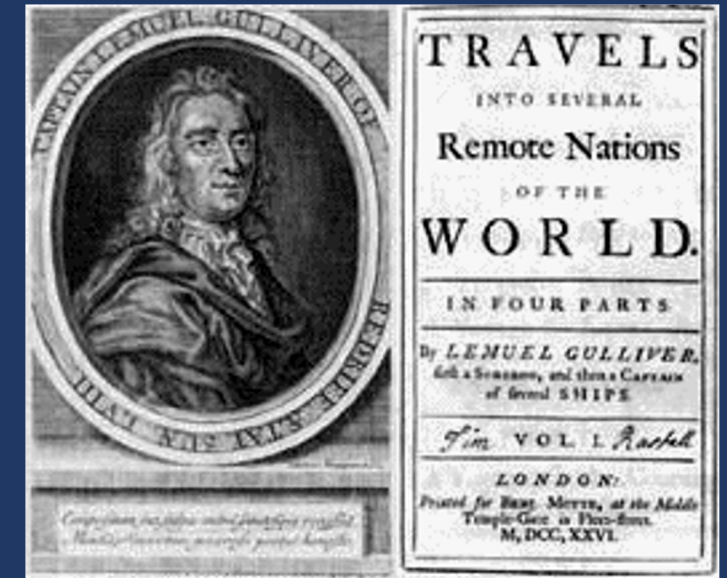
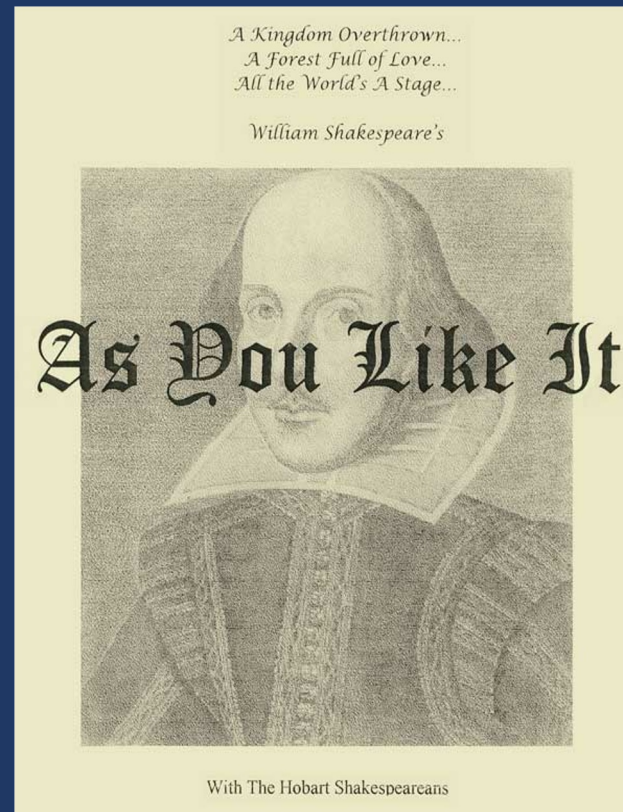
Gresham lecture
5 April 2022







Ptah-hotep Egyptian 5th 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.

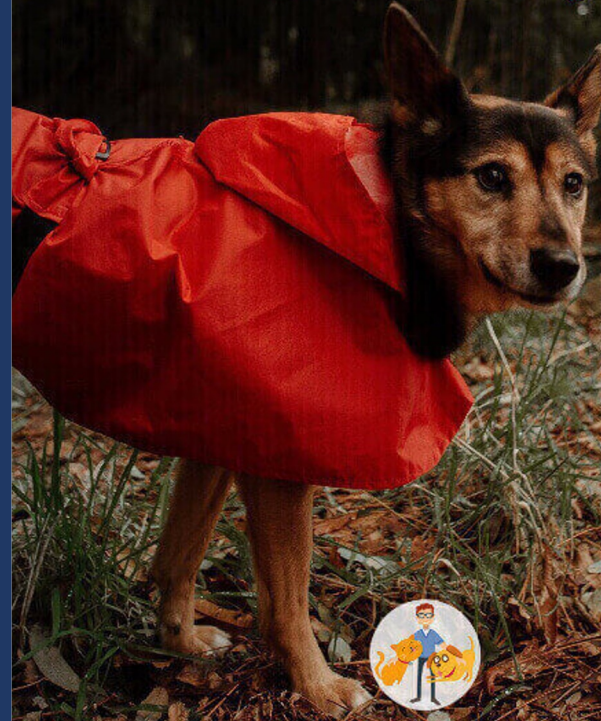
Last scene of all, that ends this
strange eventful history, is second
childishness and mere oblivion, sans
teeth, sans eyes, sans taste, sans
everything.

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		
		TOTAL	235

A Treatise on Insanity - Esquirol, 1845



Städt. Irren-Anstalt Frankfurt a. M.

No. _____

Aerztliche Acten

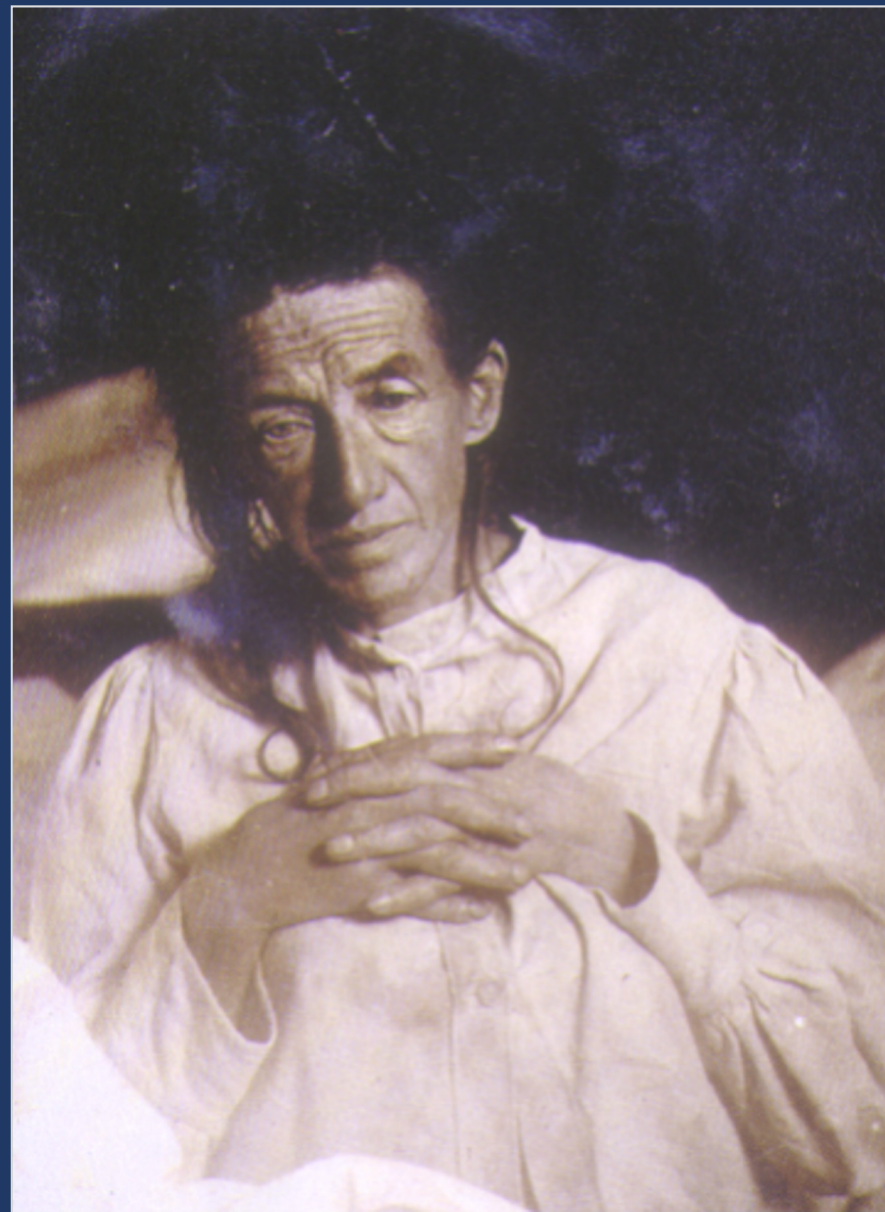
über

Auguste *D* geb. *SD*
 Alter: 31 Jahre. Religion: *evangelisch*

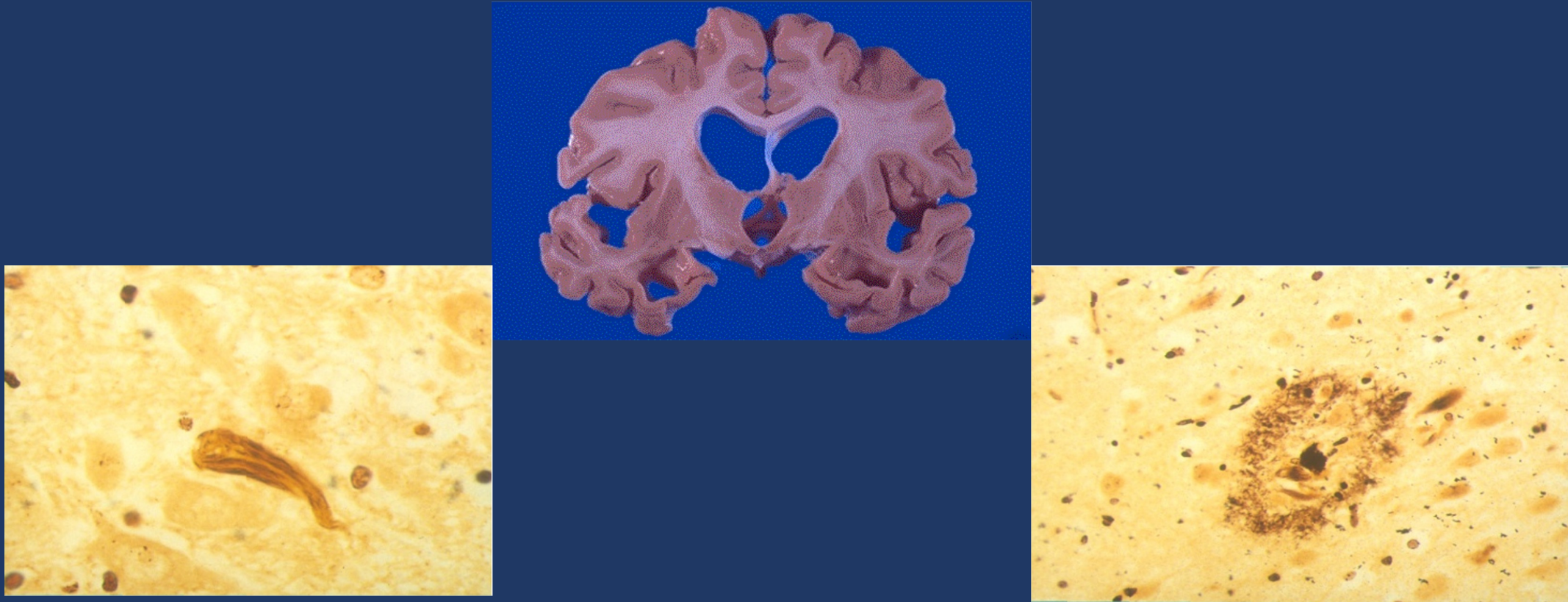
Tag No.	Aufgenommen	Entlassen
1.	am 25. November 1901	
2.	"	"
3.	"	"
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6.	"	"
7.	"	"
8.	"	"
9.	"	"
10.	"	"
11.	"	"
12.	"	"

Gestorben am 8. April 1902.

26. II. Frau Auguste D. Frankfurt/Main
 für
 Auguste D.
 für
 für
 für
 für
 Frankfurt



Alzheimer's Disease



Neurofibrillary tangles and neuritic amyloid plaques

Dementia is a syndrome
NOT a disease diagnosis

Dementia means
severe and multiple cognitive impairments

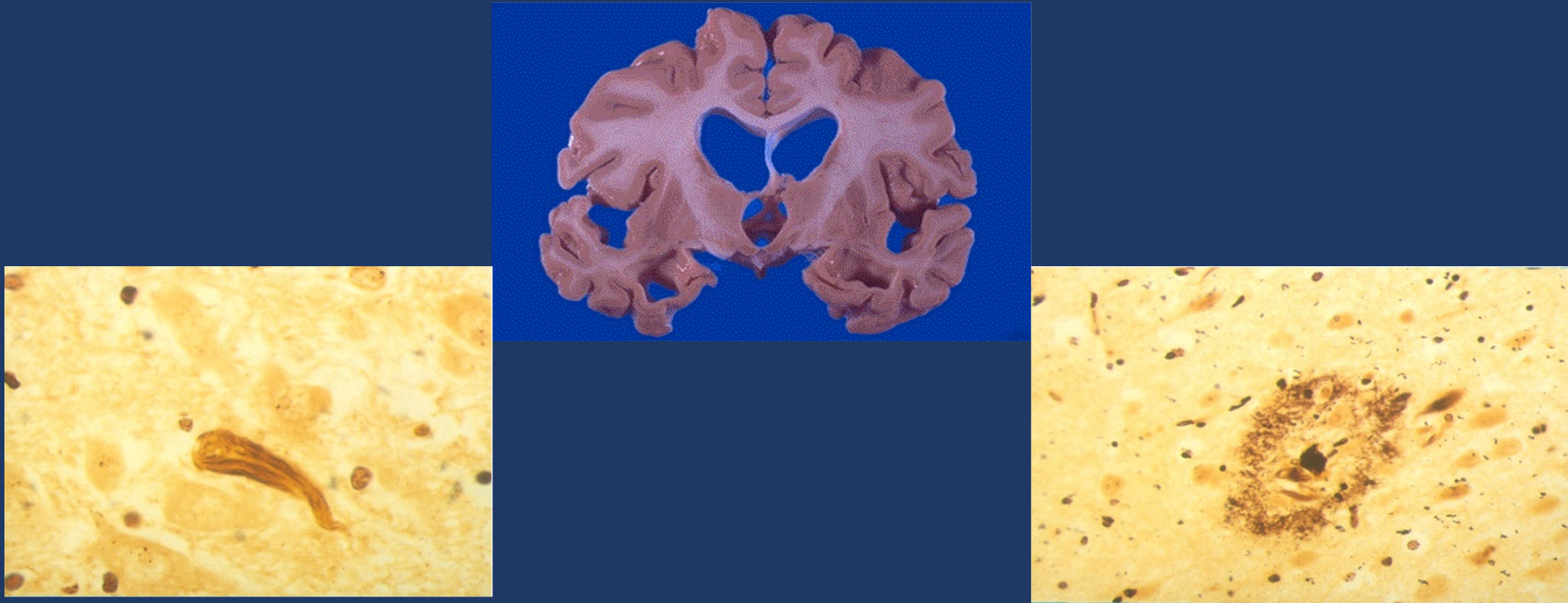
Dementia is not the same as Alzheimer's Disease

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.

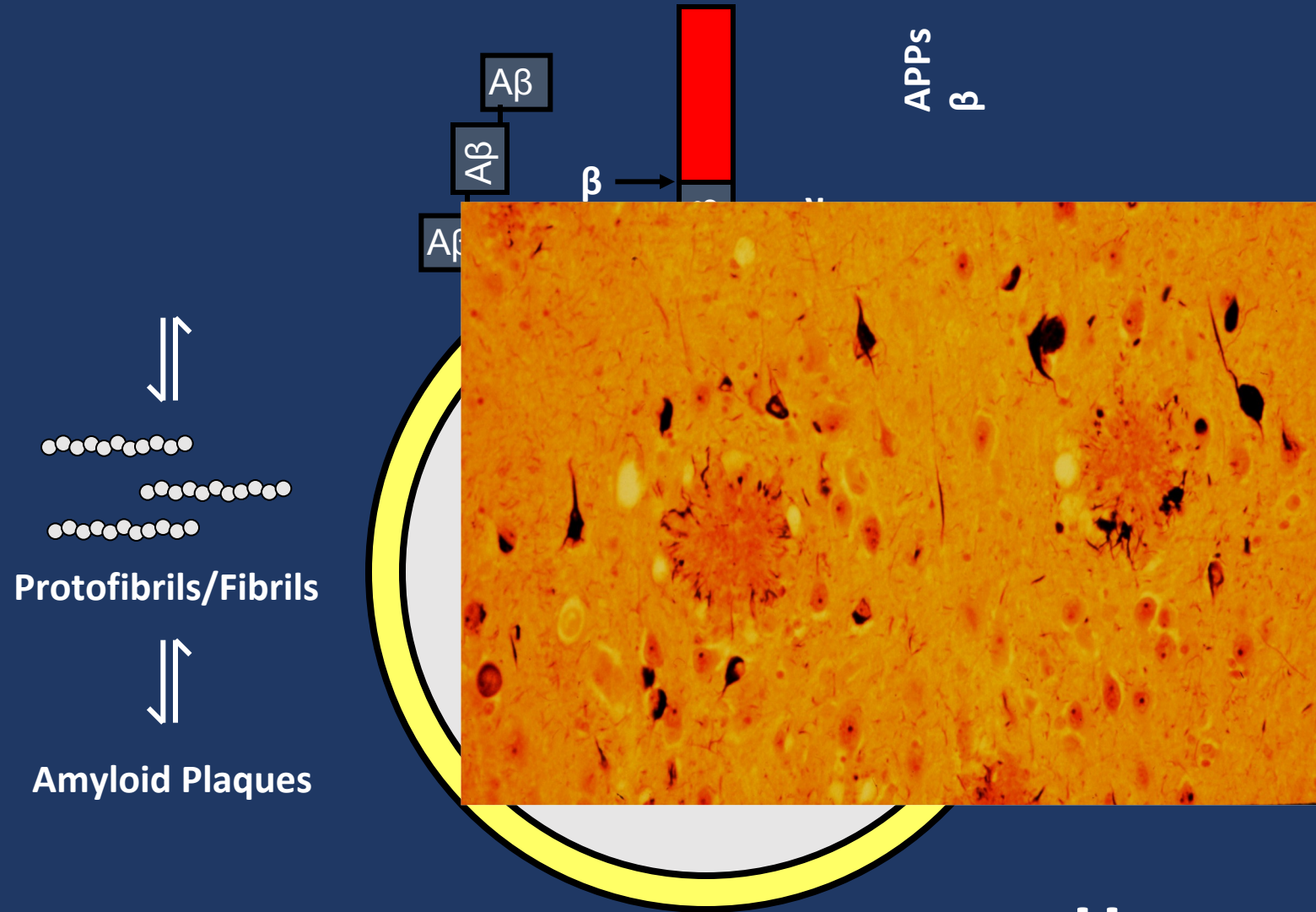
Royal College of Physicians 1981

Alzheimer's Disease



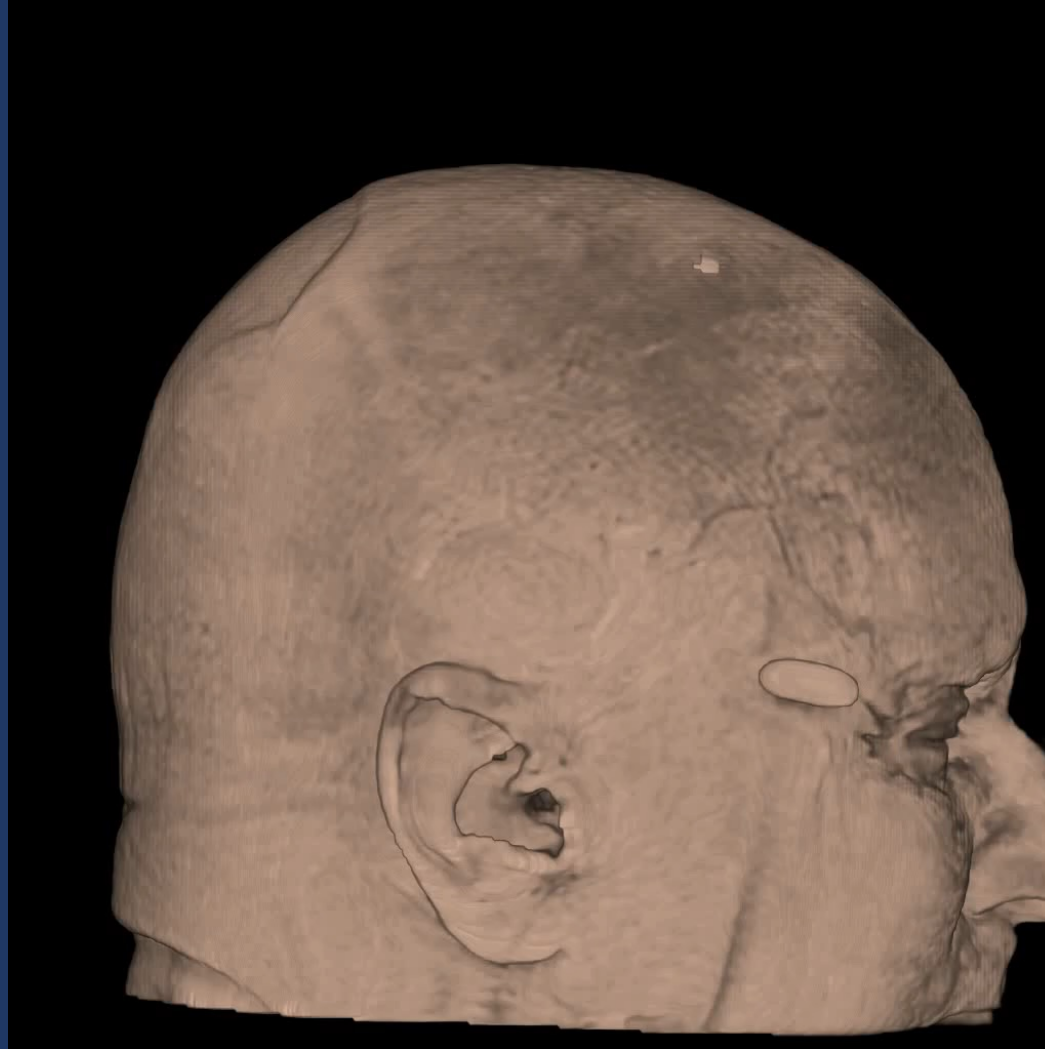
Neurofibrillary tangles and neuritic amyloid plaques

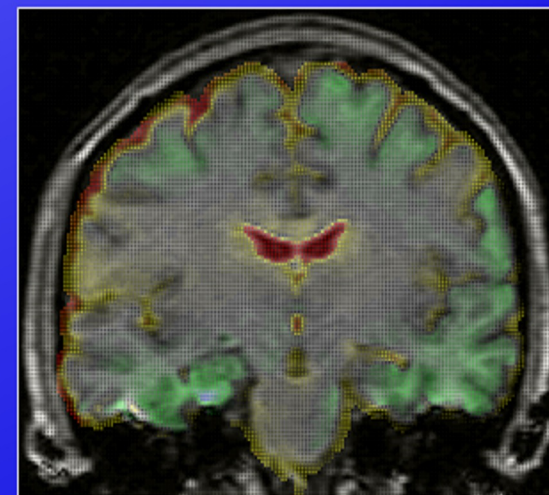
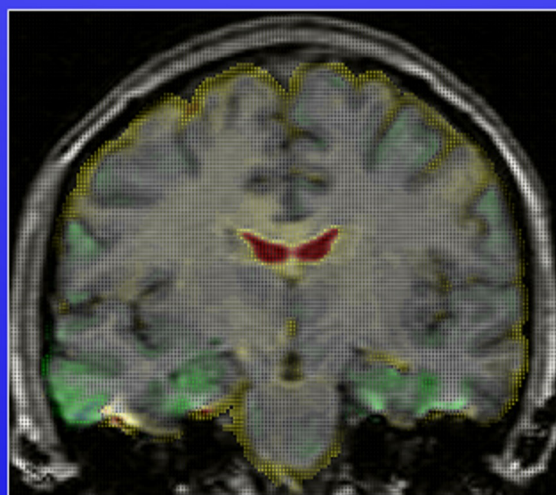
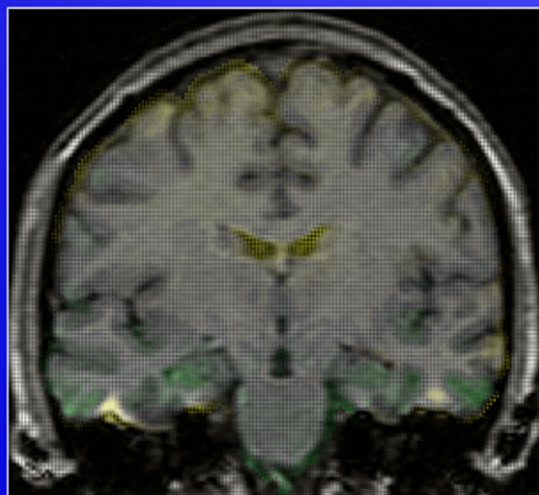
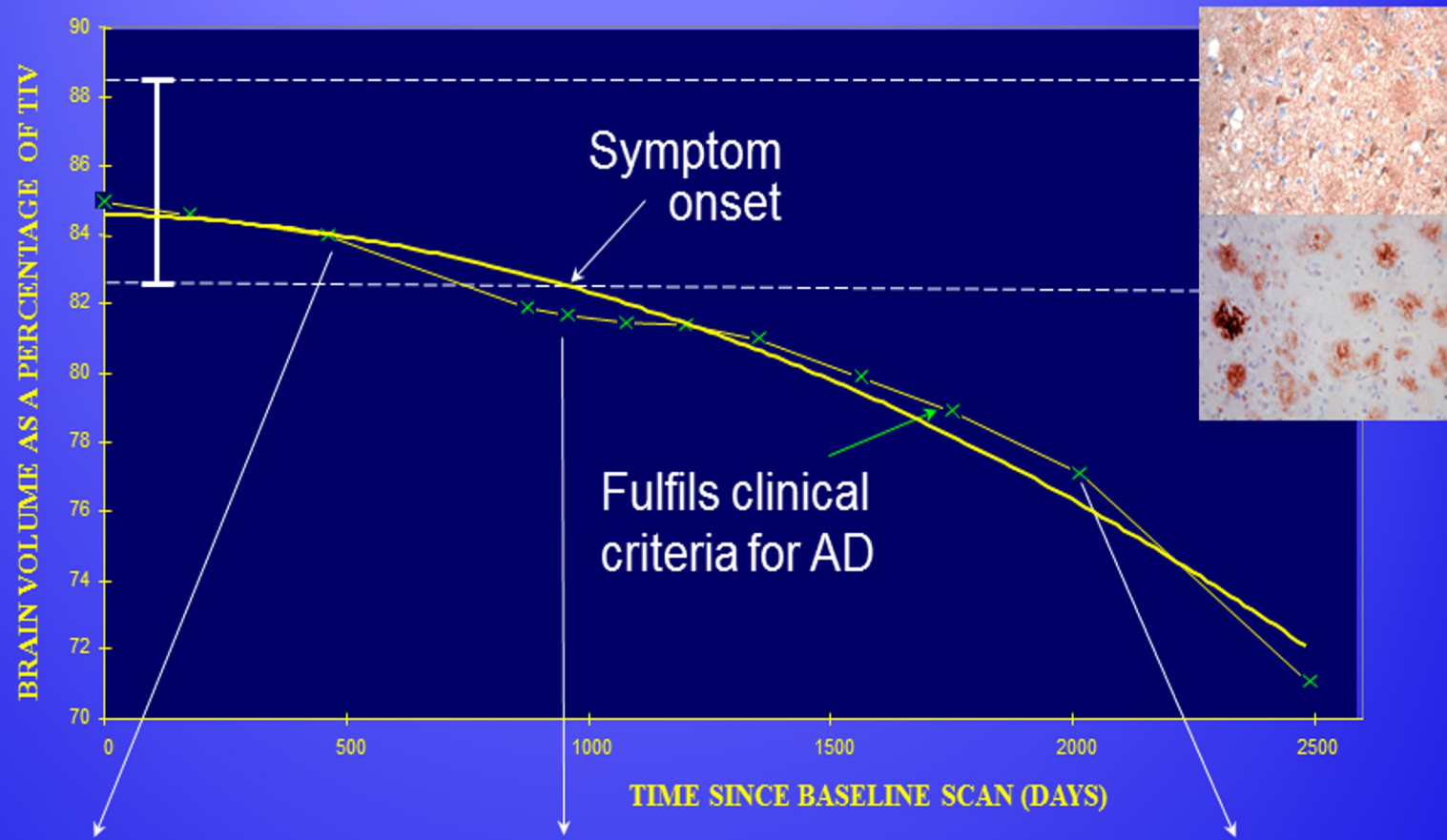
APP processing, A β aggregation, and amyloid pathology



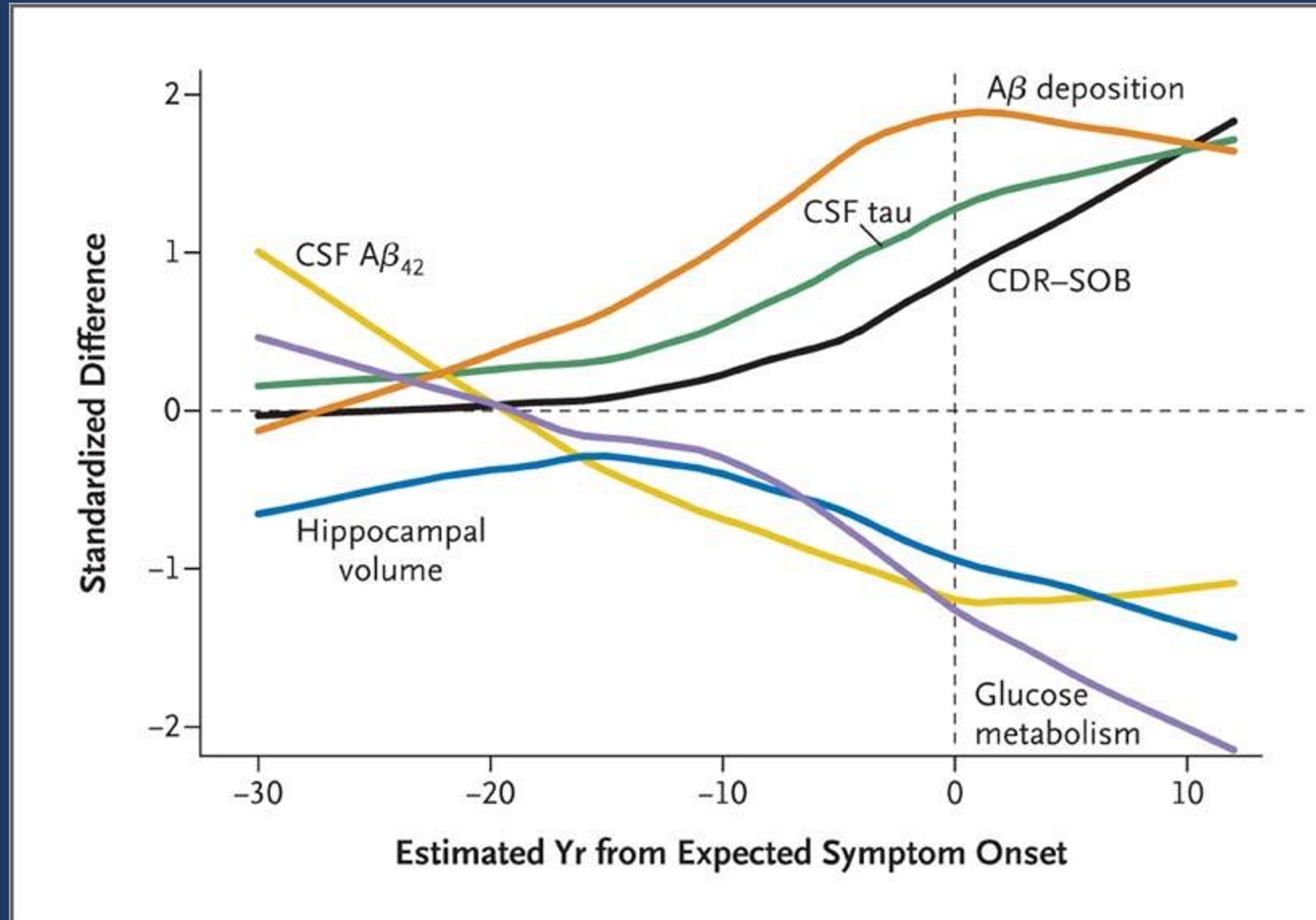
Haass et al

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





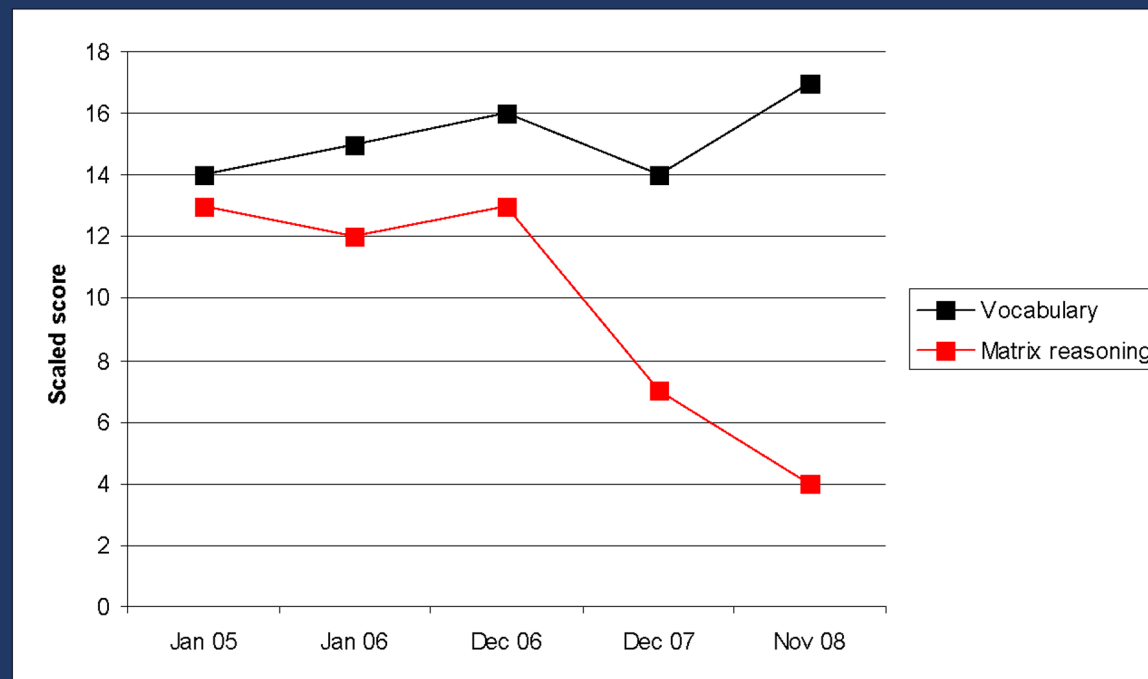
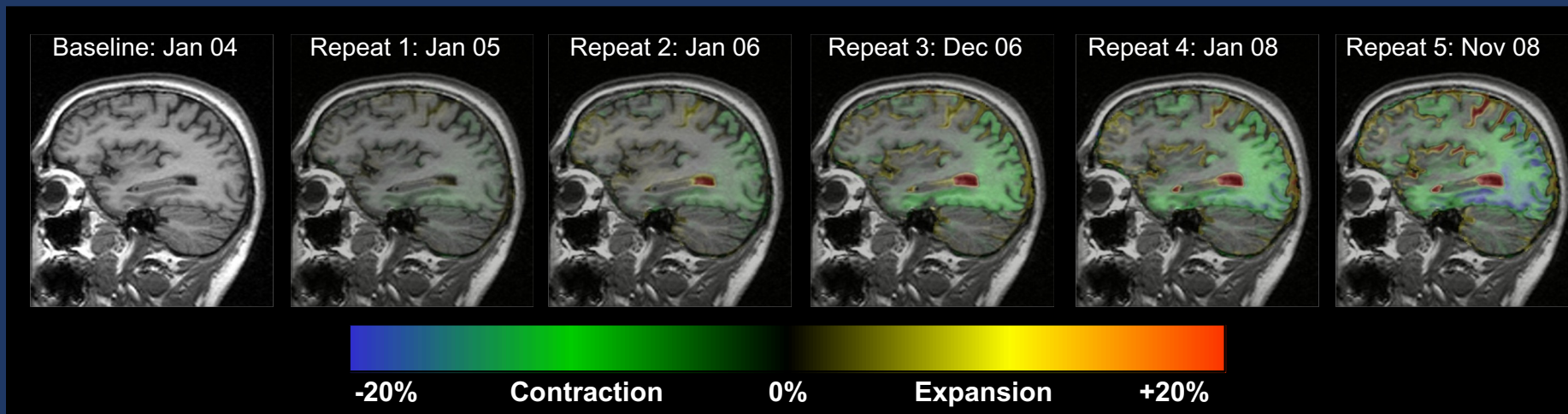
Comparison of Clinical, Cognitive, Structural, Metabolic, and Biochemical Changes as a Function of Estimated Years from Expected Symptom Onset



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

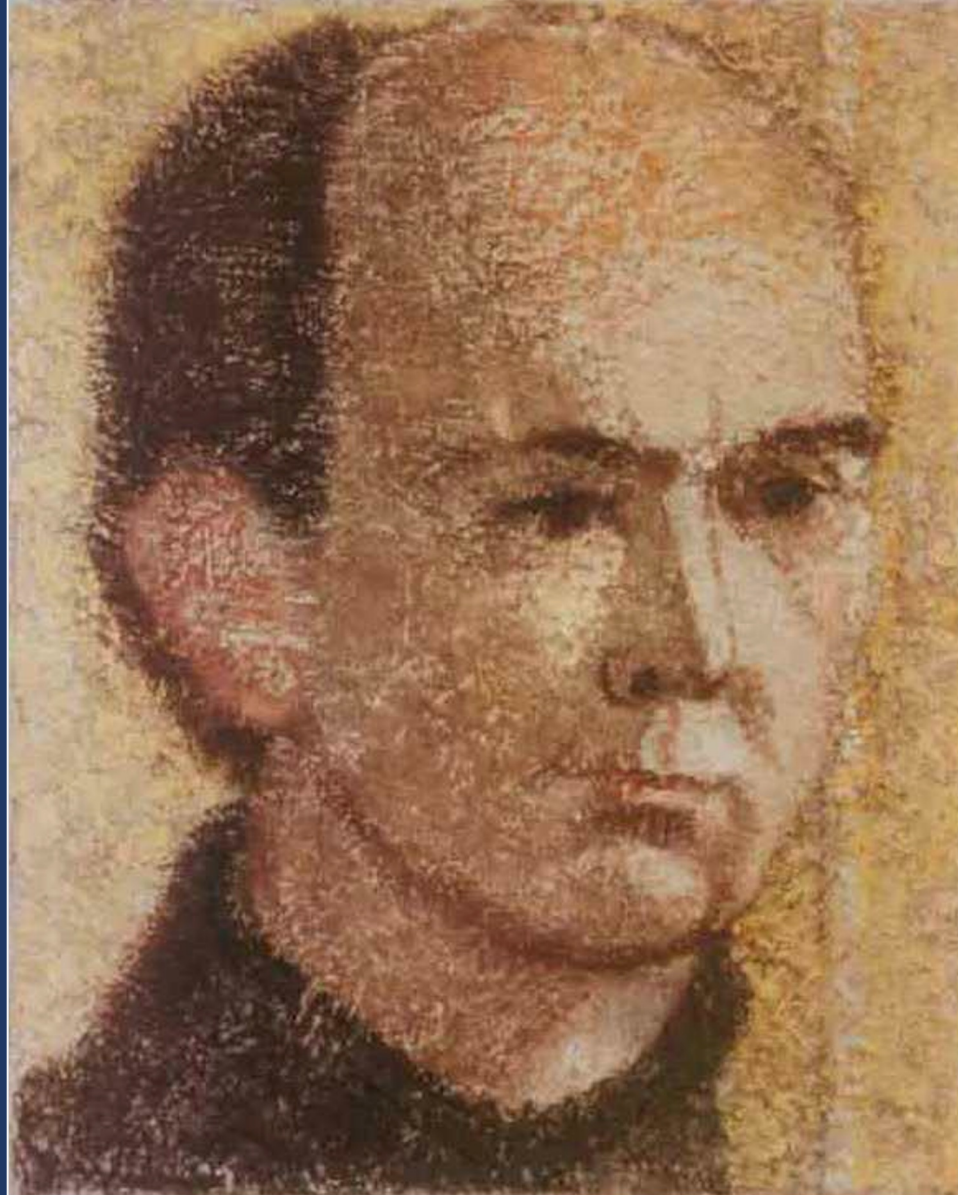


The NEW ENGLAND
JOURNAL of MEDICINE



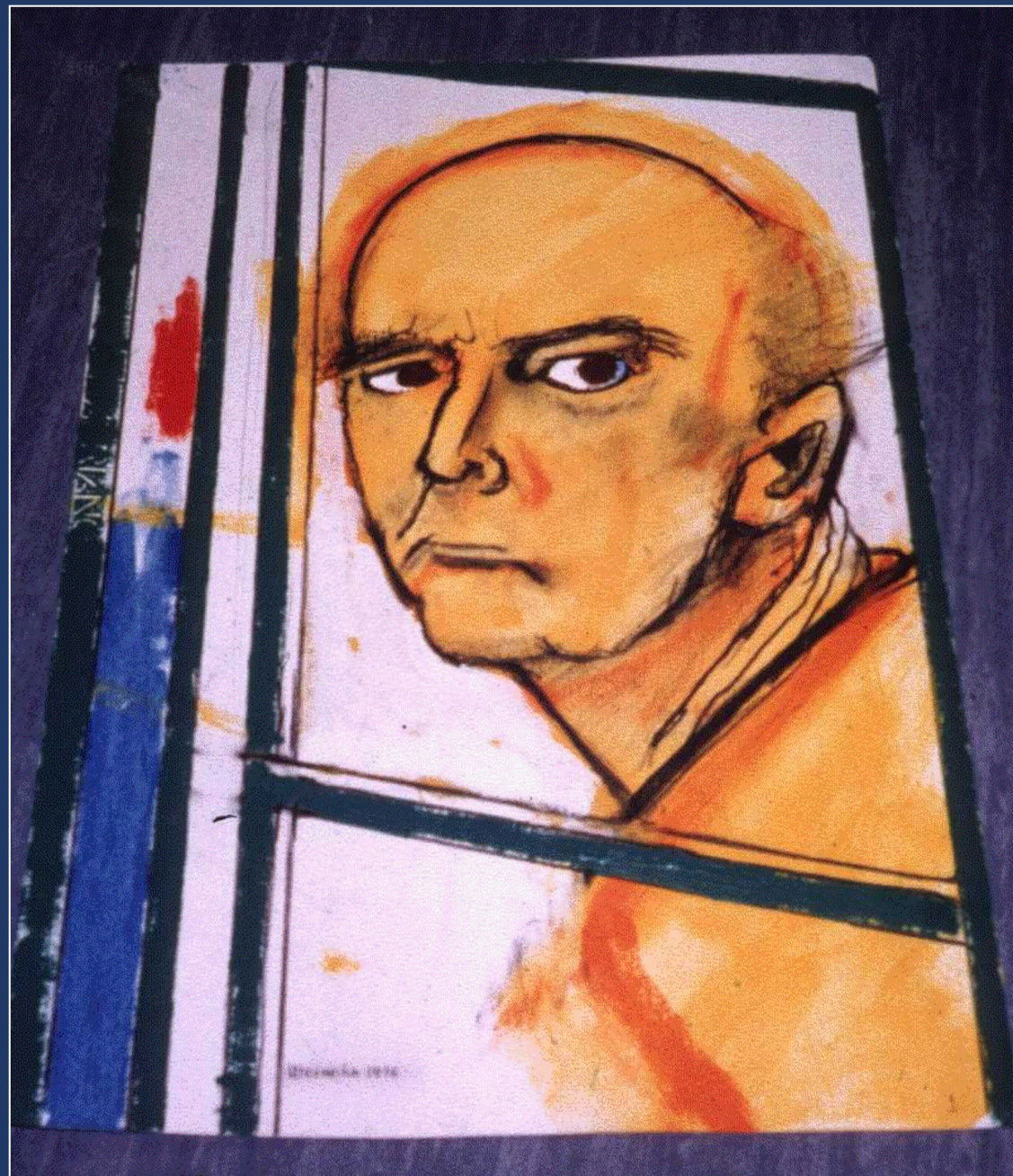


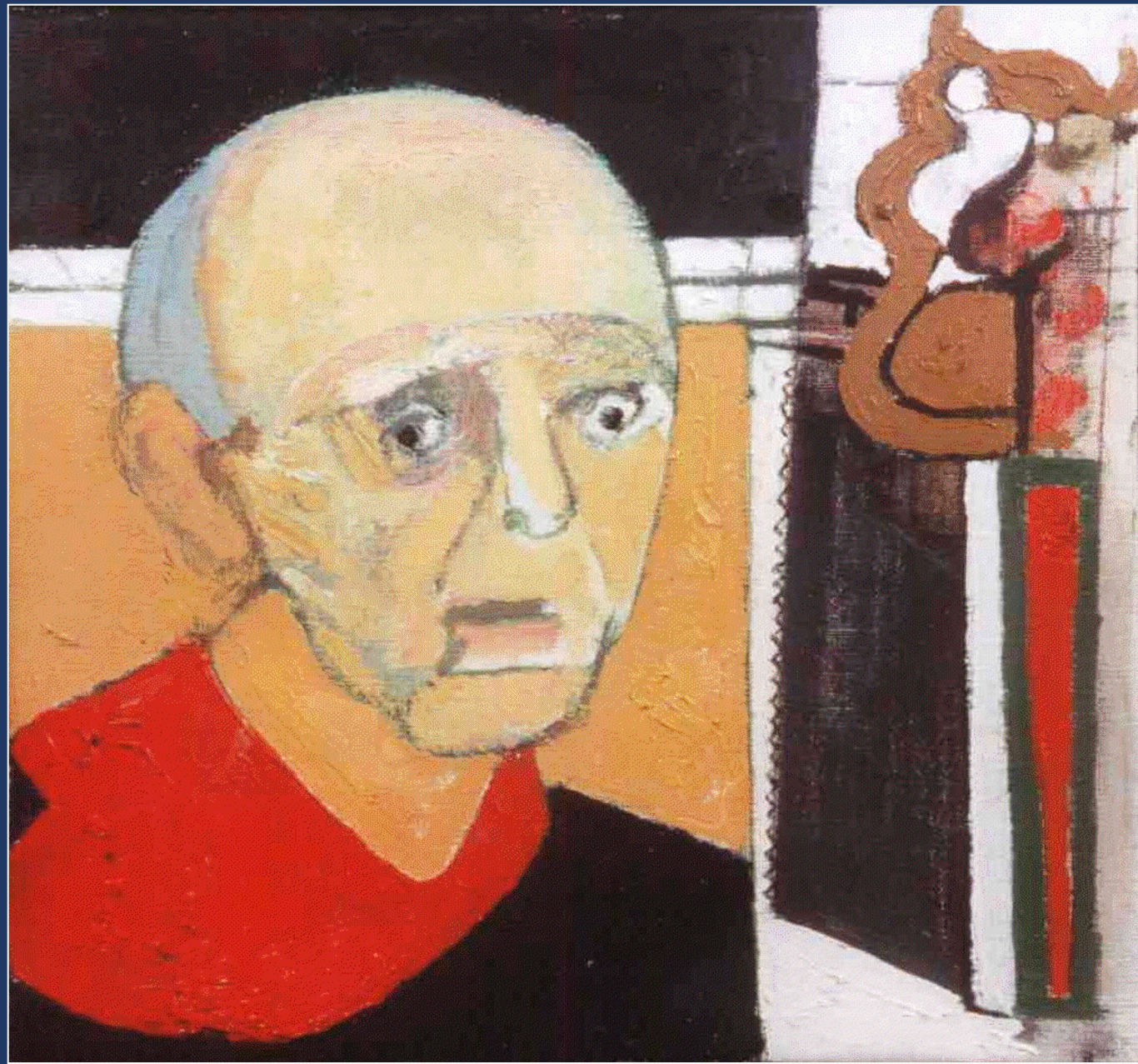


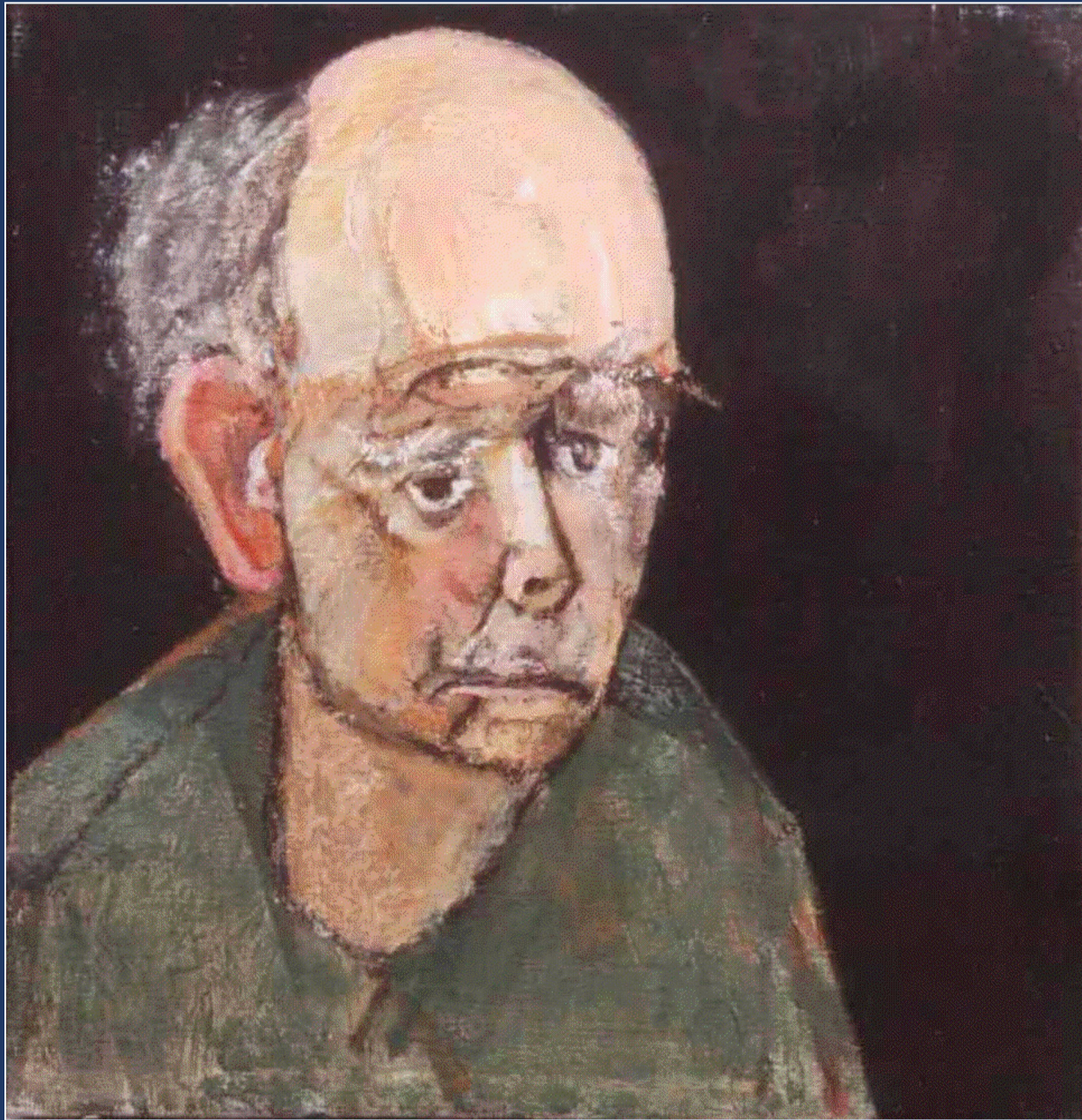


William
Utermohlen
1933-2007

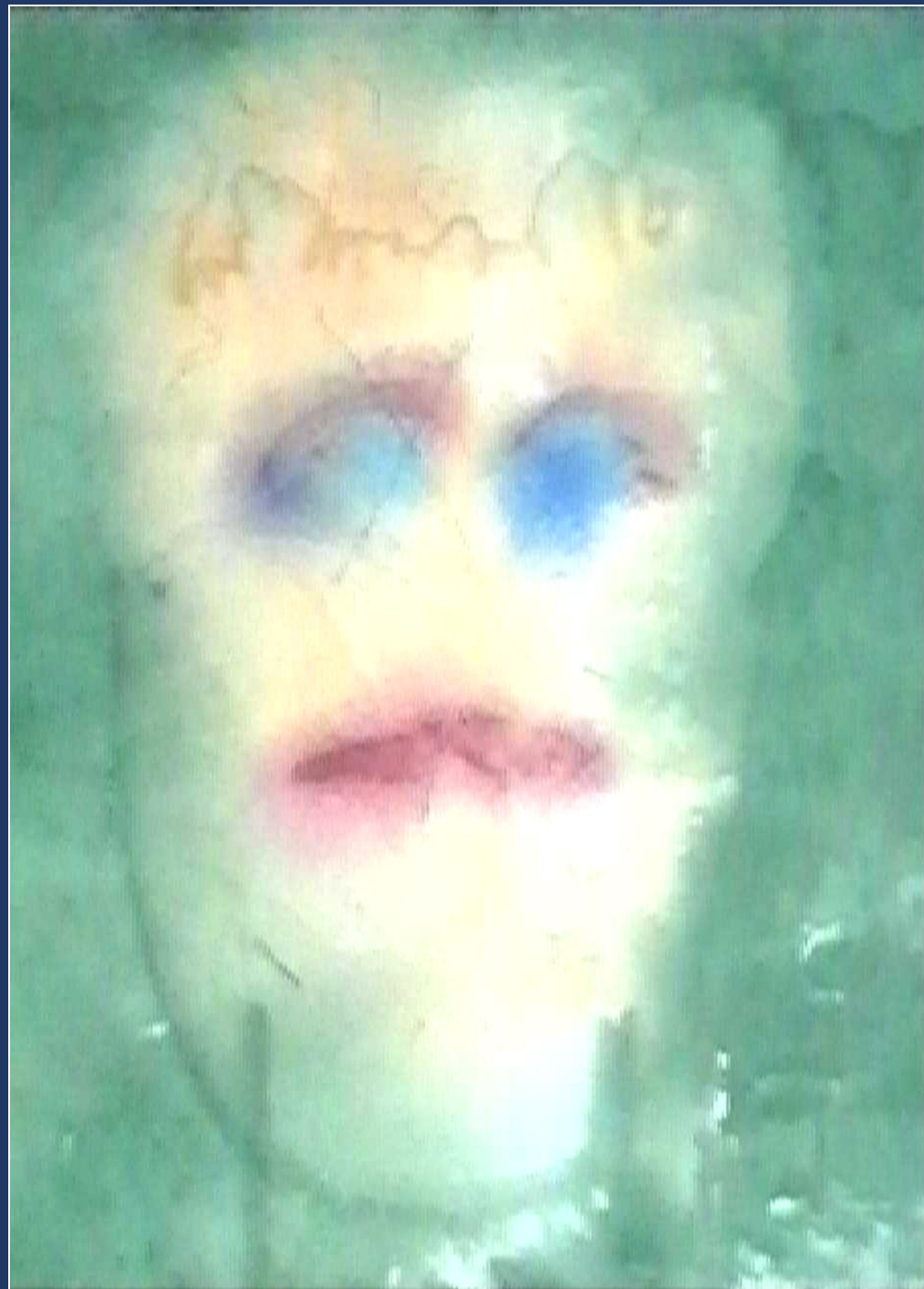
Crutch, Isaacs and Rossor
Lancet 2001









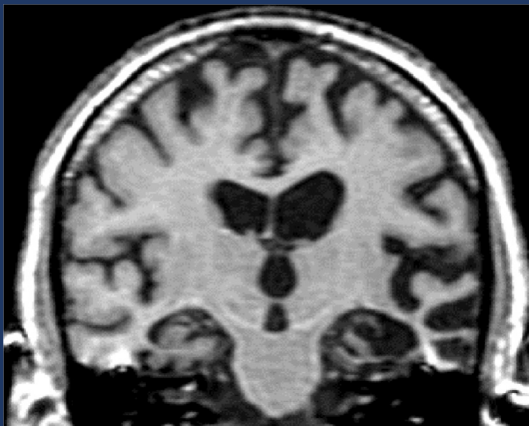
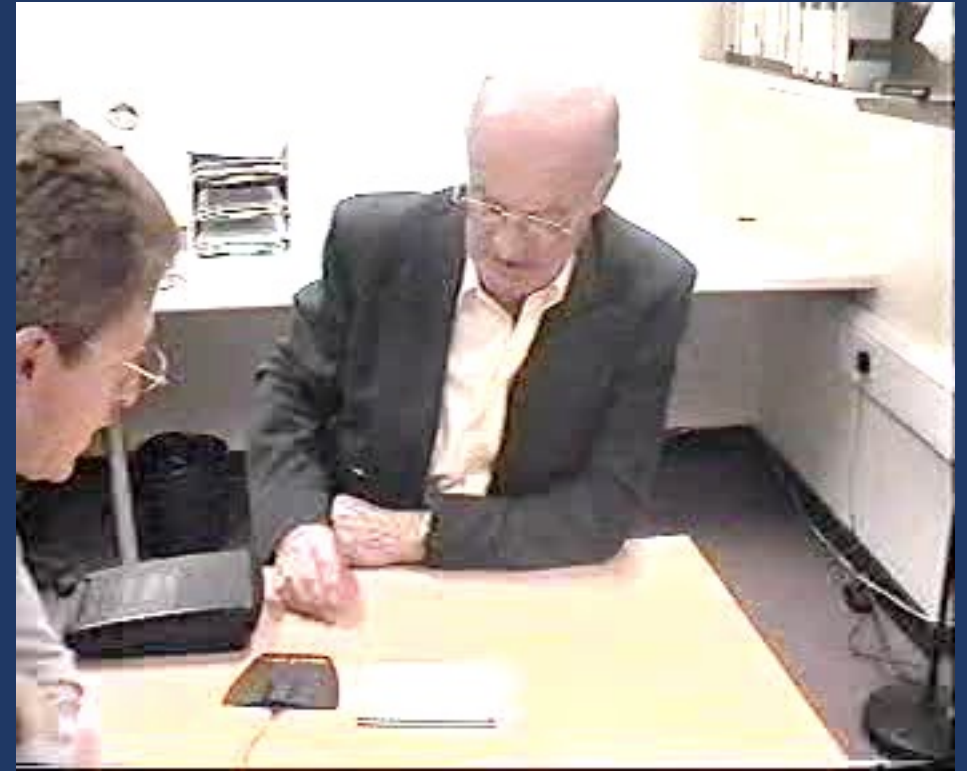


Dementia is a syndrome
NOT a disease diagnosis

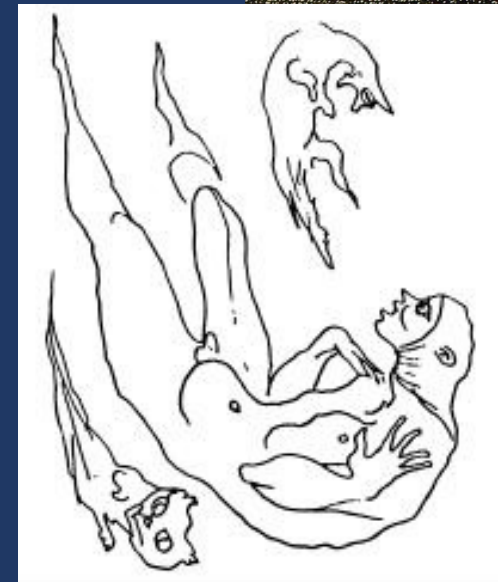
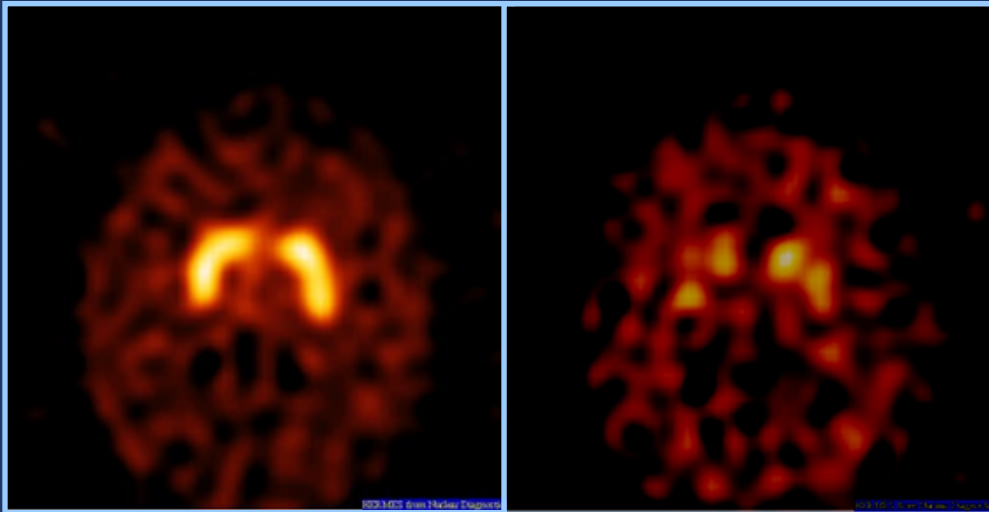
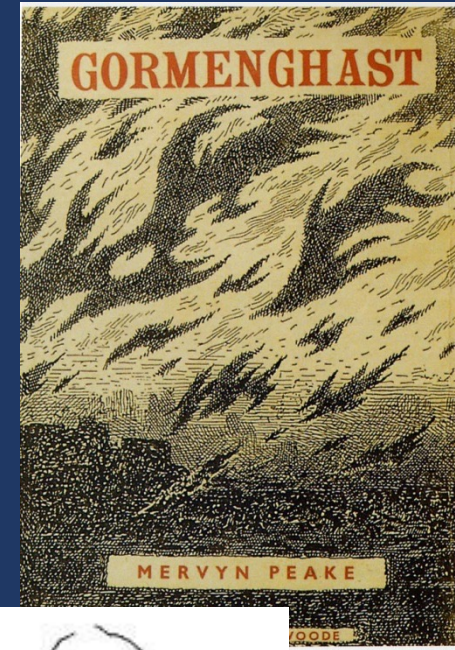
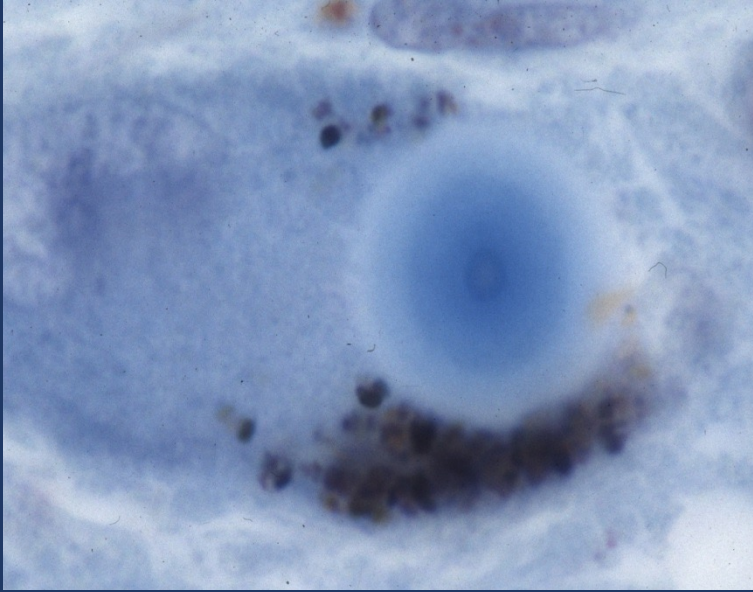
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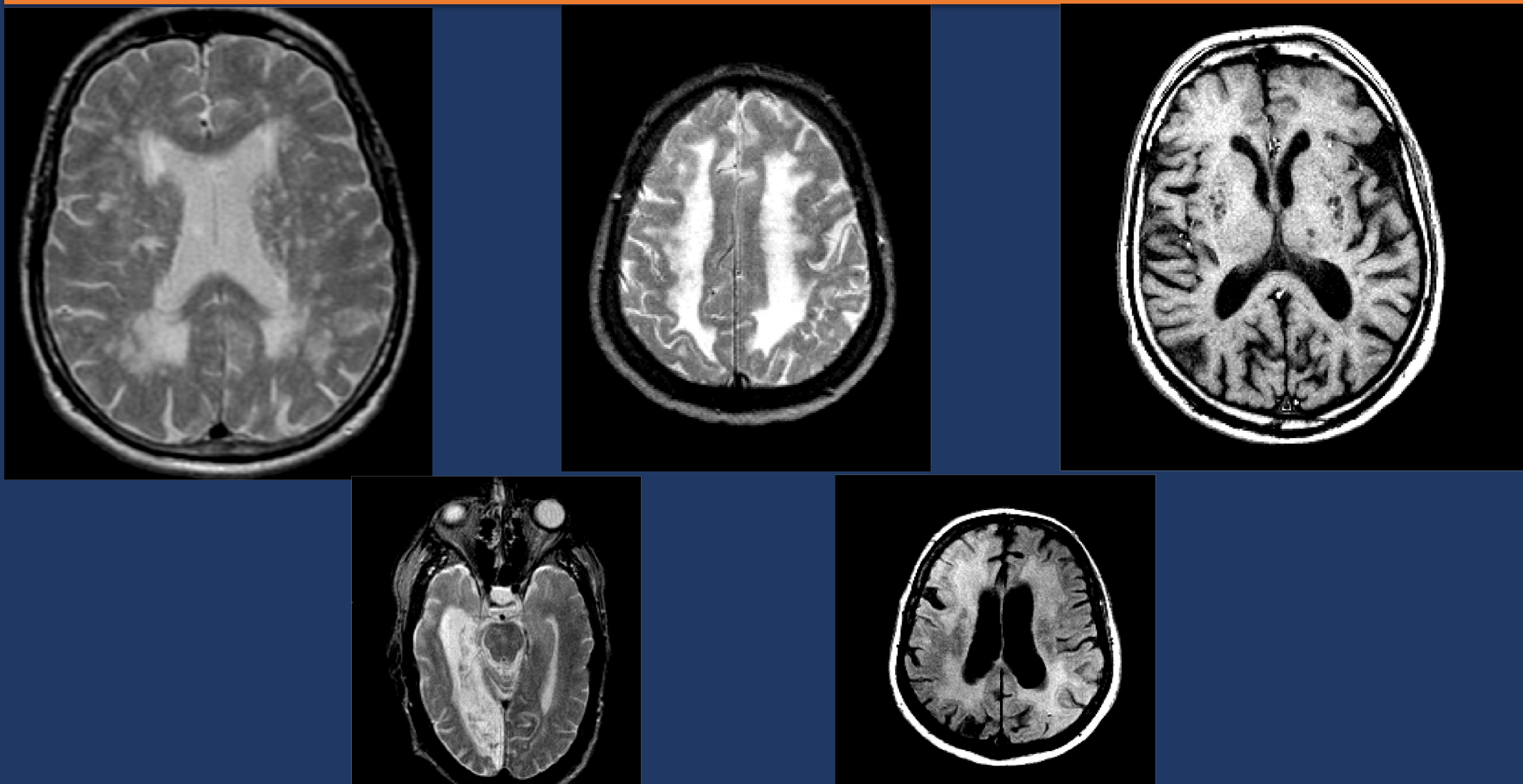
Semantic Dementia



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

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



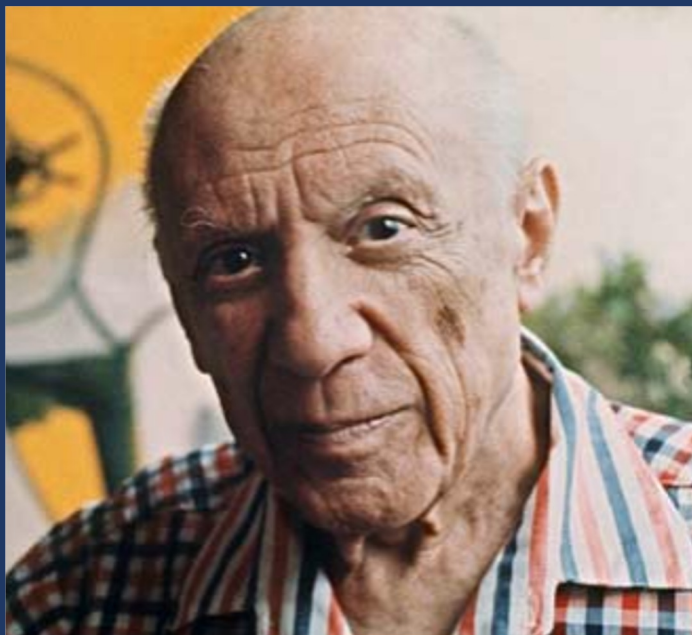
Memorandum

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Jeanne Calment 1875-1997





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SCANDAL OF 'TAX' ON DEMENTIA
Thousands forced to pay for care

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STATINS HA ALZHEIMER

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HEALTHY HEA IS KEY TO FIGHTING DEMENTIA

HEALTHY HEA IS KEY TO FIGHTING DEMENTIA

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50 IN LOVE...THE CHARMING COUPLE, AGED JUST 22, WHO WON £45m LOTTO JACKPOT

DRUG TO CURE ALZHEIMER'S

SKID PAN BRITAIN: ICE AND SNOW CAUSE CHAOS ON OUR ROADS

THE LANCET

July 2017

www.thelancet.com

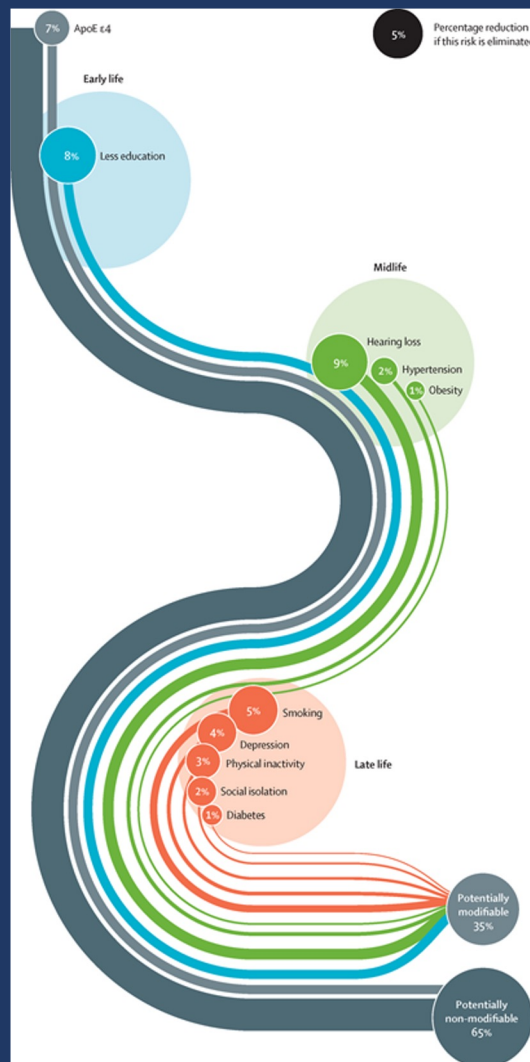
The Lancet Commission on dementia



"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	Communality	PAF	Weighted PAF*
Early life (age <18 years)					
Less education (none or primary school only)	1.6 (1.26–2.01)	40.0%	64.6%	19.1%	7.5%
Midlife (age 45–65 years)					
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%
Later life (age >65 years)					
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 fraction. *Weighted PAF is the relative contribution of each

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

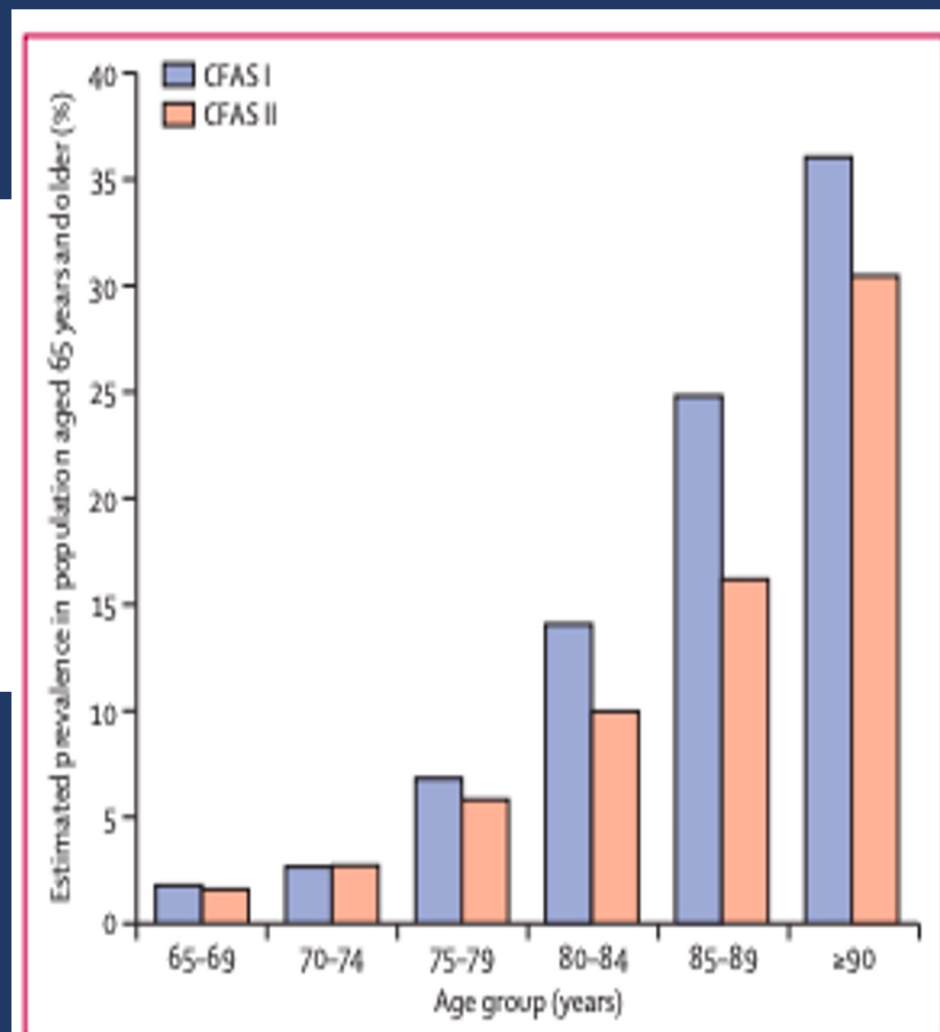


Figure 1: CFAS I and CFAS II age-specific dementia prevalence
CFAS=Cognitive Function and Ageing Study.

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 base is submerged. Various risk factors for dementia are listed around the submerged part of the iceberg, illustrating that the visible symptoms are only a small fraction of the underlying causes.

Ill-health

Stress

Injury

Poverty

Poor education

Pollution

Medication

Early progressive
disease

Loneliness

Cognitive Health

- 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

Gresham lecture
5 April 2022

