MANCHESTER 1824
The University of Manchester

Psychology Divisional Seminar

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Manchester Cognitive Ageing Cohort

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The University of Manchester Longitudinal Study of Cognition in Normal Healthy Old Age (UMLCHA)

Beginning of the study

Phenotypes/biological material

Main findings

Future plans

Virtual reality demo

Medical history taking (mental health case)

Study started in 1983

Prof Patrick Rabbitt
1983-2004

Prof Neil Pendleton
Prof Mike Horan
2004-2019

>6500 volunteers aged 50yrs +
Manchester and Newcastle
66% female
Almost all Caucasian
Dementia was exclusion criteria

Follow-up of up to ~35 yrs

Phenotypes

Sociodemographics

PDQ (159)
Job Questionnaires

Cognition (28)

Fluid, memory, processing speed, vocabulary

Mental Health

Depression, personality, life events, life satisfaction

Phenotypes

General Health

Cornell Medical Index (263)

Clinical Measures

Balance, BP, BMI, Lung Volume, MRI (brain region volumes), Cortisol, Pain, Dysphagia, Hearing loss

Sleep

Pittsburgh Sleep Quality index
Sleep Timing Questionnaire
Sleep efficiency measures

Overall 889 unique phenotypes

Phenotypes

Largely summary data entered electronically

Most itemised data not yet entered

>100,000 questionnaires

- **20 filing cabinets**
- **1 large storage cabinet**
- **1 safe**
- **lots of boxes/files**

4 Admin staff entering data

Biological Material

Manchester Brain Bank
Prof Federico Roncaroli
Andy Robinson
Yvonne Davidson

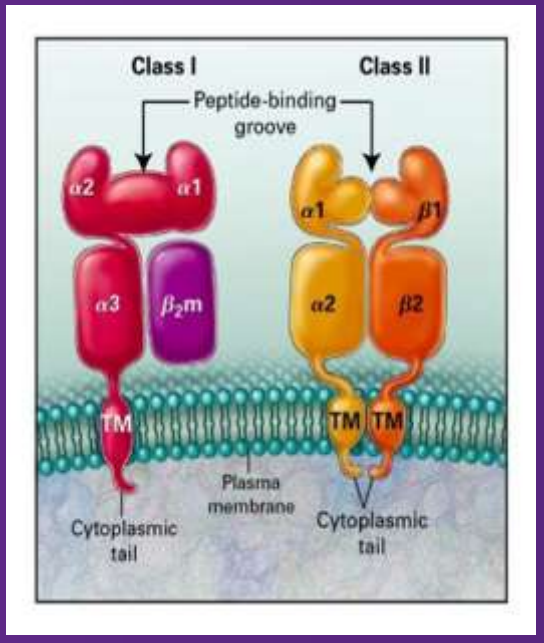
Brains (~135)
Brain Weight
Braak Stage
CERAD Score
Primary age-related tauopathy
Clinical diagnosis
WMH
Cerebral blood flow

Biological Material

1563 DNA samples

GWAS imputed to 1000 genomes, HRC, HLA (Impute 2)
Epigenetic, CNVs, Transcriptomic

Plasma, Serum



Cognitive Genetics

Identification of genetic variants which regulate the level of cognitive ability/decline in a non-pathological population

Memory
Novel Problem Solving
Vocabulary Ability
Processing Speed

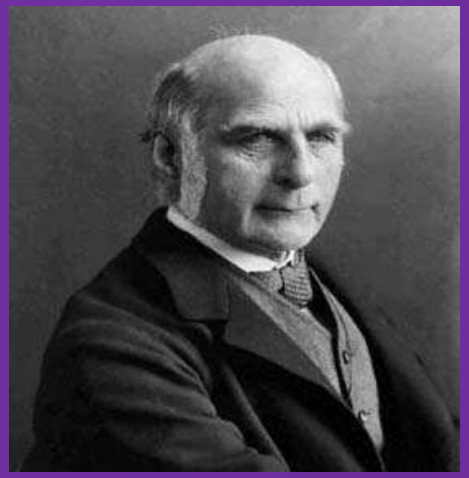
Historically and ethically controversial

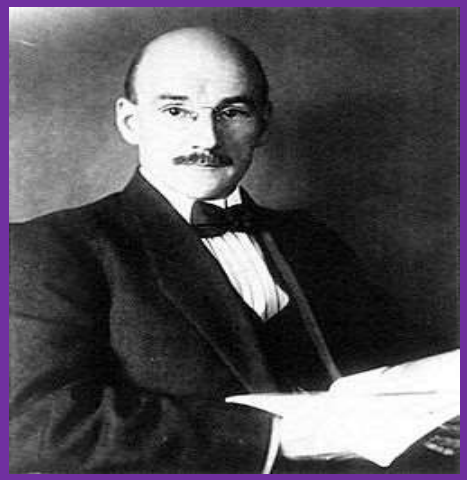
Identifying genes associated with intelligence:

Designer babies

Cognitive enhancing drugs

Eugenics





Eugenics

1883 - Francis Galton

"supplanting inefficient human stock by better strains, by such efforts as may be reasonable, to further the ends of evolution more rapidly"

Galton F. (1883). Inquires into human faculty. Macmillan. London

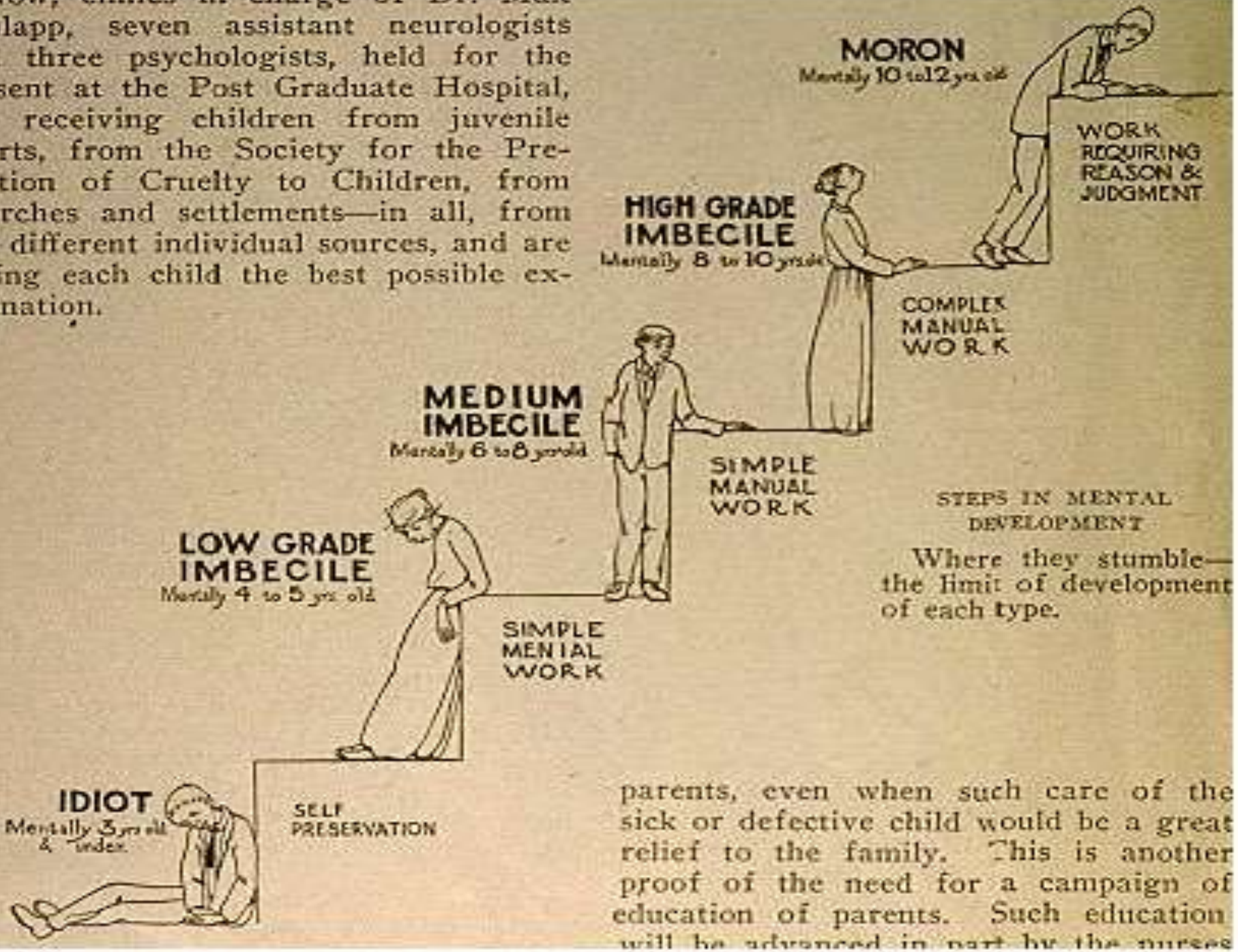
1900 - Henry Goddard

IQ test rankings: "idiots, imbeciles, and morons"

1912 - Tests used at Ellis Island

Discovered that large percentages of the new immigrants were "feeble-minded".

Now, clinics in charge of Dr. Max Schlapp, seven assistant neurologists and three psychologists, held for the present at the Post Graduate Hospital, are receiving children from juvenile courts, from the Society for the Prevention of Cruelty to Children, from churches and settlements—in all, from 47 different individual sources, and are giving each child the best possible examination.



STEPS IN MENTAL DEVELOPMENT

Where they stumble—the limit of development of each type.

parents, even when such care of the sick or defective child would be a great relief to the family. This is another proof of the need for a campaign of education of parents. Such education will be advanced in part by the nurses

The scale of the challenge

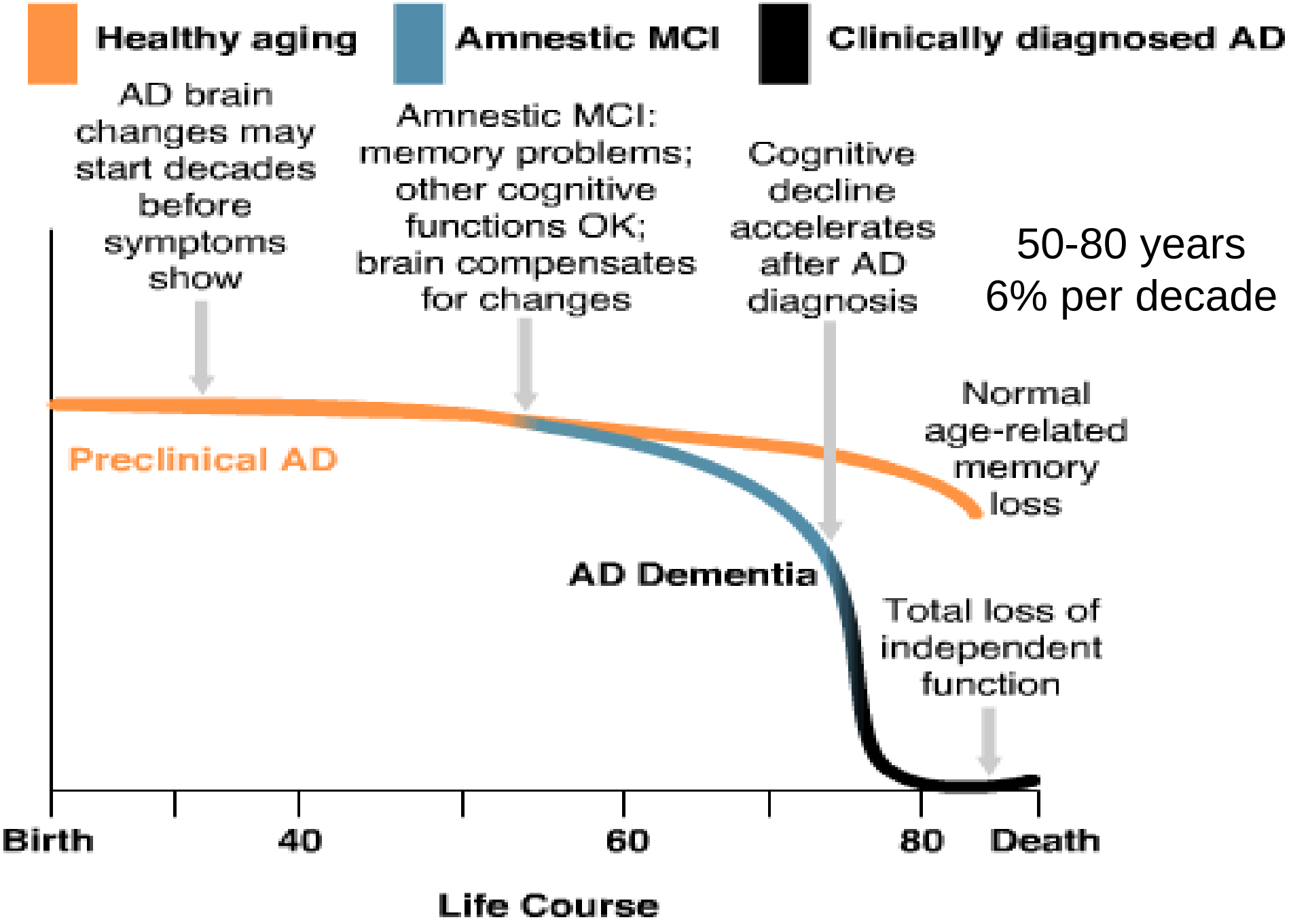
850,000 people living with dementia in the UK

By 2025

over **one million** people could have dementia in the UK

By 2050

this figure will exceed **2 million**


Healthy aging
Amnestic MCI
Clinically diagnosed AD
AD brain changes may start decades before symptoms show
Amnestic MCI: memory problems; other cognitive functions OK; brain compensates for changes
Cognitive decline accelerates after AD diagnosis
50-80 years
6% per decade
Preclinical AD
Normal age-related memory loss
AD Dementia
Total loss of independent function
Birth
40
60
80
Death
Life Course

>100 publications with ~75 genetic

Cognition, Pain, Dysphagia, Depression, Longevity, Diabetes, Dementia

1. Manchester-Edinburgh Collaboration

GWAS cognitive ability and non-pathological decline

BBSRC £1.3 mill, 2008

3500 elderly volunteers

MANCHESTER 1824
The University of Manchester

BBSRC
bioscience for the future

LBC
1936

THE UNIVERSITY of EDINBURGH

Cognition is heritable (51%)

GWAS unrelated individuals

Consistent with twin studies

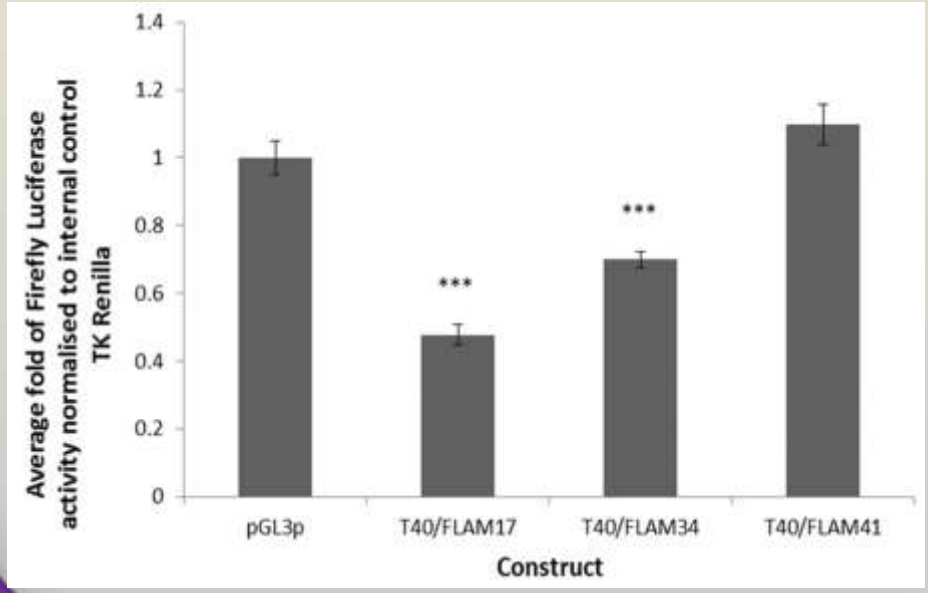
Davies et al. Mol Psych. 2011. 16: 996-1005

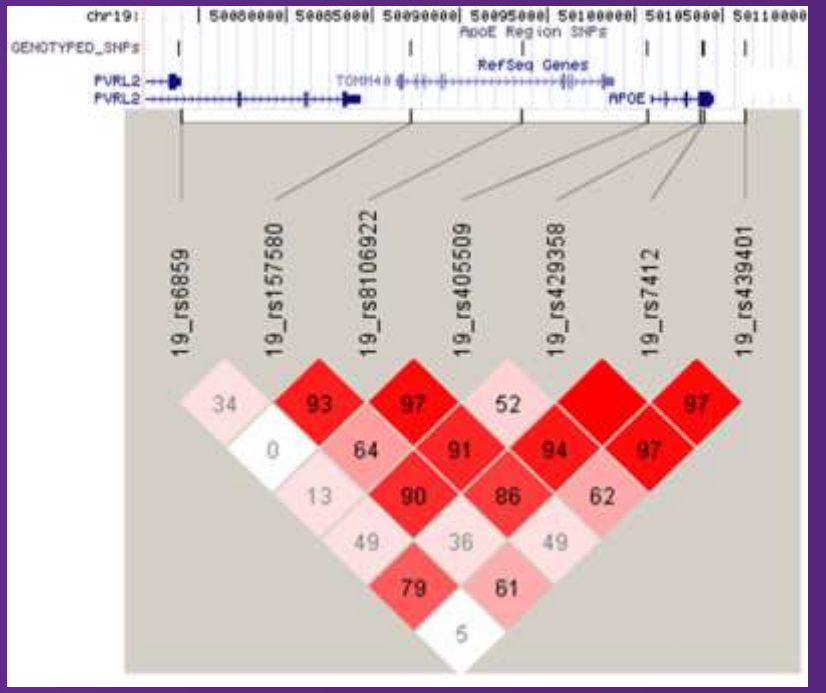
TOMM40/APOE locus

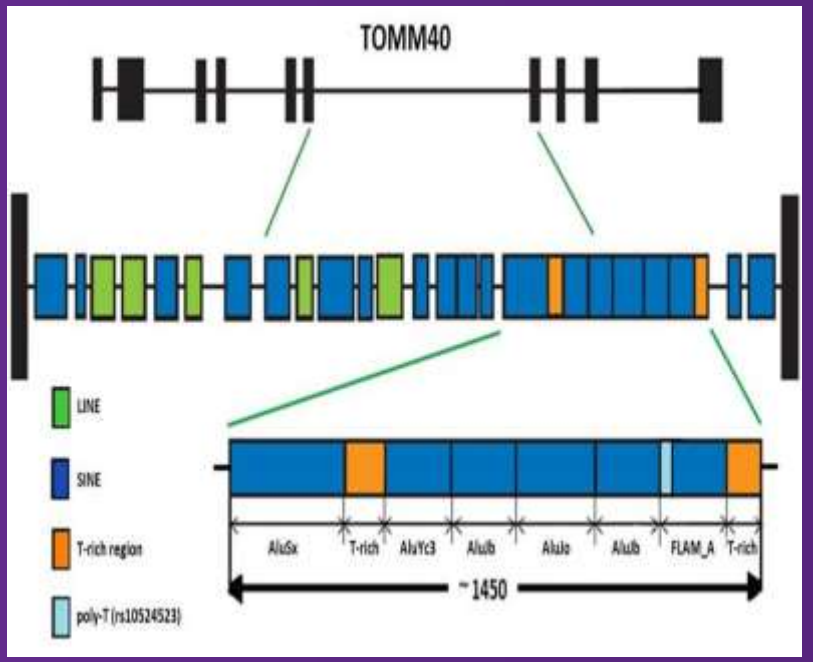
Associated with cog decline

Davies et al. Mol Psych. 2014. 19: 76-87

Payton et al. Neurobiol Aging. 2016.39:217.e1-7

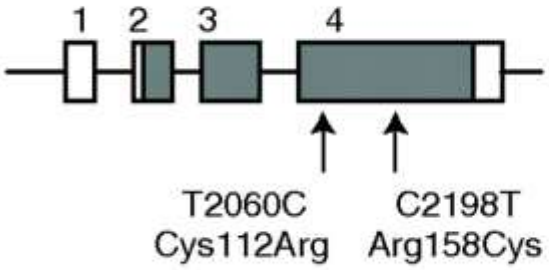






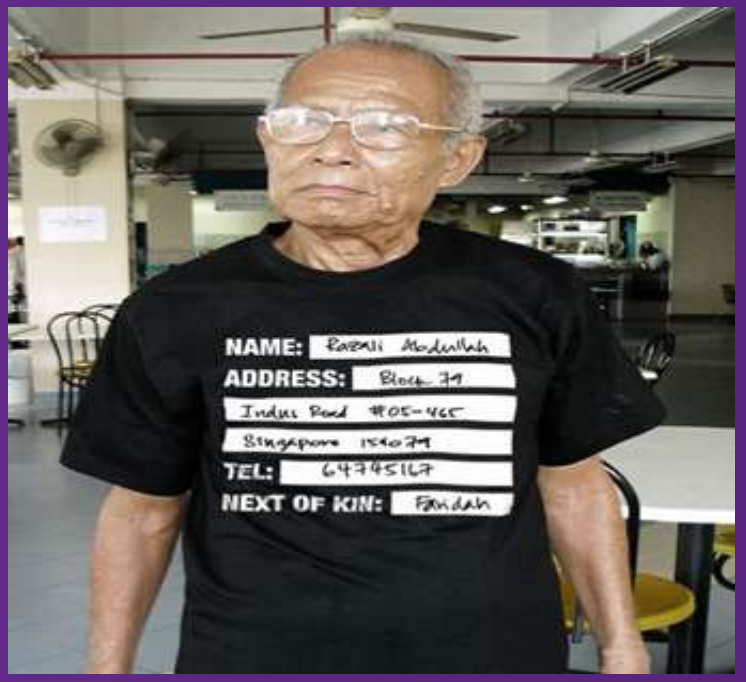
Apolipoprotein E and Alzheimer's disease

A



B

Isotype	aa Position 112	158
ε2	TGC (Cys)	TGC (Cys)
ε3	TGC (Cys)	CGC (Arg)
ε4	CGC (Arg)	CGC (Arg)



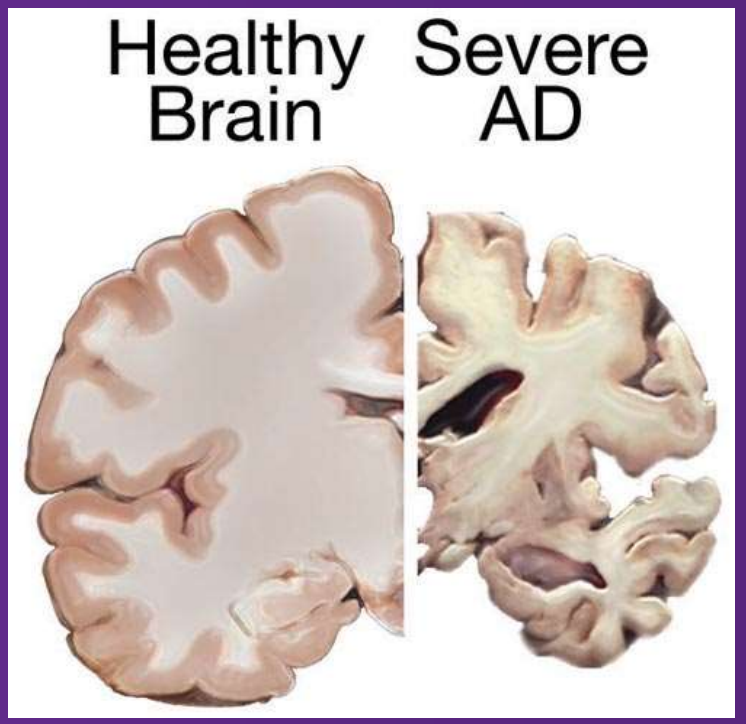
Risk of developing AD

20% no ε4 mean age onset 84yrs

47% one ε4 mean age onset 75yrs

91% two ε4 mean age onset 68yrs

ε4 allele frequency: 14%

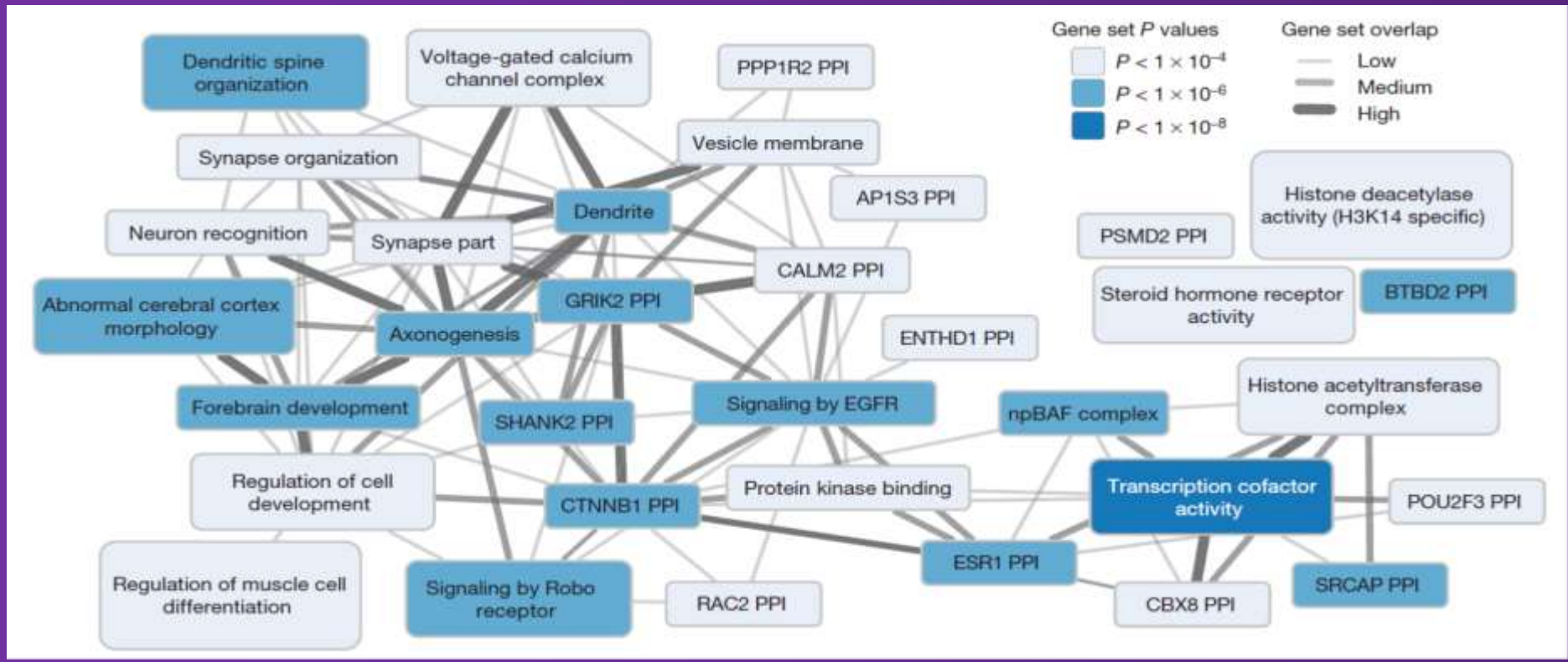


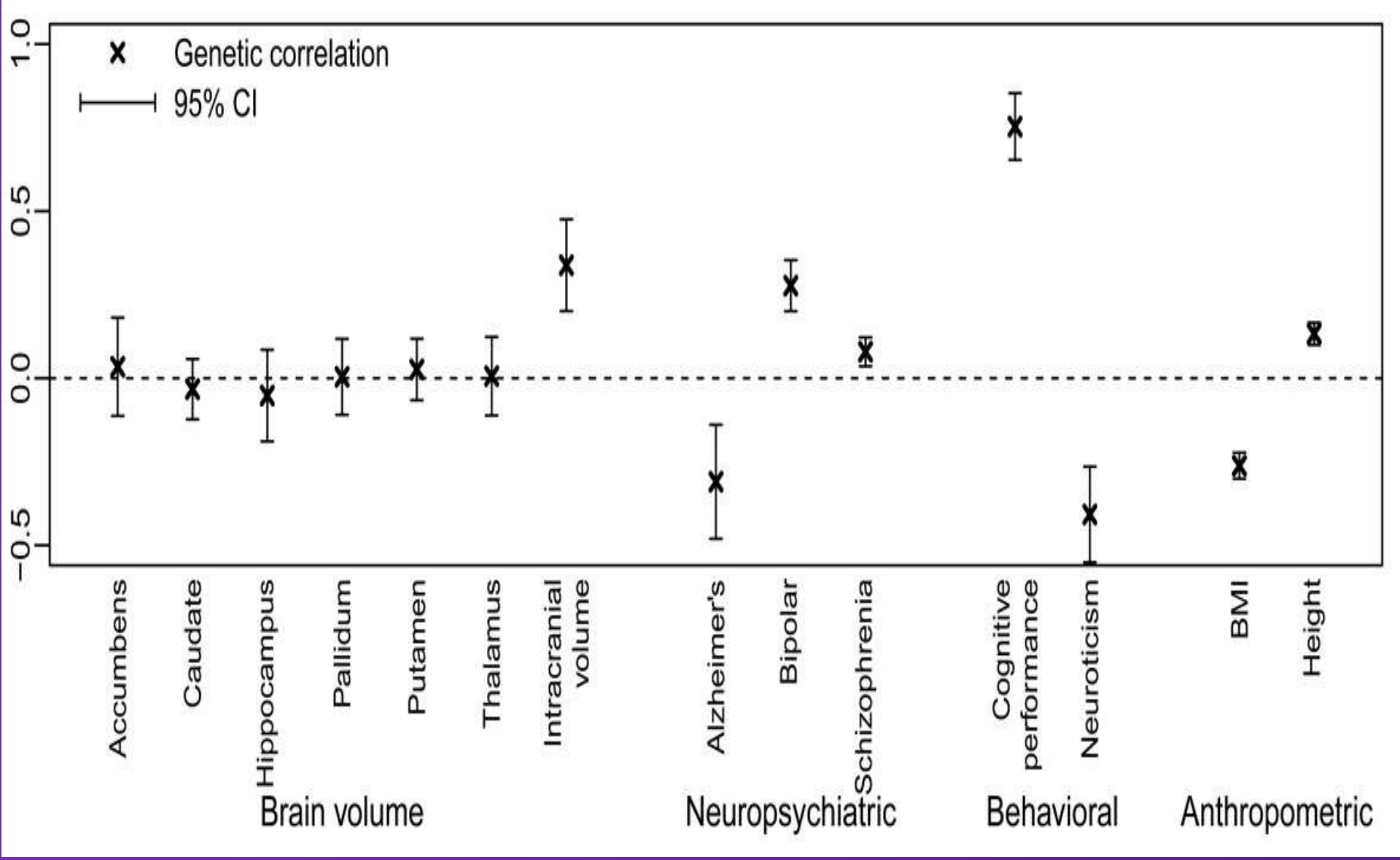
2. Educational Attainment (COGENT consortium)

293,723 individuals, 30+ yrs, European decent, ~9.3M SNPs

74 independent genome-wide significant ($5x10^{-8}$) loci identified
Okbay et al. 2016. Nature. 533: 539-42.

3 million individuals; 3592 independent SNPs identified
Okbay et al. 2022. Nature Genetics. 54(4):437-449





Genetic correlations between EduYears and other traits

Scientists identify 40 genes that shed new light on biology of intelligence

Study significantly adds to the tally of genes connected to intellect – but researchers caution genius isn't all down to genetics

theguardian

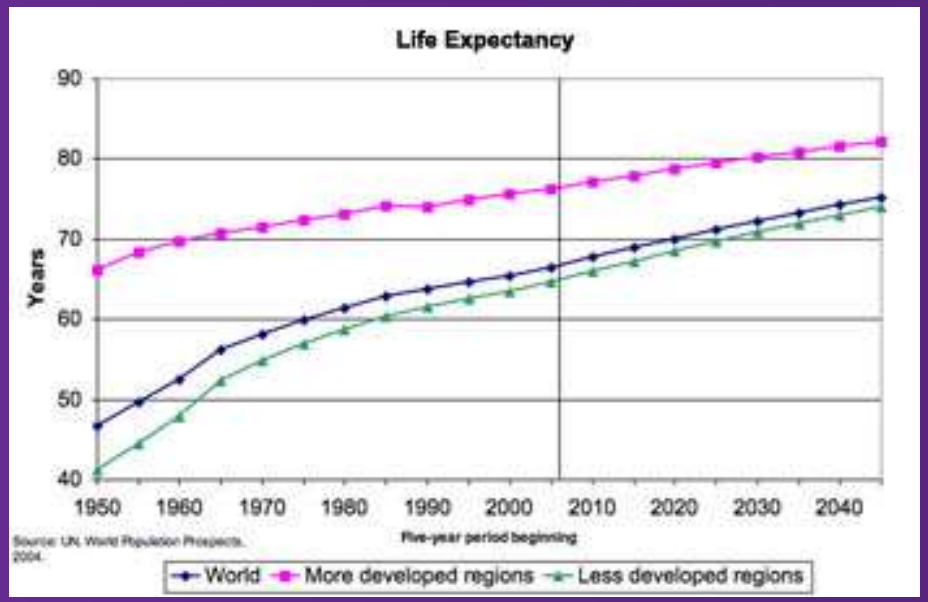
Scientists identify 40 genes that shed new light on biology of intelligence Photograph: Chung Sung-Jun/Getty Images

3. Human Lifespan (LifeGen consortium)

Up to 25% of variance in lifespan has a genetic basis

606,059 parental lifespans (>40 yrs)
Kin-cohort method. Parent phenotype-offspring genotype GWAS

HLA-DQA1/DQB1 and LPA: ↓ lifespan 0.6-0.7 yrs, resp. per allele
APOE and CHRNA3/5: ↓ lifespan 0.9, 0.4 yrs, resp. per allele
FOXO3, SH2B3 and CDKN2A/B: ↓ lifespan 0.15-0.25 yrs per allele
Joshi et al. Nature Communications 2017

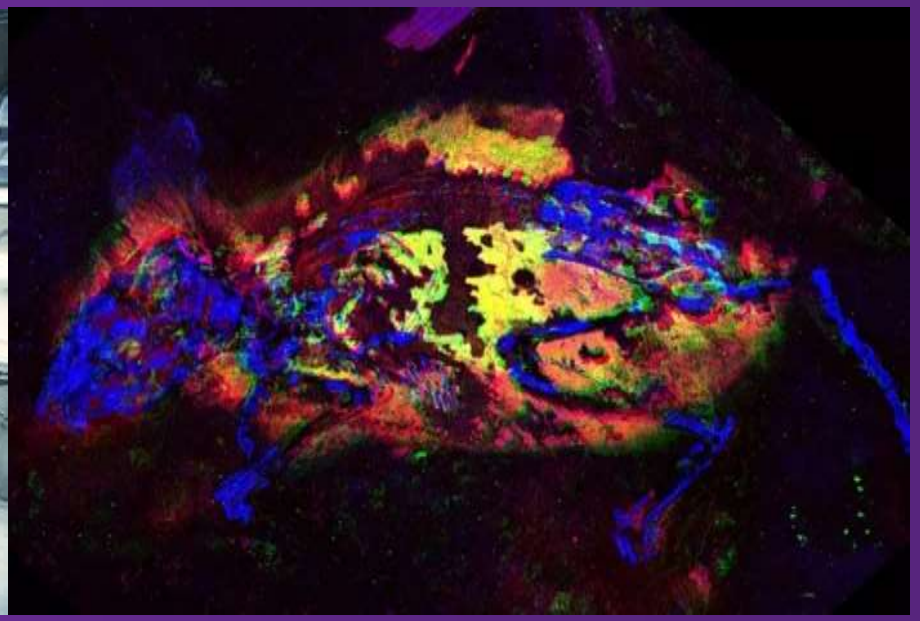


4. Current work

Sleep and Health (mental and physical)
Mech Ageing Dev. 2020

Brain studies: expression of IL6, APOE, PART/episodic memory, TICS/cognitive decline/dementia
Neurobiol Aging. 2020
Alzheimer's Disease. 2021

Stanford University Synchrotron



Future studies

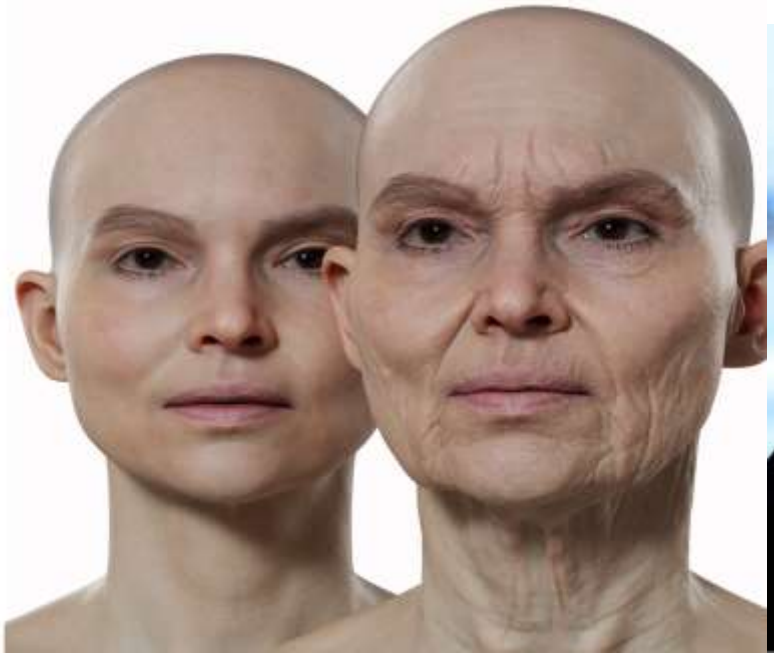
Most of the research has used cognitive measures, but there's a lot of data that hasn't been investigated in detail:

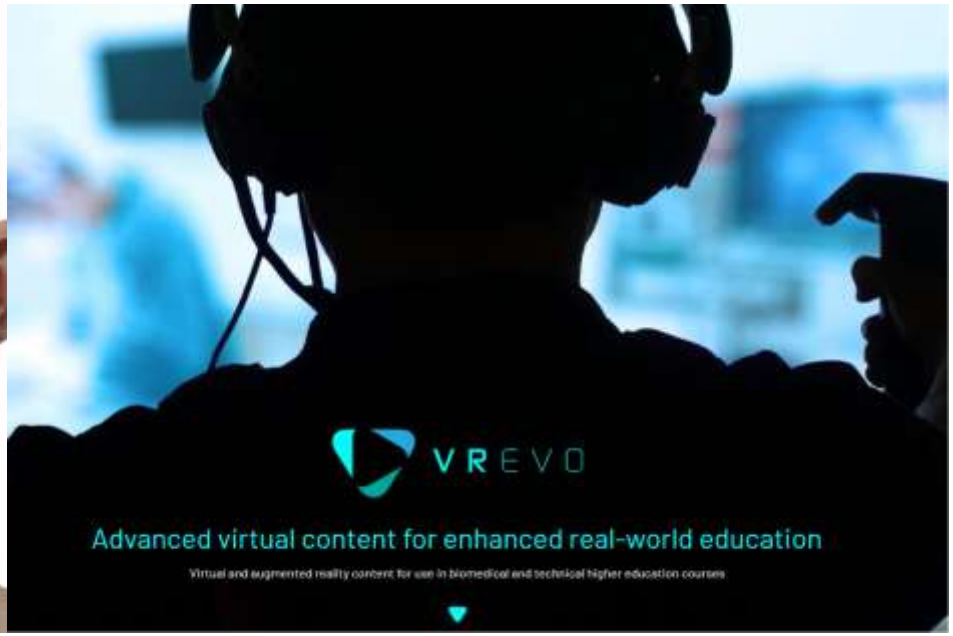
Depression
Personality
General Health
Imaging (WMH, brain volumes)
Pollution
25% data still not entered

NGS, other OMICs

Phenotype	Measures	Longitudinal	Time Points	Years	Number of Volunteers	Number of measures
01_Sociodemograpic	Karasek Job Content Questionnaire	N			3788	2
	Personal Details Questionnaire	Y	7	24	6372	159
02_Cognition	Multiple tests for memory, processing speed, fluid intelligence and vocabulary (inc. TICS)	Y	11	35	6356	26
	Cognitive Failures Questionnaire	N			4071	1
	Telephone Interview for Cognitive Status (TICS)	Y	5	13	865	1
03_General Health	Cornell Medical Index	Y	4	12	2809	263
	Hearing Loss	N			265	3
04_Mental Health	Beck, Yesavage and Geriatric Depression Tests	Y	11	29	5482	3
	Eysenck Personality Questionnaire	N			3523	4
	Negative Life Events	Y	4	19	3510	2
	Personality Intellectual Ageing Contexts	Y	2	11	1881	3
	Satisfaction with Life Scale	N			549	6
	Self Awareness Questionnaire	N			3719	4
05_Clinical	Various (inc. balance, blood pressure, BMI, lung volume)	N			580	33
	Heamoglobin A1C and Cortisol	N			580	10
	Pain	N			751	67
	Dysphagia	N			627	18
06_Sleep	Loughborough Sleep Diary	Y	7	1	465	92
	Personal Details Questionnaire: Sleep	Y	4	25	6000	21
	Pittsburgh Sleep Quality Index	N			477	34
	Sleep Study Health Questionnaire	N			477	92
	Sleep Timing Questionnaire	N			467	25
07_Death Registrations	Date of death and dementia status	N			6000	8
08_Brain/Neuopathology	Brain weight, neuropathology diagnosis, clinical diagnosis, CERAD, Thal, Braak, Synaptic Density	N			126	12

VR in Health Education





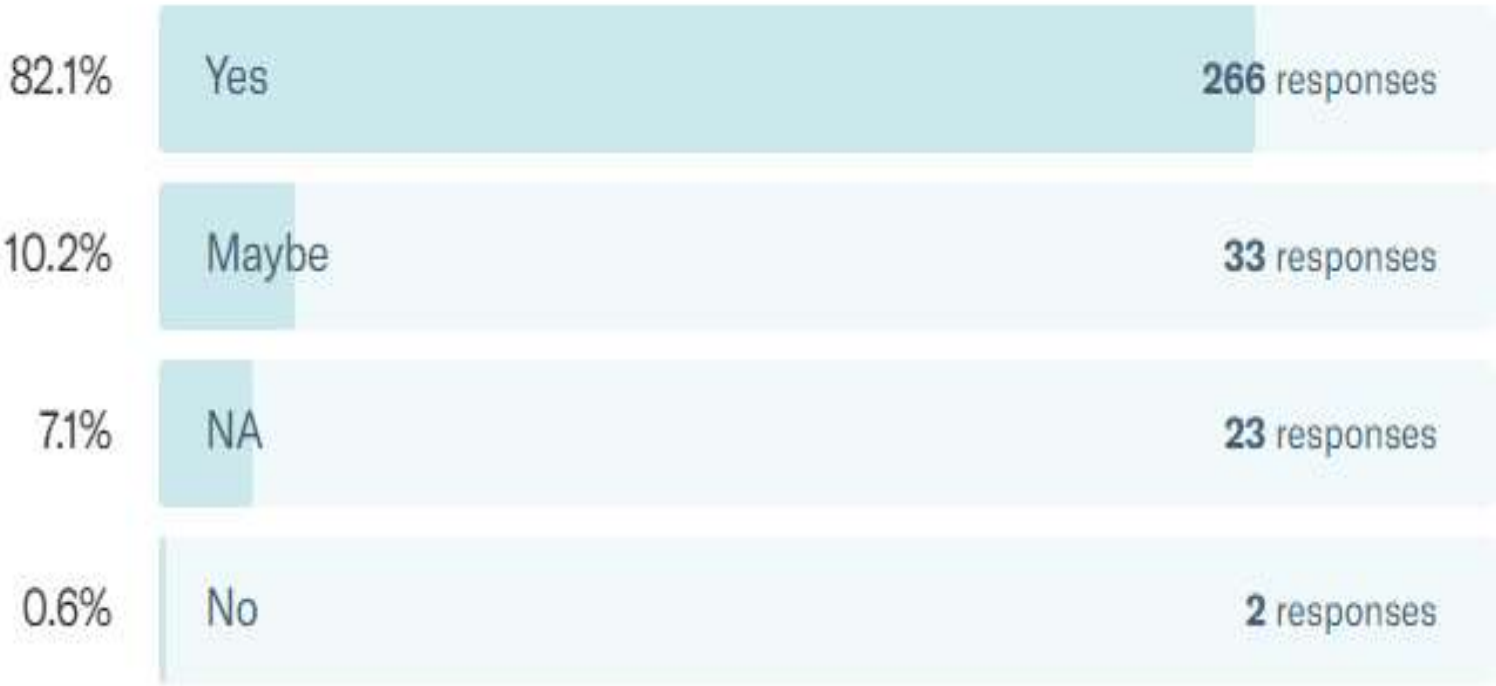
Natural Language Processing
Realistic Avatars
Standalone VR headsets

VR Evaluation

✓ 16

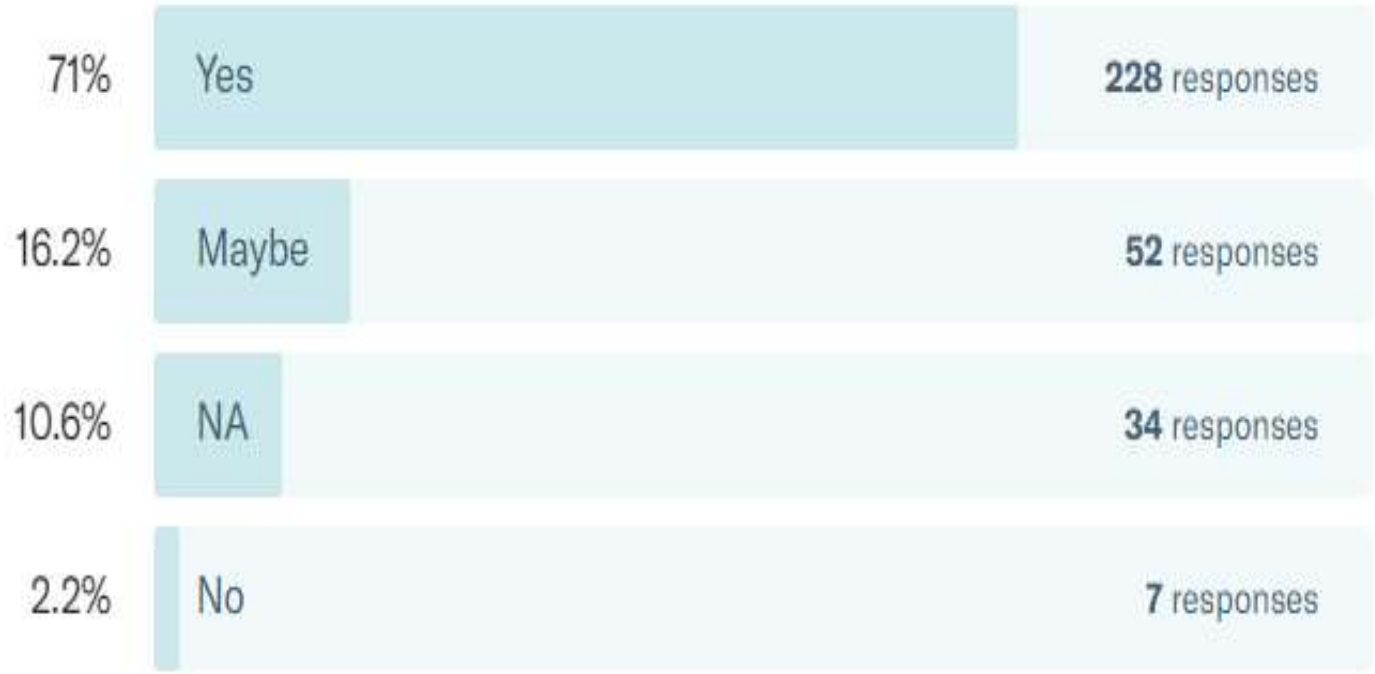
Would VR enhance your learning experience?

324 out of 333 people answered this question



✓ 17 **Would you more likely enrol on a course that includes VR as a teaching tool?**

321 out of 333 people answered this question




“
엄마, 어디 있었어?
항상... 네 곁에...