A Primer from Pathology to Protection: Brain changes, risk factors & maximizing brain health in menopausal women

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Jean Hailes, February 28, 2026

MONASH University

Acknowledgements

- I work, live and play on the lands of the Wurundjeri Woi-Wurrung people of the Kulin nation
- I acknowledge their Elders past, present, and emerging, and any First Nations Elders viewing this presentation

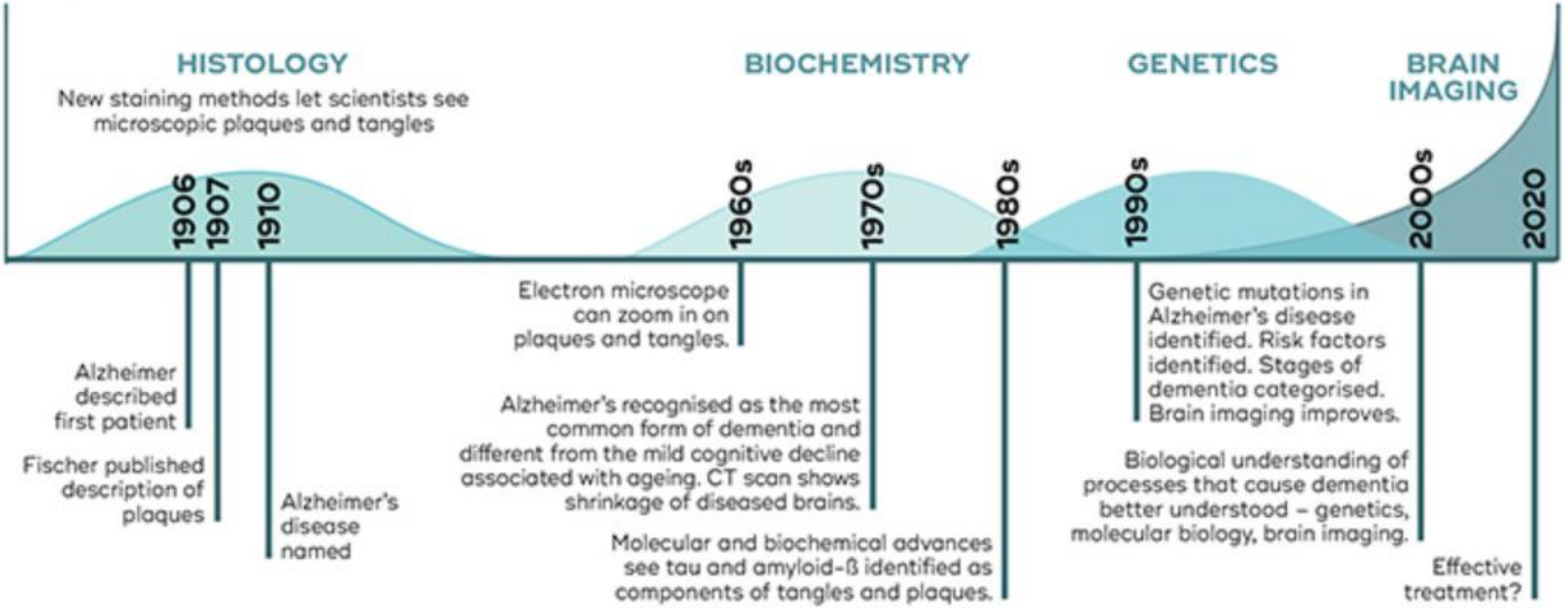
Overview

- prevalence and pathology of neurodegeneration
- what is dementia and how do we diagnose it
- the risks: concept of vascular health = brain health
- midlife vascular risk factors determine late life cognition for women
- neuroprotective behaviours – get fit, get tested

Nuns and orthodoxies: Facts, pathologies, incidence

Greatest health problem in the world: Dementia facts 2026 (WHO, Dementia Australia)

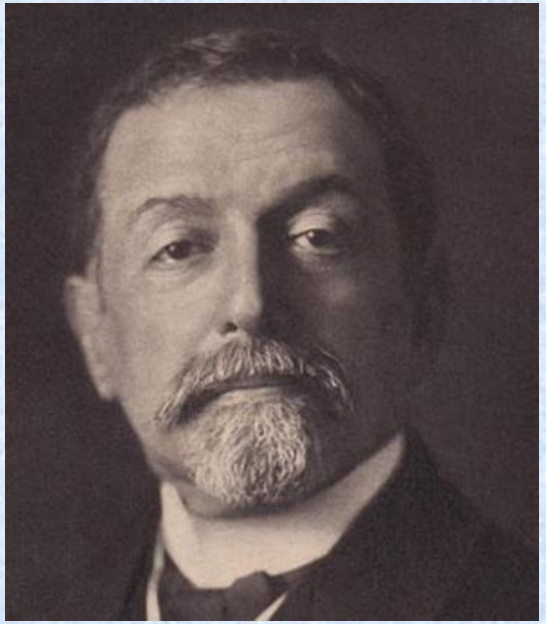
- **dementia is the leading cause of death in Australia**
- estimated 446,500 Australians living with dementia, 1.7 million people are involved in the care of someone living with dementia
- number of Australians living with dementia is expected to increase to more than 1 million by 2065
- 10 million people are diagnosed each year with dementia globally
- women are disproportionately affected by dementia, both directly and indirectly
- dementia due to Alzheimer disease (AD) is commoner in women than men
- women experience higher disability-adjusted life years and mortality due to dementia
- women provide 70% of care hours for people living with dementia
- Costs ~$USD1.6 trillion annually


HISTOLOGY
New staining methods let scientists see microscopic plaques and tangles
BIOCHEMISTRY
GENETICS
BRAIN IMAGING
1906
1907
1910
1960s
1970s
1980s
1990s
2000s
2020
Alzheimer described first patient
Fischer published description of plaques
Alzheimer's disease named
Electron microscope can zoom in on plaques and tangles.
Alzheimer's recognised as the most common form of dementia and different from the mild cognitive decline associated with ageing. CT scan shows shrinkage of diseased brains.
Molecular and biochemical advances see tau and amyloid-ß identified as components of tangles and plaques.
Genetic mutations in Alzheimer's disease identified. Risk factors identified. Stages of dementia categorised. Brain imaging improves.
Biological understanding of processes that cause dementia better understood – genetics, molecular biology, brain imaging.
Effective treatment?

ALOIS ALZHEIMER

OSKAR FISCHER

EMIL VON KRAEPELIN



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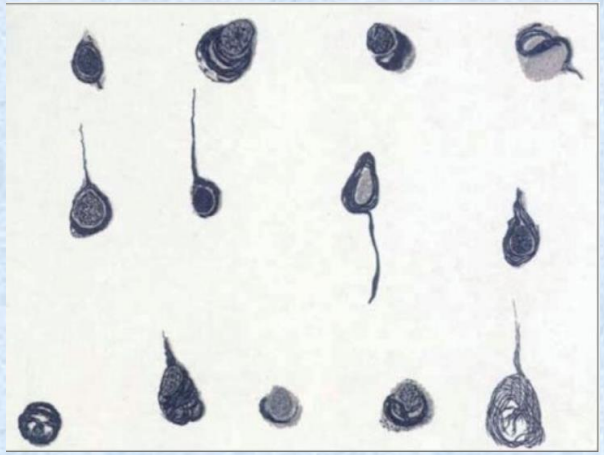

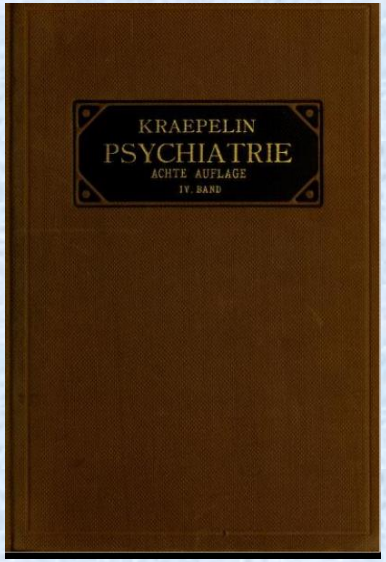

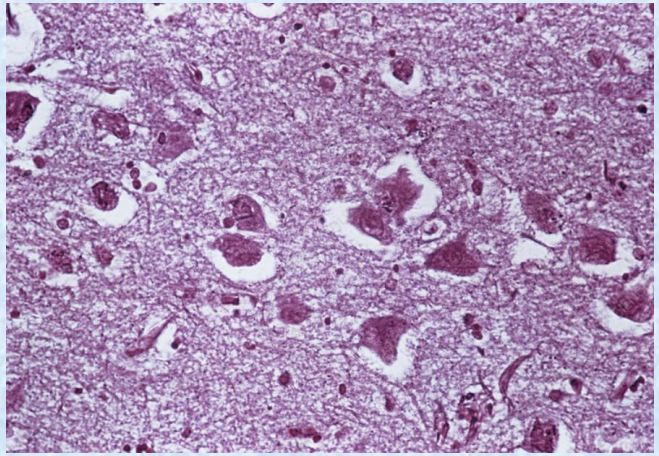

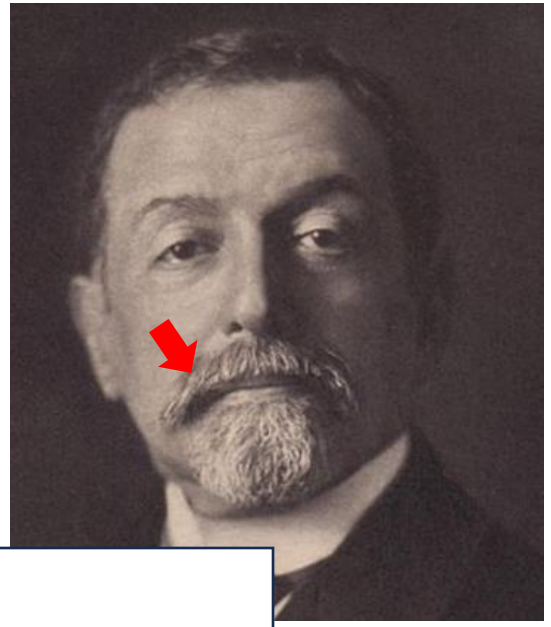

ALOIS ALZHE

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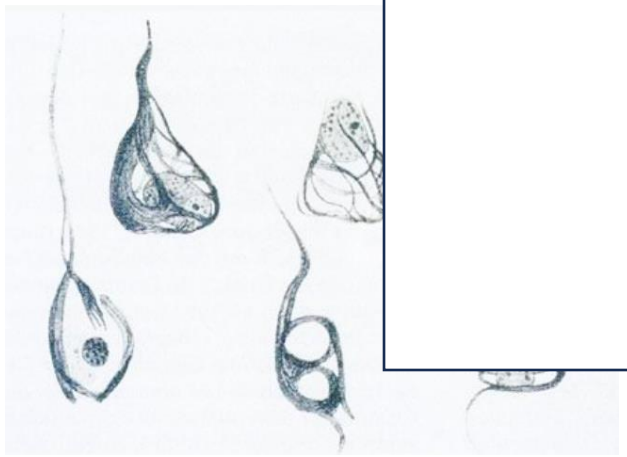
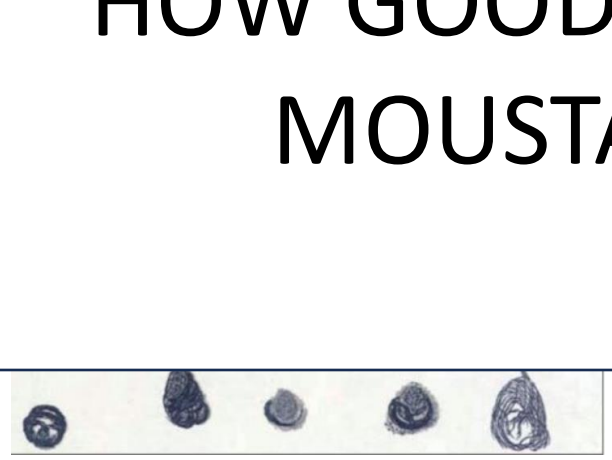
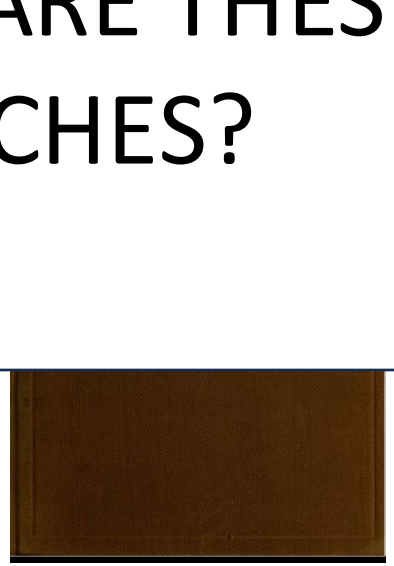
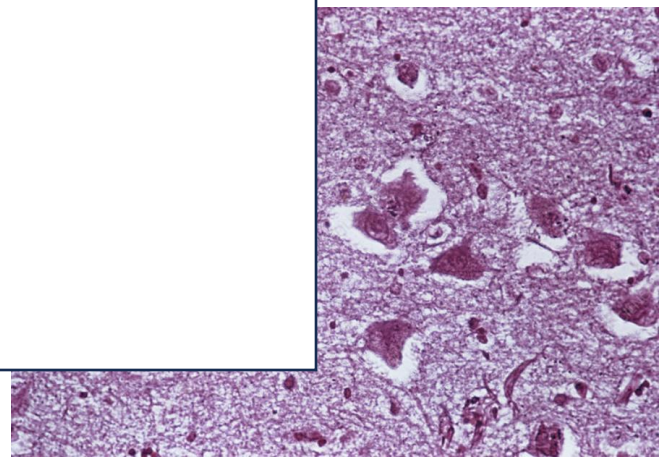
HOW GOOD ARE THESE MOUSTACHES?









Orthoxies: age of "causal" toxic proteins

- 1906 Alois Alzheimer presented the case of Auguste Deter, Fischer confirmed
- 1910 Emil Kraepelin named the disease in his honour
- 1963 Terry and Kidd imaged neurofibrillary tangles (NFTs) via EM
- 1976 Davies and Maloney proposed cholinergic hypothesis of AD
- 1984 Glenner and Wong described amyloid-beta (Aβ) in AD brains
- 1987 first genetic association reported Chr21 amyloid precursor protein
- 1991-2 Hardy, Allsop, Higgins publish the amyloid hypothesis *"deposition of Aβ is the causative agent of AD pathology … other lesions … follow directly from this deposition"*
- 1993 first genetic risk factor *APOE ε4* described on Chromosome 19

The ascent of the amyloid hypothesis

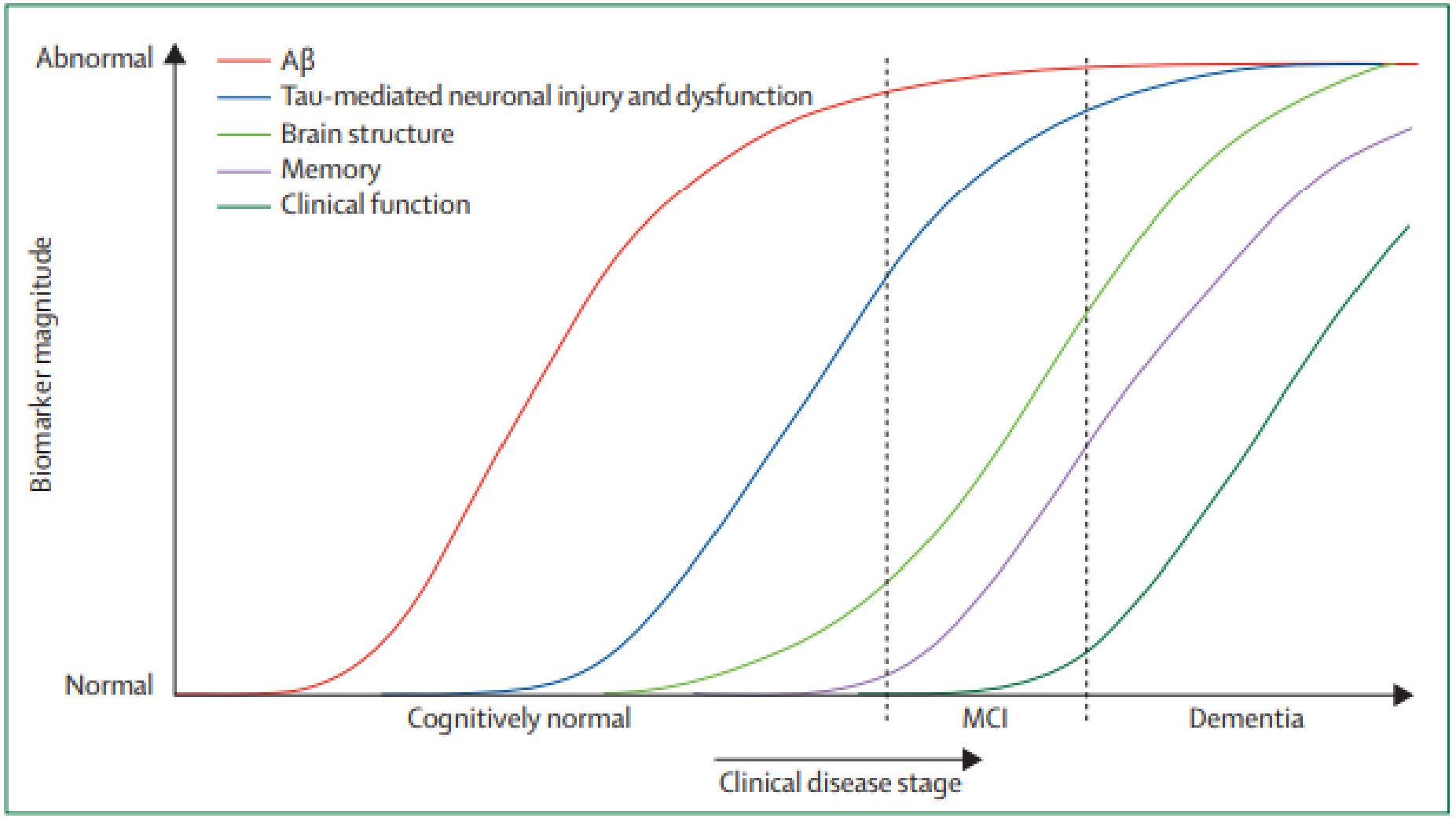


Figure 1: **2010 model of dynamic biomarkers of the Alzheimer's disease pathological cascade**
Aβ is identified by CSF $A\beta_{42}$ or PET amyloid imaging. Tau-mediated neuronal injury and dysfunction is identified by CSF tau or fluorodeoxyglucose PET. Brain structure is measured by structural MRI. Aβ=amyloid β. MCI=mild cognitive impairment. Reproduced from Jack and colleagues,[18] by permission of Elsevier.

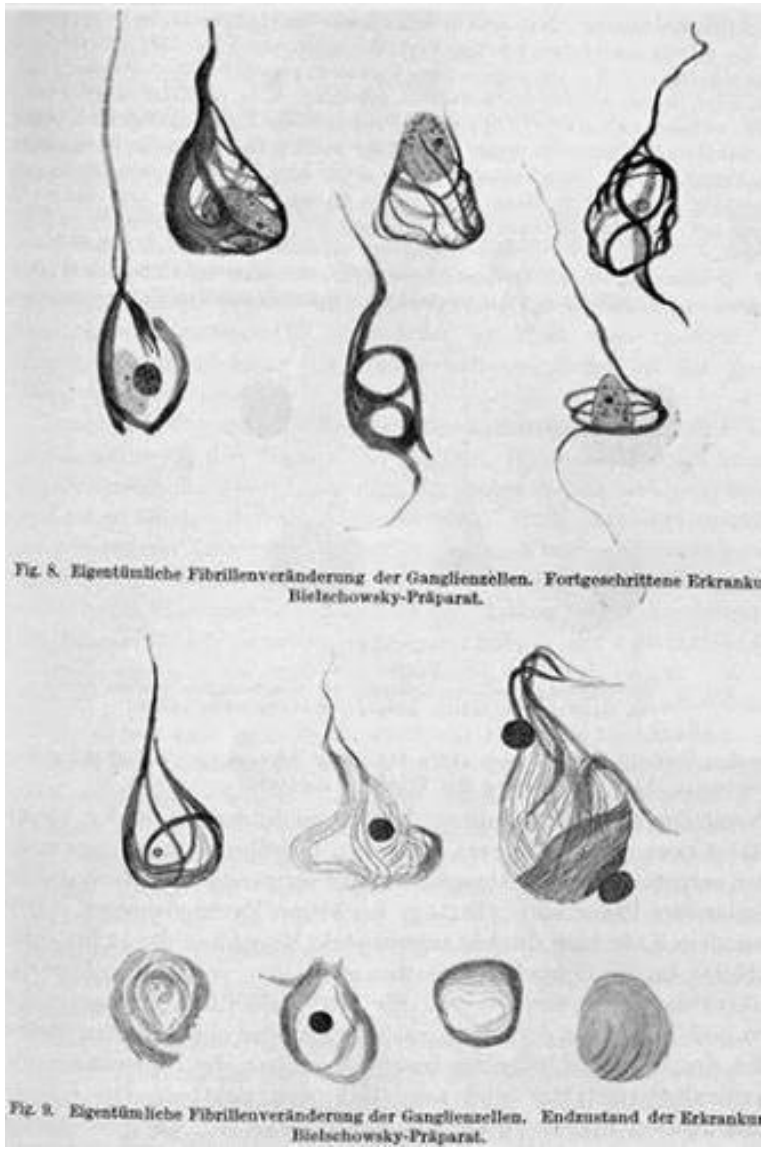
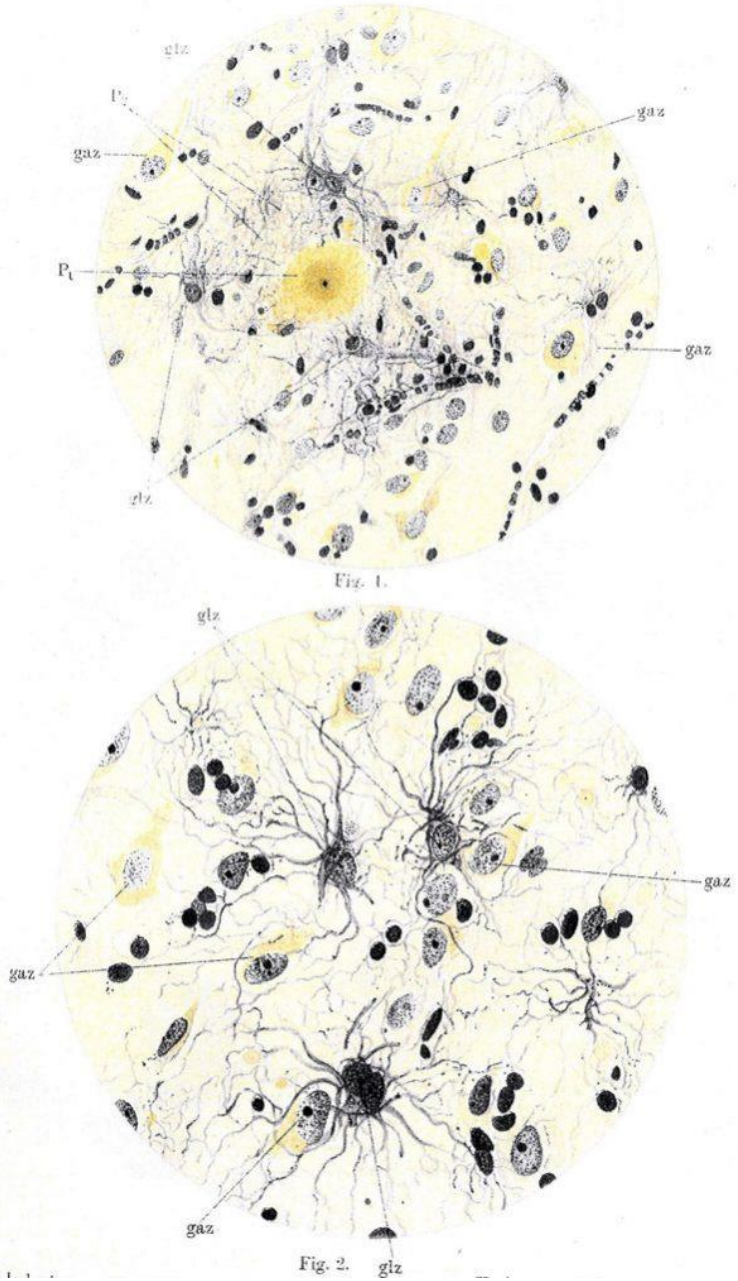
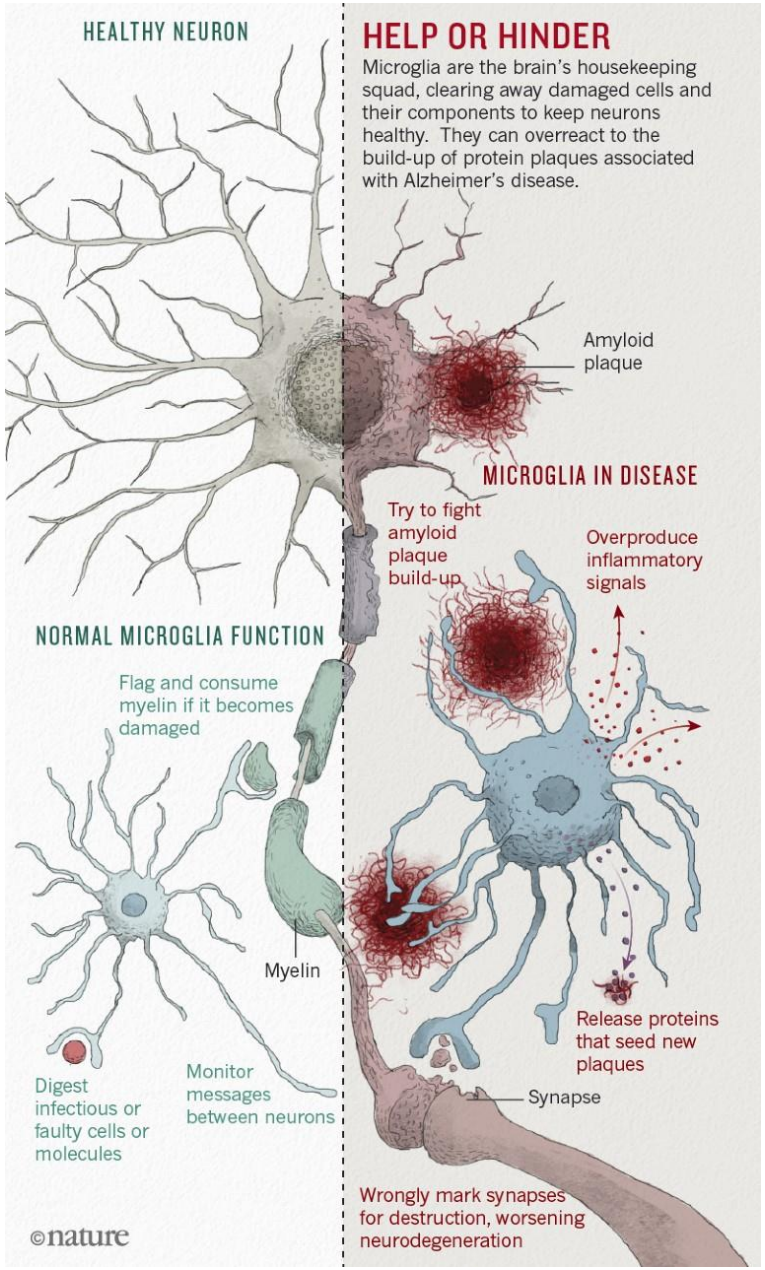


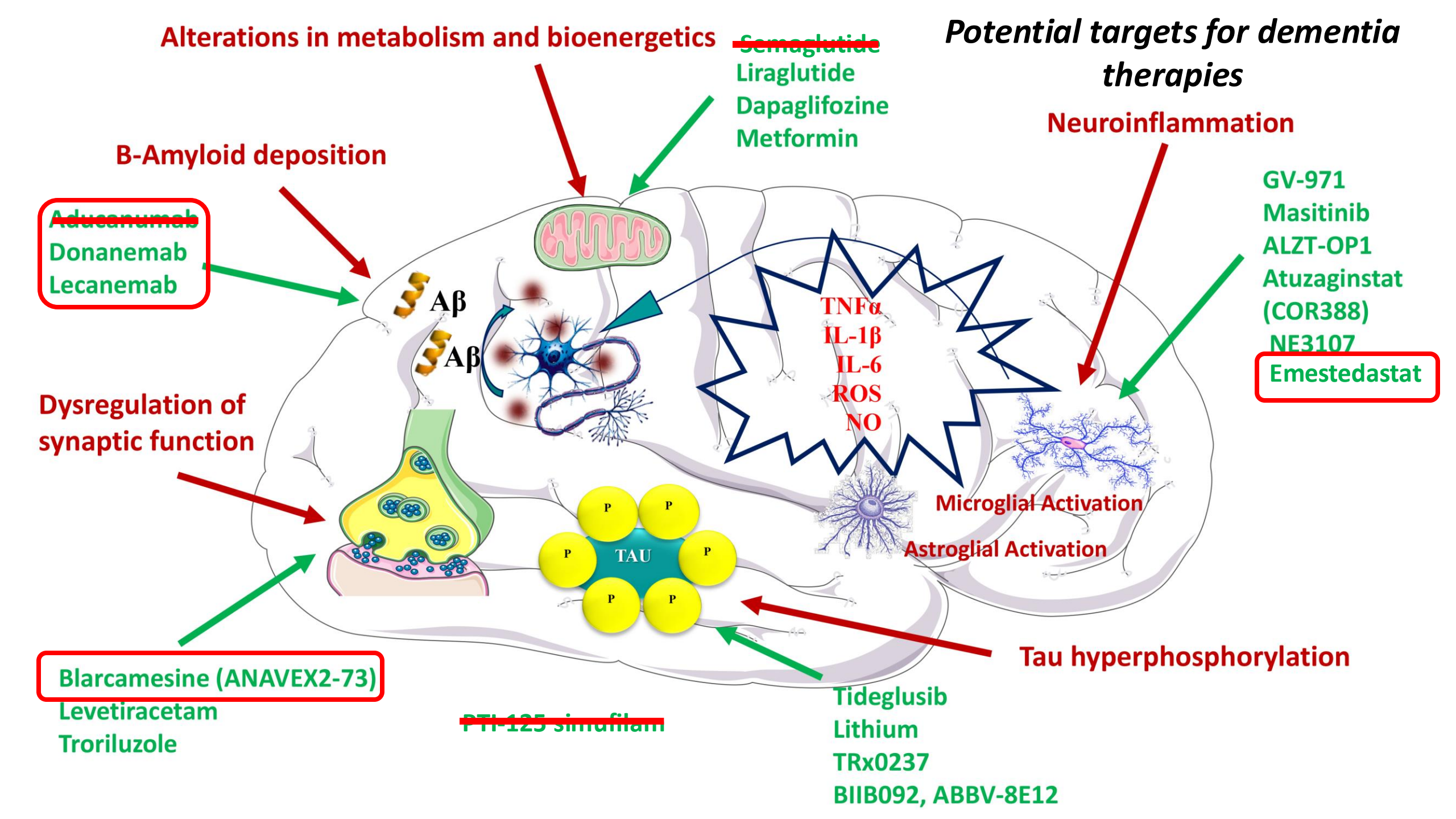
Fig. 8. Eigentümliche Fibrillenveränderung der Ganglienzellen. Fortgeschrittene Erkrankung
Bielschowsky-Präparat.

Fig. 9. Eigentümliche Fibrillenveränderung der Ganglienzellen. Endzustand der Erkrankung
Bielschowsky-Präparat.

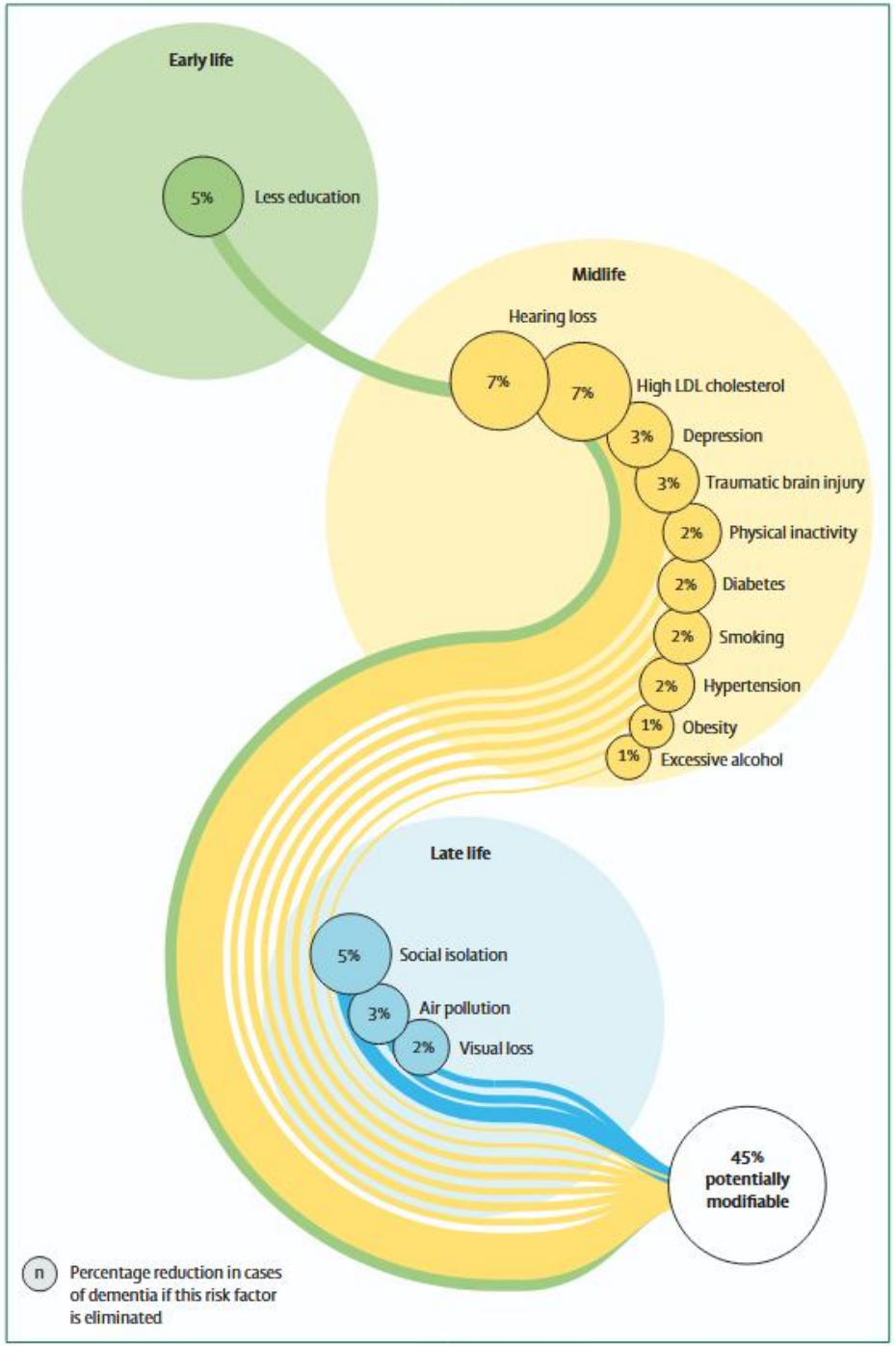




TAU, AMYLOID, VASCULAR DEGENERATION, MICROGLIAL ACTIVATION


Potential targets for dementia therapies
Alterations in metabolism and bioenergetics
~~Semaglutide~~
Liraglutide
Dapaglifozine
Metformin
B-Amyloid deposition
~~Aducanumab~~
Donanemab
Lecanemab
Aβ
Aβ
Neuroinflammation
GV-971
Masitinib
ALZT-OP1
Atuzaginstat
(COR388)
NE3107
Emestedastat
TNFα
IL-1β
IL-6
ROS
NO
Dysregulation of synaptic function
Microglial Activation
Astroglial Activation
P
TAU
Blarcamesine (ANAVEX2-73)
Levetiracetam
Troriluzole
~~PTI-125 sinufilam~~
Tau hyperphosphorylation
Tideglusib
Lithium
TRx0237
BIIB092, ABBV-8E12

Epidemiological and brain bank findings



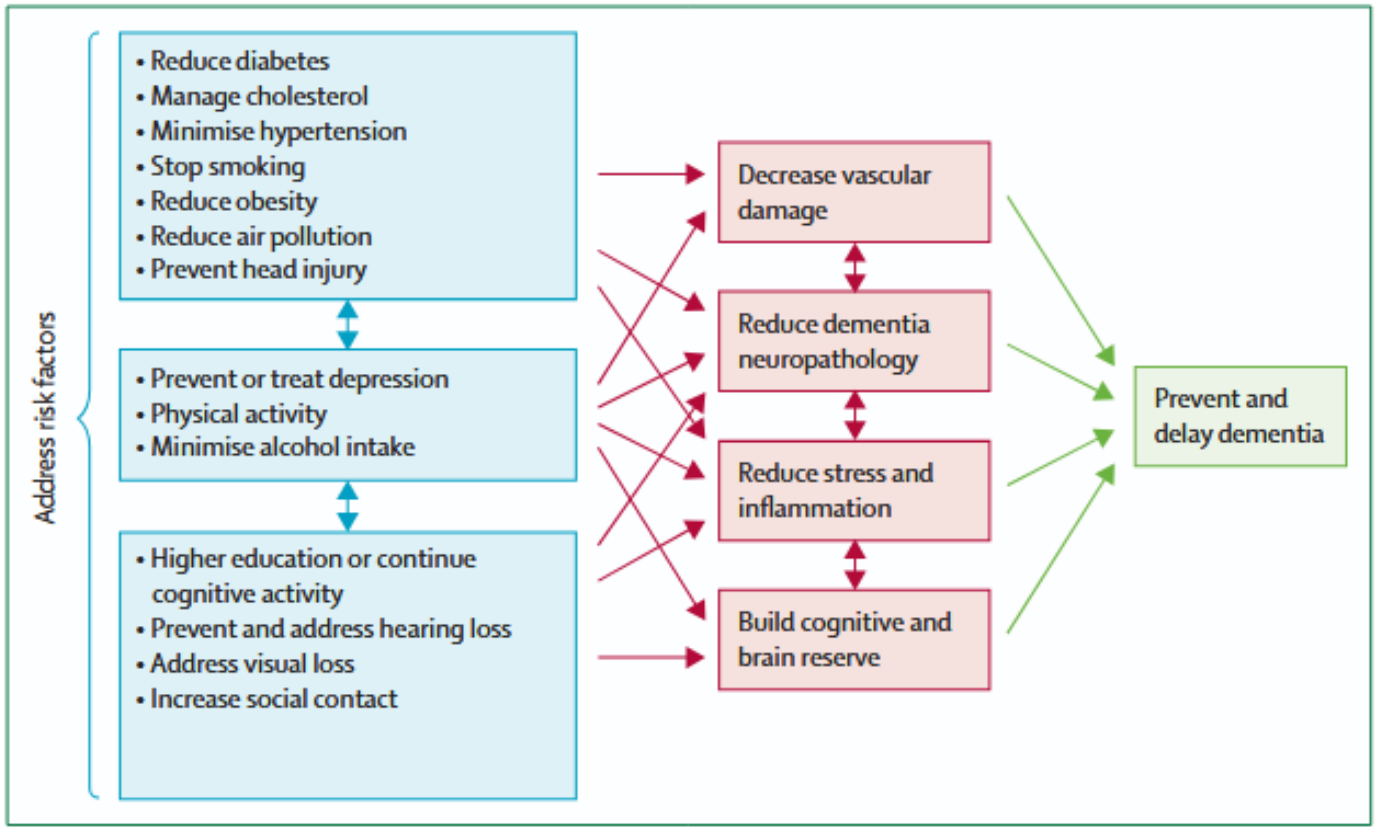


Figure 2: **Possible brain mechanisms for enhancing or maintaining cognitive reserve and risk reduction of potentially modifiable risk factors in dementia**

Livingston, et al., *The Lancet,* 2024

Vascular health is the greatest determinant of brain health

- ***AD, cerebro- and cardiovascular disease share the same risk factors***
- ***Including education, as educational attainment is one of the strongest determinants of health literacy***
- many pivotal studies have shown that mid-life vascular disease is a strong risk factor for all cause late-life dementia, especially hypertension
- true for all CVRF, including physical inactivity, obesity, T2DM, etc.
- cognitive effects like slowed speed of processing and executive impairments are seen in non-demented individuals with CVRF
- large studies, such as PROGRESS and SPRINT-MIND, suggest that treatment may reduce risk of dementia
- healthy lifestyle associated with lowered dementia risk AND slower cognitive decline

The Nuns:
Religious Orders Study and Rush Memory and Aging Project

- ROS (Nun study): women with strokes had poorer cognitive function and a higher prevalence of dementia than those without them (Snowdon, et al., *JAMA*, 1997)
- amyloid status bore little correlation with their cognitive profile during life
- especially high prevalence of dementia in women with small vessel and *microvascular* disease
- severity of dementia correlated with number of brain infarcts better than extent of amyloid protein deposition (Troncoso, et al., *Ann Neurol*, 2018; 179 autopsies)
- "*initiator, stimulator, or additive contributor to neurodegeneration*"

Mixed brain pathology is the norm in normal aging

- co-pathologies are the norm in normal aging and dementia
- n = 1,079 brains from ROSMAP normal aging, MCI and AD (Boyle, et al., *Ann Neurol* 2018;83:74–83)
- **mixed neuropathology was ubiquitous**
- 94% of participants 1+, 78% 2+, 58% 3+, and 35% 4+
- AD was most frequent (65%) but rarely occurred in isolation (9%)
- **236 different neuropathologic combinations** were observed
- AD pathology accounted ~55% cognitive loss

Table 3. Proportions of Cognitive Loss Associated with Specific Neuropathologies

Neuropathology	No.	Mean	SD	Median	Q1	Q3
AD	704	57.9%	19.9%	53.7%	42.7%	72.4%
Gross infarcts	388	28.8%	23.7%	20.1%	16.1%	27.6%
Cerebral amyloid angiopathy	386	20.6%	19.0%	15.7%	11.9%	22.1%
TDP-43	377	30.5%	19.3%	23.8%	20.5%	34.1%
Atherosclerosis	358	27.4%	23.1%	18.5%	14.9%	27.7%
Arteriolosclerosis	338	27.5%	21.5%	19.8%	15.8%	28.1%
Cortical Lewy bodies	143	45.1%	17.2%	41.0%	33.7%	49.0%
Hippocampal sclerosis	112	28.1%	12.6%	24.9%	21.3%	28.9%

Boyle, et al., *Ann Neurol* 2018;83:74–83

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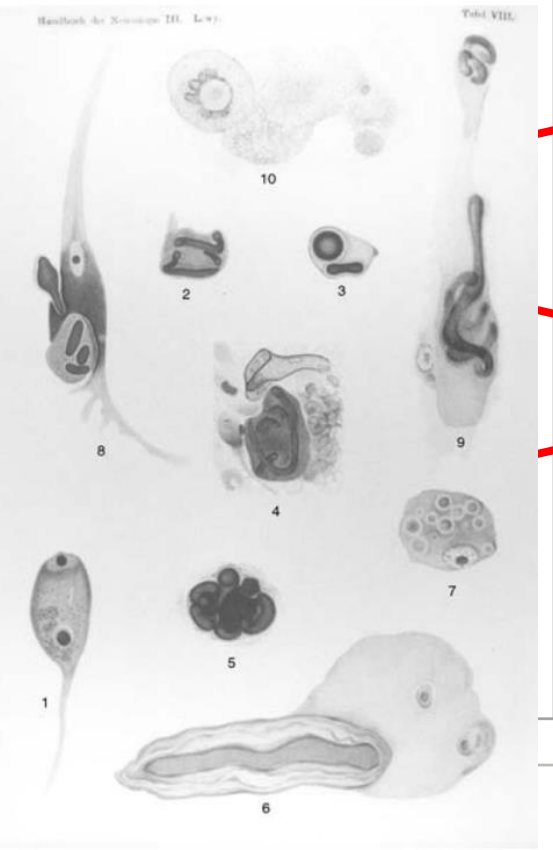

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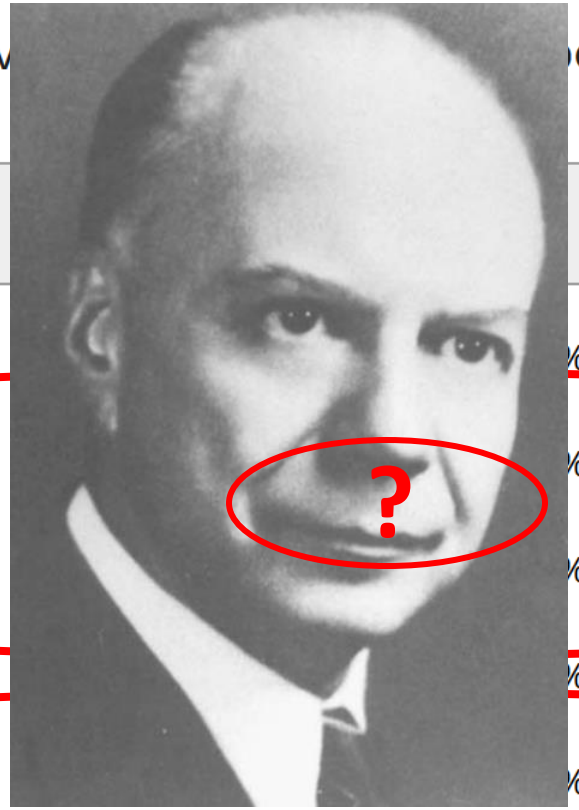
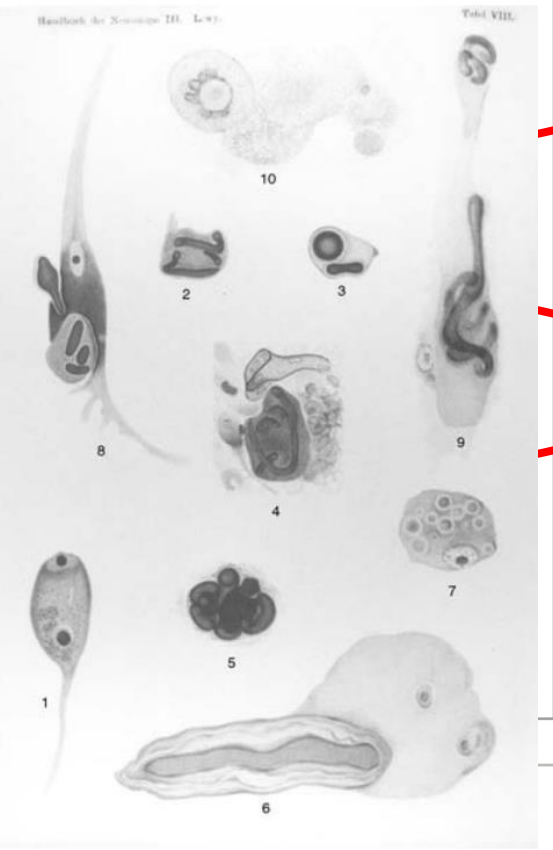




Boyle, et al., *Ann Neurol* 2018;83:74–83

Dementia incidence is declining

- some studies found a 26% drop in dementia incidence between 2015 and 2022, with more pronounced declines in women
- sex specific differences are emerging, women with CVD 1.5 x risk AD than men but 15% less risk VaD than men (Dong, *Biol Sex Differ*, 2022)
- average decrease of 13% per decade over the past 30 years
- people in more recent birth cohorts have a lower risk of developing dementia at any given age compared to previous generations, with a potential 67% reduction in age-specific risk over 40 years.
- Doblhammer, et al., *Alzheimers Dement*, 2014.; Norton, et al., *Lancet Neurol*, 2014
- Satizabal, et al., *NEJM*, 2016 decline over 3 decades in Framingham study
- Matthews, et al., *Nature Communications*, April 2016; 20-year incidence has reduced in UK CFAS studies

Pooled data and meta-analyses

Mukadam, et al. *The Lancet Public Health*, 2024

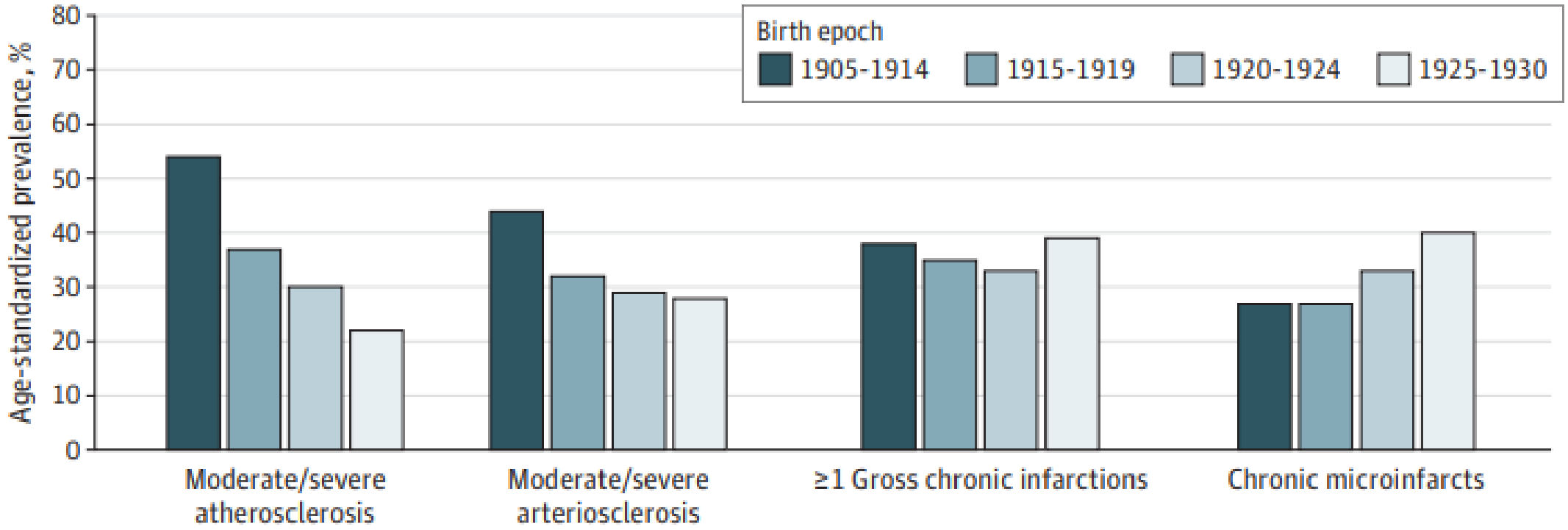
- Reviewed evidence on changes in dementia prevalence and incidence over time using published population-based cohort studies
- aimed to quantify associated changes in risk factors over time using population attributable fractions (PAFs)
- 1925 records, five eligible systematic reviews, 71 potentially eligible primary papers, 27 included
- lifestyle interventions such as compulsory education and reducing rates of smoking through country-level policy changes could be associated with an observed reduction, and therefore future reduction, in the incidence of dementia

And is this reflected in the pathology?

- ROSMAP team examined 1554 participants (510 [33%] male; 90 [66-108] years at death)
- Examined trends across birth epochs (1905-1914: n = 374; 1915-1919: n = 360; 1920-1924: n = 466; 1925-1930: n = 354).
- **no differences** in prevalence of pathologic AD diagnosis (62-68%), mean levels of global AD pathology, or other "neurodegenerative pathologies"
- greater density of tau tangles in later birth cohorts
- ***'In contrast, atherosclerosis and arteriosclerosis were dramatically lower over time'***
- age-standardized prevalence of moderate to severe atherosclerosis was 54% in 1905-1914 cohort but 22% for 1925-1930
- they concluded that any improvements over time in clinical dementia may be associated with improved resilience to pathology rather than reduced AD pathology AND *'vessel pathologies were markedly lower over birth cohorts, indicating the association with brain health of population-wide improvements in several vascular risk factors'*

Vascular pathologies are declining in brain banked participants

Figure 3. Time Trends in Postmortem Cerebrovascular Pathology Across 4 Birth Epochs



Grodstein, et al. *JAMA Neurology*, 2023

What defines dementia? How do you diagnose it?

Cognitive impairment and dementia

- Subjective cognitive impairment is the term we use for people who experience cognitive symptoms
- Brain fog falls in this category, but so does almost every major life experience
- Mild cognitive impairment is a research category for people with cognitive impairments on testing that are not affecting their ability to function
- Dementia is the term we use when people have progressive cognitive impairments that are affecting their ability to function
- Most dementia is due to degenerative processes in the brain –these cause neurodegeneration

How do we detect neurodegeneration?

- On brain imaging, sometimes CT but mostly MRI scans
- We can see many things: brain shrinkage (atrophy), changes in the white matter (white matter hyperintensities, WMH), strokes, bleeds
- Most of the changes we can see are vascular or shrinkage
- PET scans can allow us to see changes in brain metabolism associated with neurodegeneration
- Newer PET scans allow us to image the distribution of amyloid and tau in the brain
- Can measure brain proteins via CSF and now blood tests too

Brain volumes, cognition, HRT

- Our brains reach peak volume in the third to fourth decades
- Decline after ☹
- no effect of lifetime estrogen exposure on grey matter volumes in the Women's Healthy Aging Project (Kwan, et al., 2025)
- UK Biobank: 125K women, examined grey matter volume in 2 areas, HRT and mental health – found that menopause was linked to mental health problems and grey matter decline (Zuhlsdorff, et al. *Psychological Medicine*, 2025)
- UK Biobank data: no neuroprotection from HRT nor any adverse effects on predicted brain age (Barth et al., *eLife,* 2025)
- **No effect on brain volumes with HRT demonstrated**
- relationship between midlife CVRF scores and late life brain volume and cognition mediated by white matter health (WMH)
- intervention **strategies that target major cardiovascular risk factors** at midlife might be effective in reducing the development of WMH lesions and thus late life cognitive decline (Aljondi, et al., 2020)

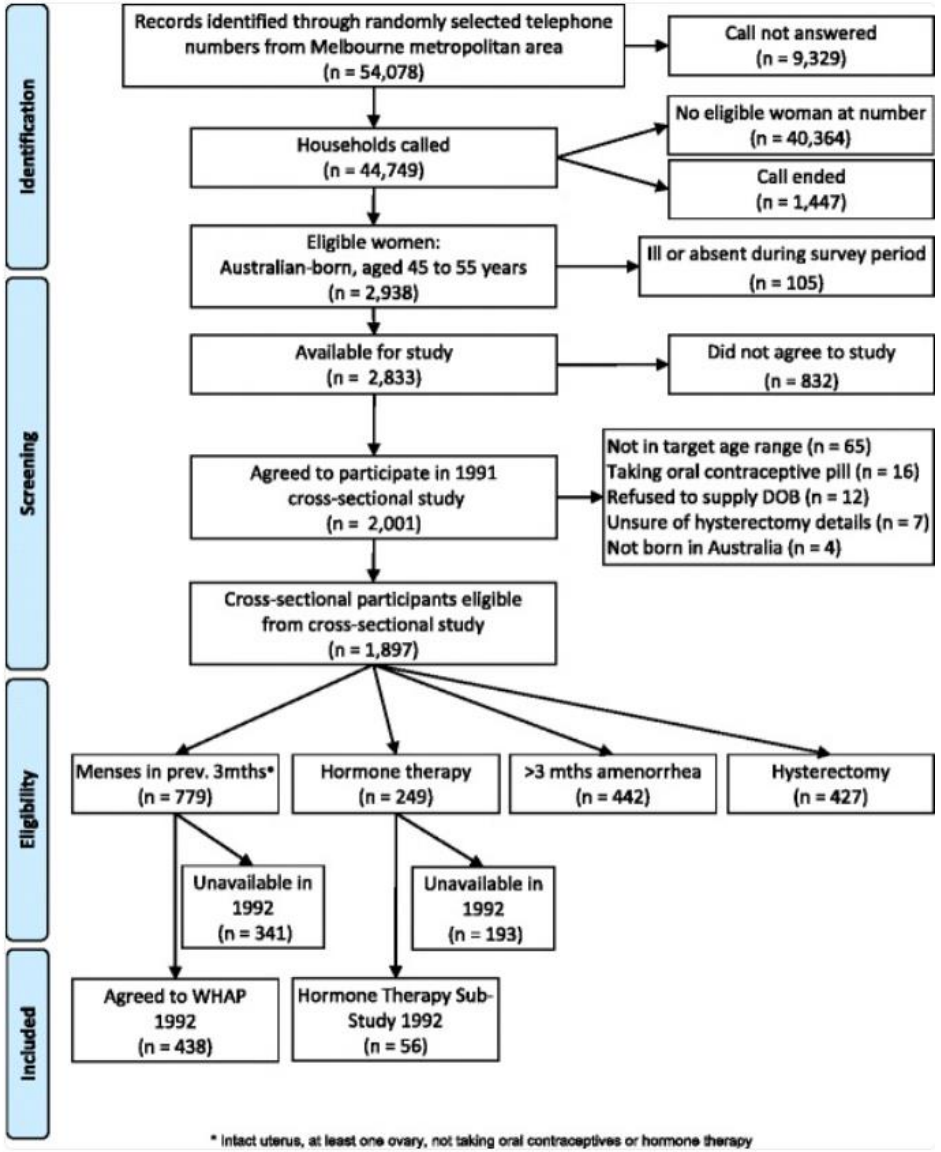
Results

Younger age and better education were associated with baseline memory test performance (CERAD). Over the 20 years of study follow-up, cumulative mid- to late-life physical activity had the strongest effect on better later life verbal memory (0.136 [0.058, 0.214]). The next most likely contributors to verbal memory in late life were the negative effect of cumulative hypertension (−0.033 [−0.047, −0.0.18] and the beneficial effect of HDL cholesterol (0.818 [0.042, 1.593]).

Conclusions

Findings suggest that midlife interventions focused on physical activity, hypertension control, and achieving optimal levels of HDL cholesterol will help maintain later-life verbal memory skills.

- Women's Healthy Aging Project (from Szoeke, 2016)
- Followed women aged 45-55 for 20 years, started by Lorraine Dennerstein with interest in women's psychological wellbeing
- now run by Cassandra Szoeke with an interest in cognitive profiles and dementia risk
- Found that women who developed impairments in memory later in life had more hypertension, physical inactivity and dyslipidaemia (Szoeke, AJGS, 2016)



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Original Article

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Emotional and cognitive effects of menopause and hormone replacement therapy

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Abstract

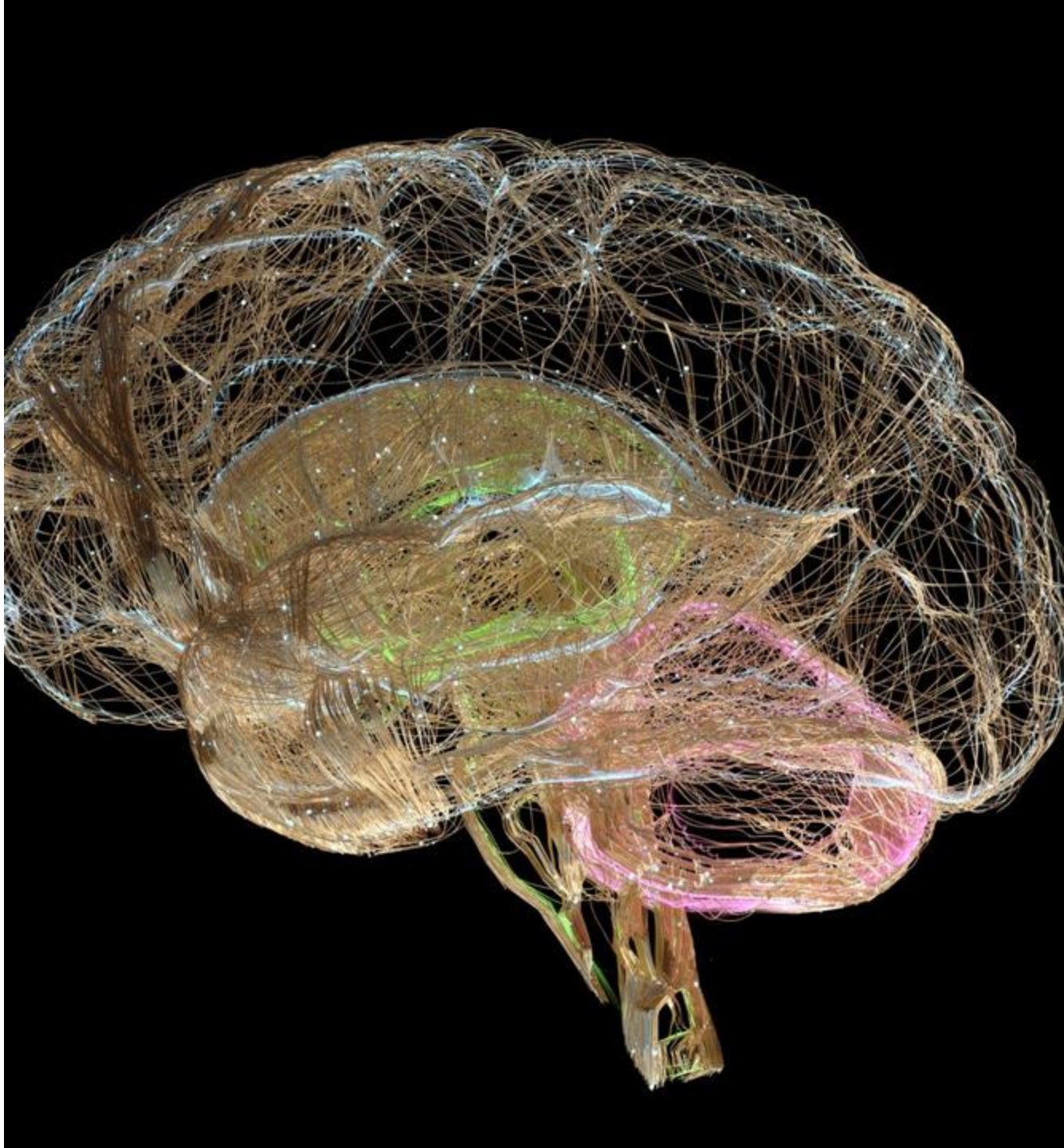
Background. Menopause is a natural physiological process, but its effects on the brain remain poorly understood. In England, approximately 15% of women use hormone-replacement therapy (HRT) to manage menopausal symptoms. However, the psychological benefits of HRT are not well established. This study aims to investigate the impact of menopause and HRT on mental health, cognitive function, and brain structure.

Methods. We analyzed data from nearly 125,000 participants in the UK Biobank to assess associations between menopause, HRT use, and outcomes related to mental health, cognition, and brain morphology. Specifically, we focused on gray matter volumes in the medial temporal lobe (MTL) and anterior cingulate cortex (ACC).

Results. Menopause was associated with increased levels of anxiety, depression, and sleep difficulties. Women using HRT reported greater mental health challenges than post-menopausal women not using HRT. Post-hoc analyses revealed that women prescribed HRT had higher levels of pre-existing mental health symptoms. In terms of brain structure, MTL and ACC volumes were smaller in post-menopausal women compared to pre-menopausal women, with the lowest volumes observed in the HRT group.

Conclusions. Our findings suggest that menopause is linked to adverse mental health outcomes and reductions in gray matter volume in key brain regions. The use of HRT does not appear to mitigate these effects and may be associated with more pronounced mental health challenges, potentially due to underlying baseline differences. These results have important implications for understanding the neurobiological effects of HRT and highlighting the unmet need for addressing mental health problems during menopause.

Brain health: the risks



Hypertension

- HTN is arguably the greatest global driver of dementia
- HTN affects women at all life stages (Srivaratharajah, 2019)
- rates of HTN increase with age & postmenopausal women have highest rates
- non-hypertensive women have 5 years longer lifespans than those with HTN (Tsao et al., 2022)
- HTN can be controlled
- In countries with a reduction in control among women from 69% to 49%, associated with a significant increase in CVD deaths and hospitalizations (Campbell et al., 2022)

Obesity and insulin resistance

- perimenopausal weight gain starts 5-10 years prior to menopause (“1 kg per year”)
- menopausal transition is associated with central body fat accumulation, a decrease in energy expenditure, weight gain, insulin resistance and a pro-atherogenic lipid profile
- these changes in our metabolic profile “syndrome X” put us at higher risk of atherosclerosis, T2DM, and HTN
- whilst HRT can help with body fat deposition, it is not associated with weight loss

Abnormal fats, sugars, sleep

- We measure high- and low-density lipoproteins in a cholesterol test
- LDLs are the baddies and are the ones that are associated with dementia risk
- During the menopause, the lipid profile for most women changes to have more LDL
- In addition, change to more central adiposity in “syndrome X” means that we have more insulin resistance, which may directly drive deposition of toxic brain proteins
- AND more sleep apneoa/disturbed sleep with higher BMIs is associated with increased dementia risk and a MAJOR factor for cognitive impairment/brain fog

Jean Hailes Women's Health Week 2025

Targeting brain health!!

Monday 1 September

Every check matters

Prioritise your health by staying up to date with your health checks.

Tuesday 2 September

Take the lead

Arm yourself with the right knowledge and tools to get more out of your health appointments.

Wednesday 3 September

Heart smart

Heart disease affects women in ways that are often overlooked. So let's talk about it.

Thursday 4 September

Pain to power

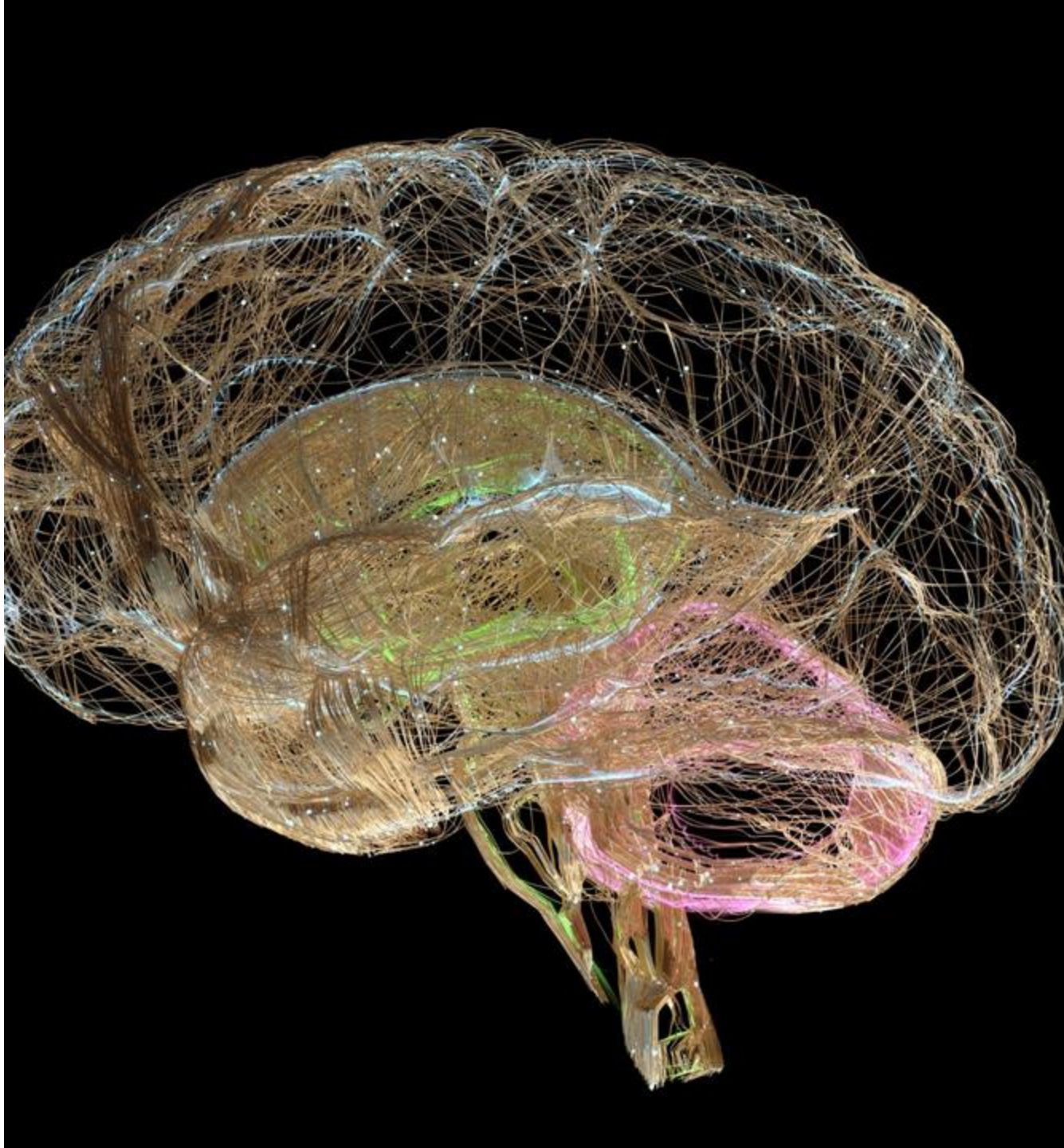
Pain isn't just 'part of being a woman'. You don't have to push through it alone.

Friday 5 September

Be kind to your mind

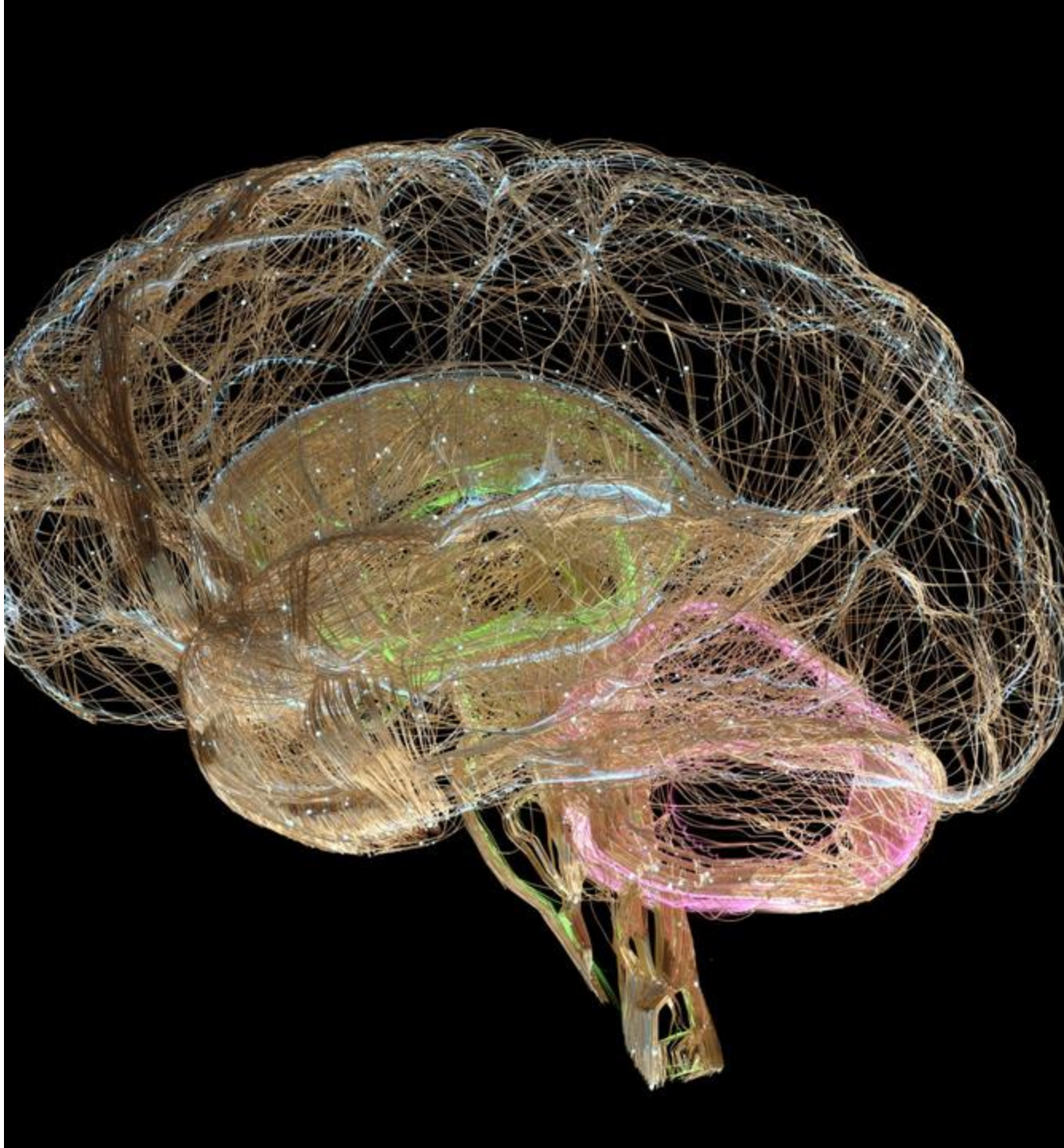
Looking after your mind is just as important as caring for your body.

Q: What reduces blood pressure, blood sugar and LDL levels, obesity, and improves our mood, sleep and longevity?

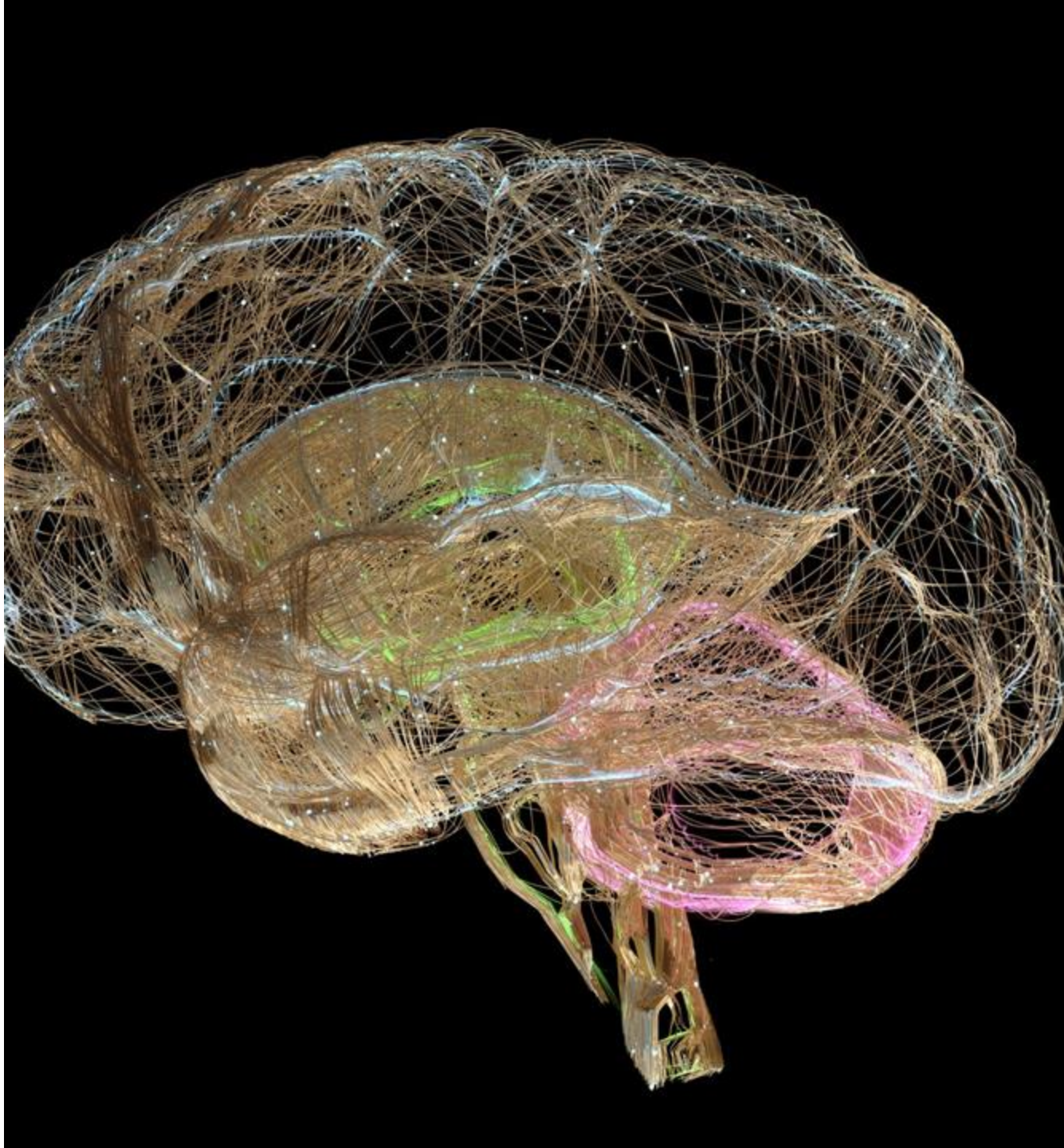


A: not HRT

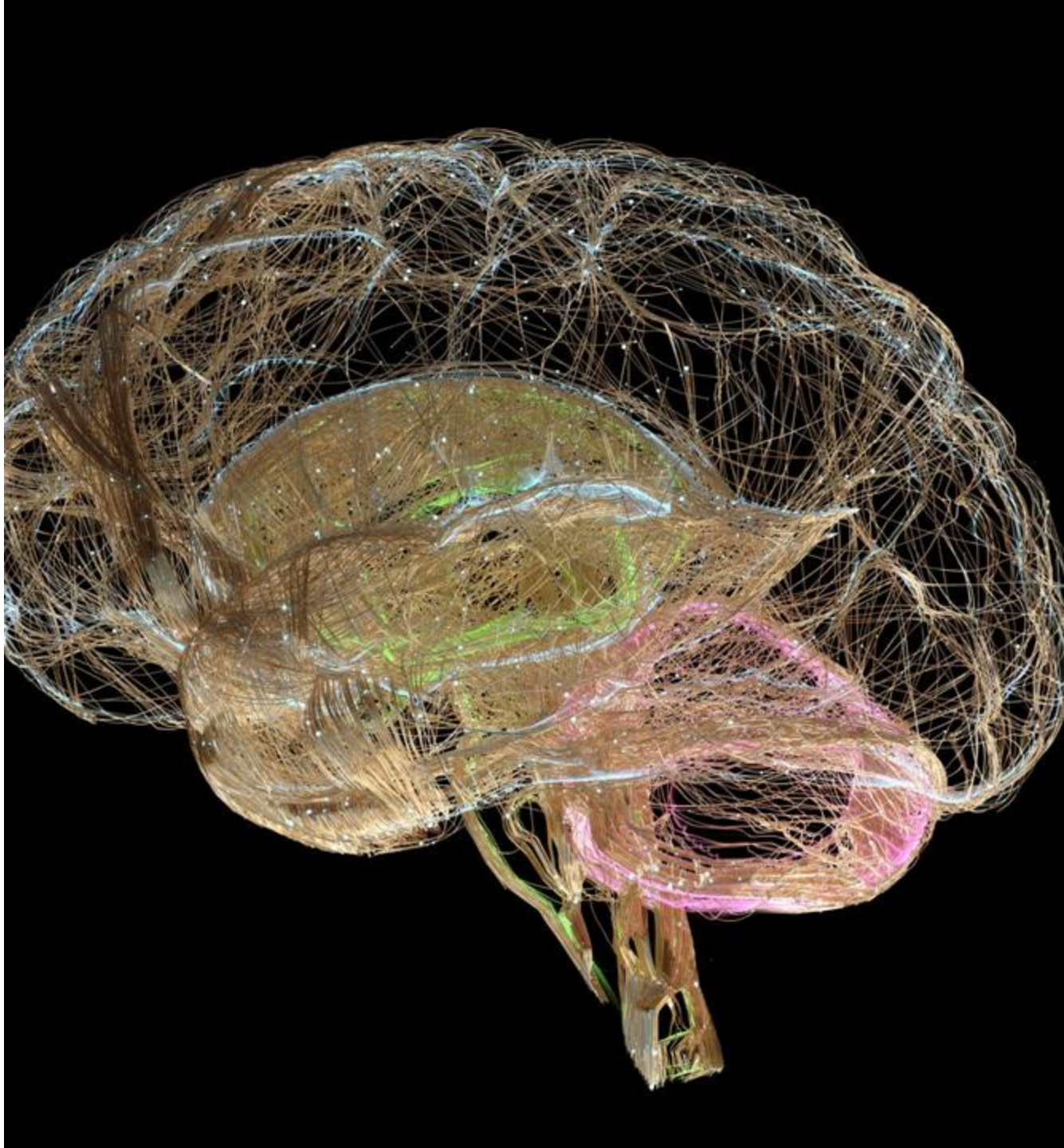
(although it can help)



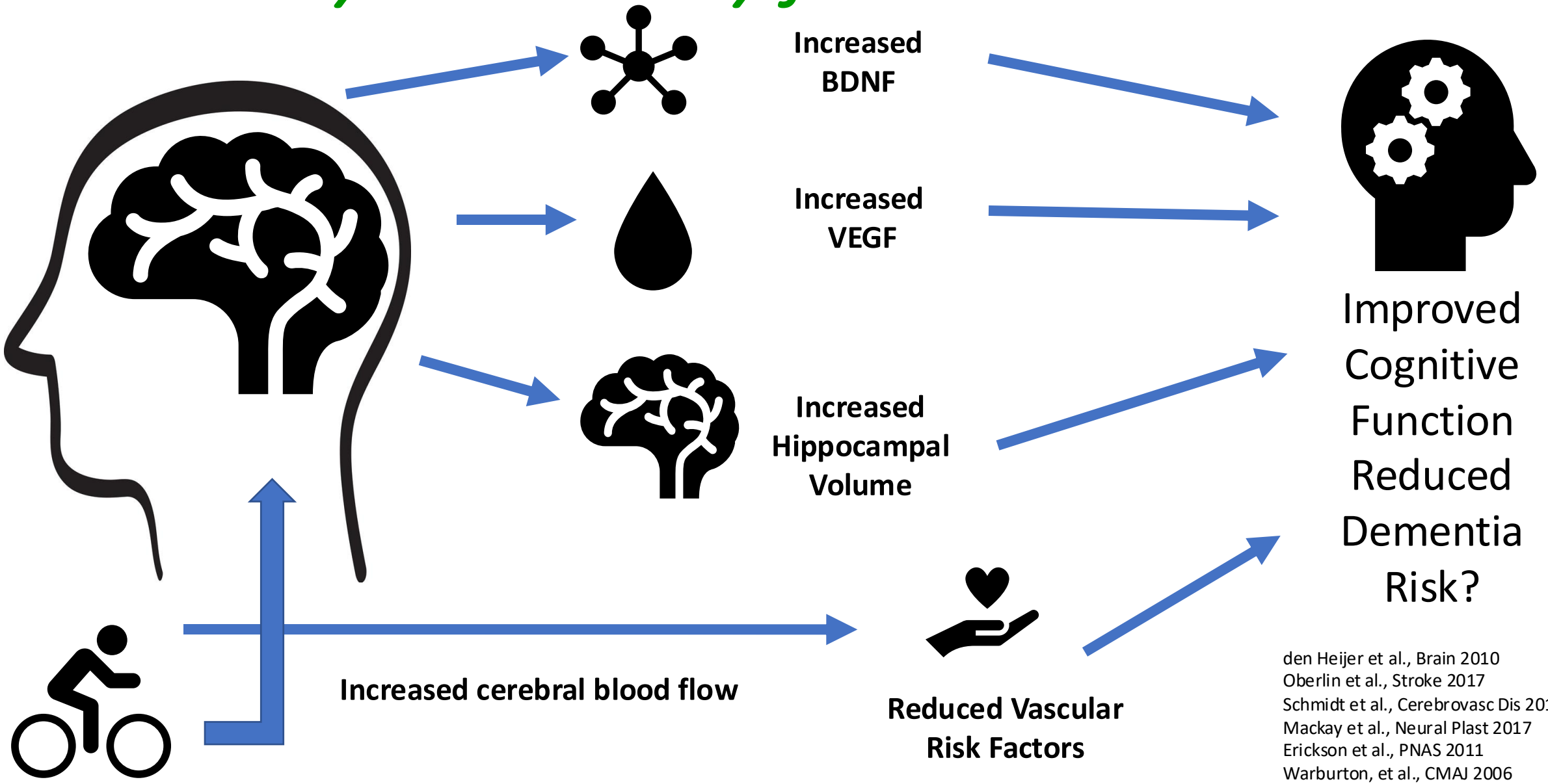
A: or Sudoku (it can't)



Brain Health: neuroprotective lifestyles at every life stage



Physical activity for brain health?



den Heijer et al., Brain 2010
Oberlin et al., Stroke 2017
Schmidt et al., Cerebrovasc Dis 2013
Mackay et al., Neural Plast 2017
Erickson et al., PNAS 2011
Warburton, et al., CMAJ 2006

Physical activity and sedentary behaviours

- higher levels of physical activity (PA) and lower levels of sedentary behaviours are associated with better global cognitive function in older adults
- greatest estimated effect sizes were found for moderate-to-vigorous and TPA, suggesting that greater duration of (any) PA and high intensity PA could be most beneficial for global cognitive function (Rojer, et al., 2021)
- lifelong PA is strongly associated with dementia risk
- evidence is probably even stronger for women
- both resistance and cardiorespiratory exercise are important
- good for heart, gut, bones and brain!

CANVAS to PISCES: Motivation to use Exercise

Original Research Article

Physical Activity After Stroke Is Associated With Increased Interhemispheric Connectivity of the Dorsal Attention Network

Michele Veldsman, PhD[1,2], Leonid Churilov, PhD[2], Emilio Werden[2], Qi Li, MEng[2], Toby Cumming, PhD[2], and Amy Brodtmann, MD, PhD[2,3,4]

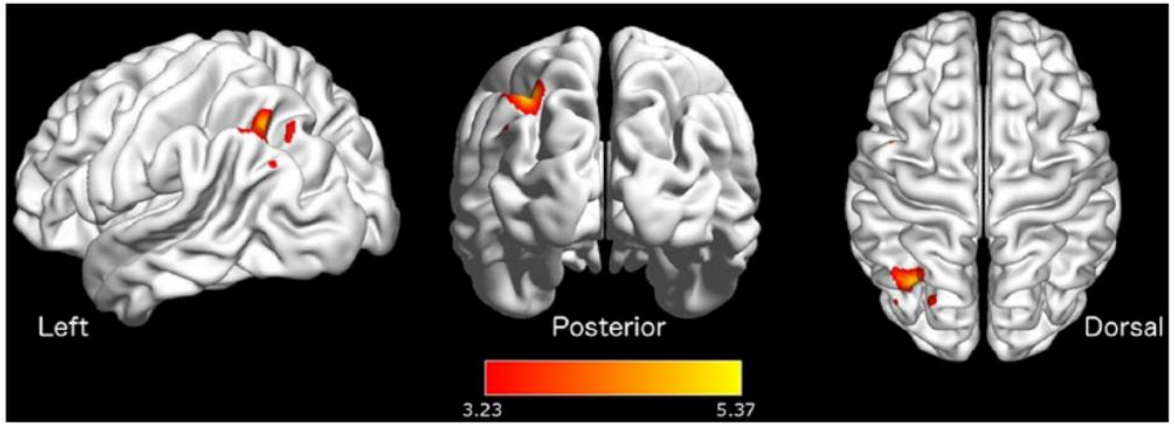
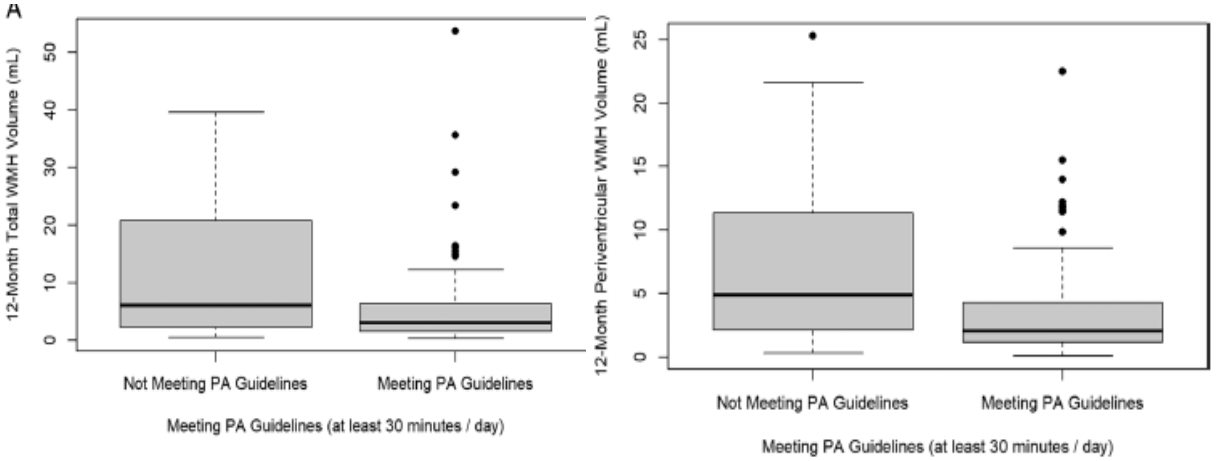


Figure 4. Dorsal attention network connectivity modulated by physical activity Significant association between strength of connectivity and daily physical activity in stroke patients in the superior parietal lobe. Height threshold uncorrected, $P < .001$; false discovery rate corrected for multiple comparisons to $P < .05$. Color maps represent *t*-values.

Poststroke White Matter Hyperintensities and Physical Activity: A CANVAS Study Exploratory Analysis

STANLEY HUGHWA HUNG[1], MOHAMED SALAH KHLIF[1], SHARON KRAMER[2,3], EMILIO WERDEN[1,4], LAURA J. BIRD[5], BRUCE C. V. CAMPBELL[1,6], and AMY BRODTMANN[1,4]



Veldsman, *NNR,* 2017
Hung, *Med Sci Sports Exerc,* 2022
Egorova-Brumley, *Sci Rep,* 2025
Hung, *J Neurol Sci*, 2025

CANVAS to PISCES: Motivation for Exercise

Dynamic Regional Brain Atrophy Rates in the First Year After Ischemic Stroke

Amy Brodtmann, MBBS, PhD; Mohamed Salah Khlif, PhD; Natali
Laura J. Bird, PhD; Emilio Werden, PhD

Neurorehabilitation and Neural Repair
Volume 31, Issue 2, February 2017, Pages 157-167
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https://doi.org/10.1177/1545968316666958

Original Research Article

Physical Activity After Stroke Is Associated With Interhemispheric Connectivity of the Dorsal Atter

Michele Veldsman, PhD[1,2], Leonid Churilov, PhD[2], Emilio Werden[2], Qi Li
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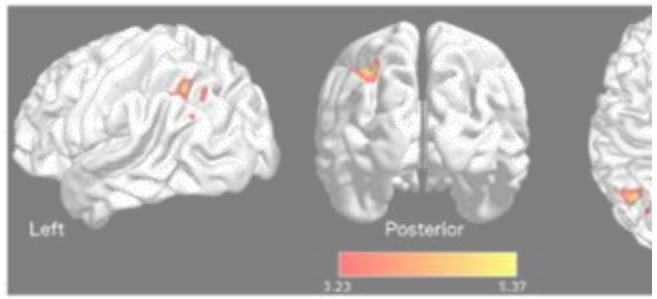

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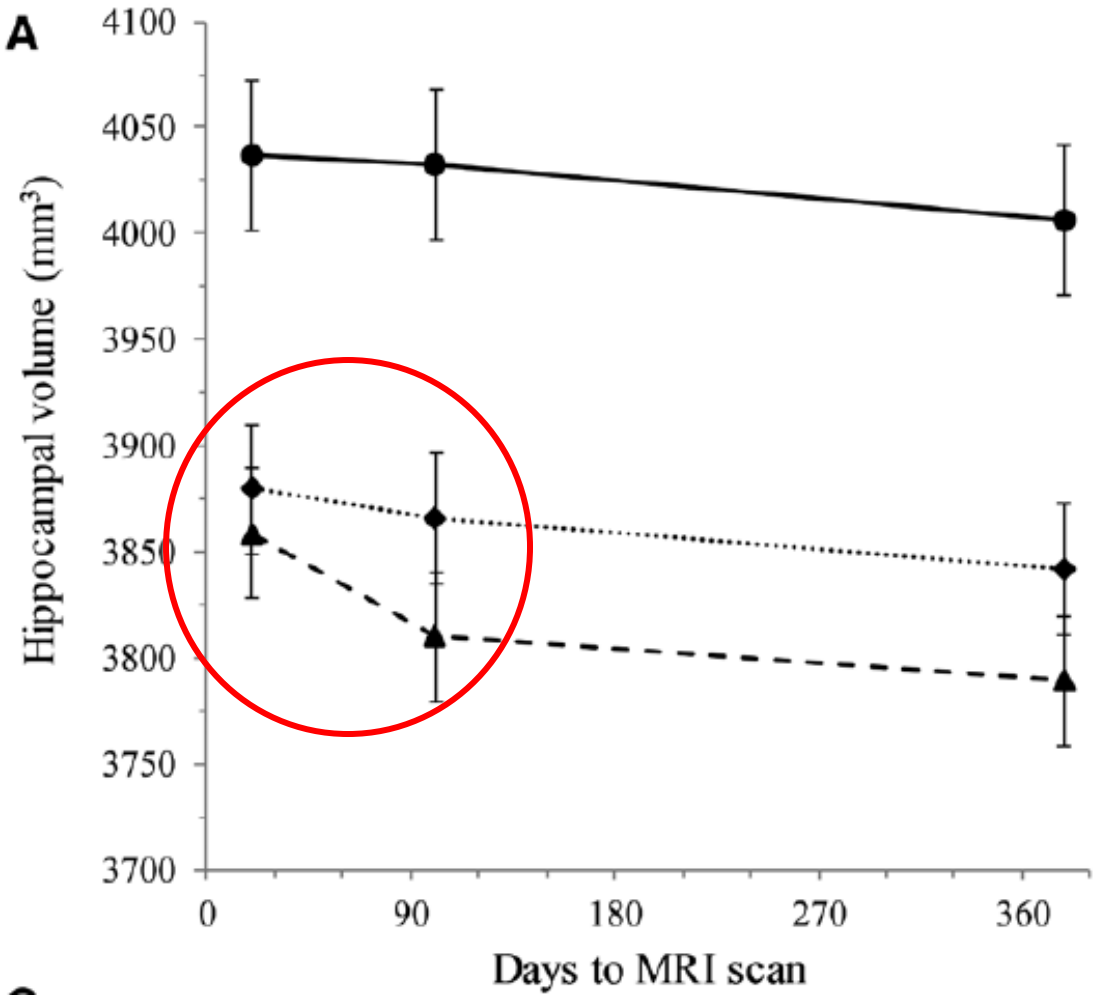

Poststroke White Matter Hyperintensities and Physical Activity: A CANVAS Study Exploratory Analysis

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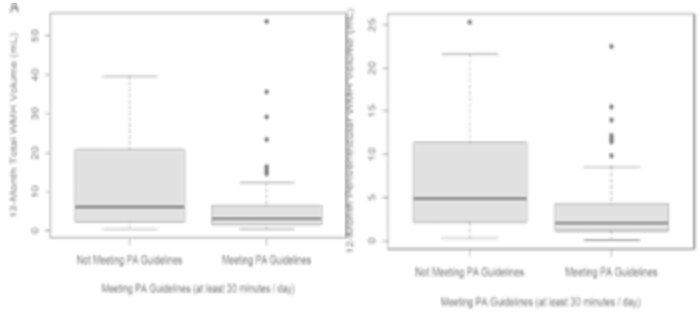
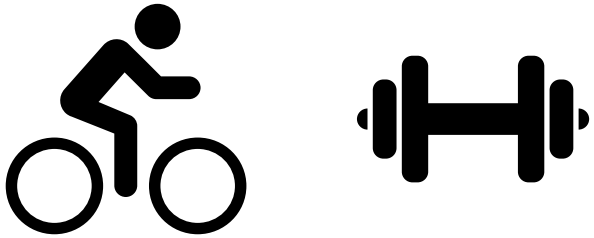


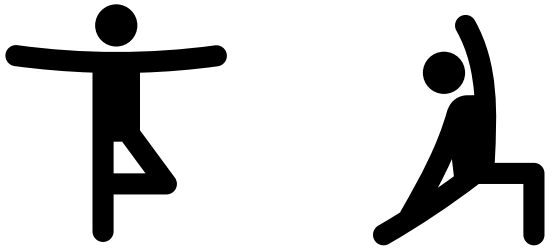
Brodtmann, *Stroke*, 2020
Veldsman, *NNR,* 2017
Hung, *Med Sci Sports Exerc* 2022

PISCES ZODIAC



CARDIORESPIRATORY (CRX)

- CRX progressive HIIT + moderate intensity continuous training
- PISCES centre-based treadmills + gym equipment for resistance training
- ZODIAC upright stationary bicycles + free- and body-weight exercises for resistance training
- moderate intensity resistance training 70-80% 3RM



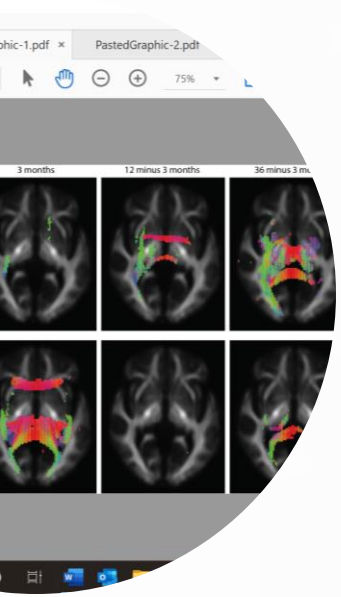
CONTROL (CON)
BALANCE & STRETCHING

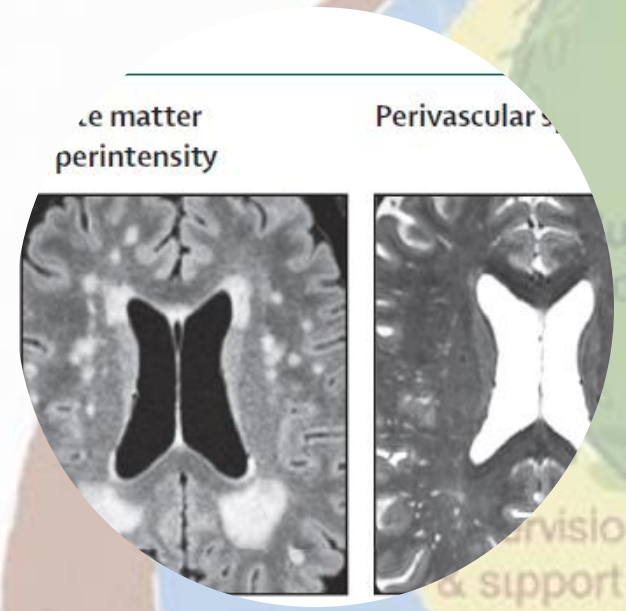
- 20 minutes of static and dynamic balance-based exercises
- 30 minutes of light, static stretching for all major joint complexes
- matched attention and dose (i.e., session duration and frequency)

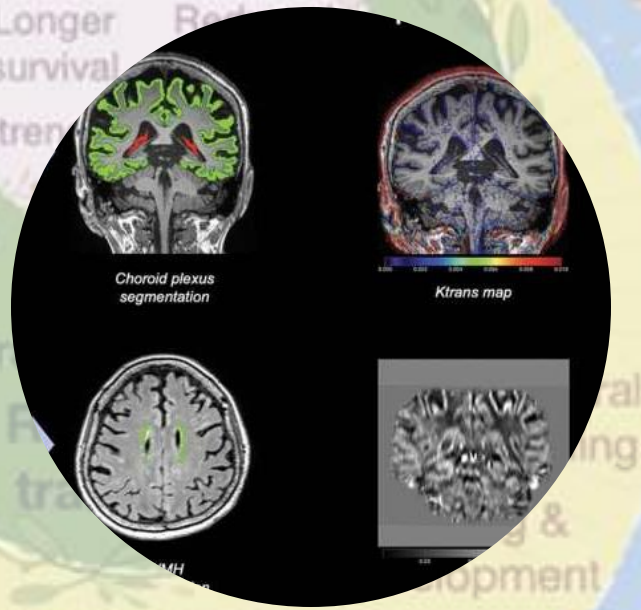
What we found

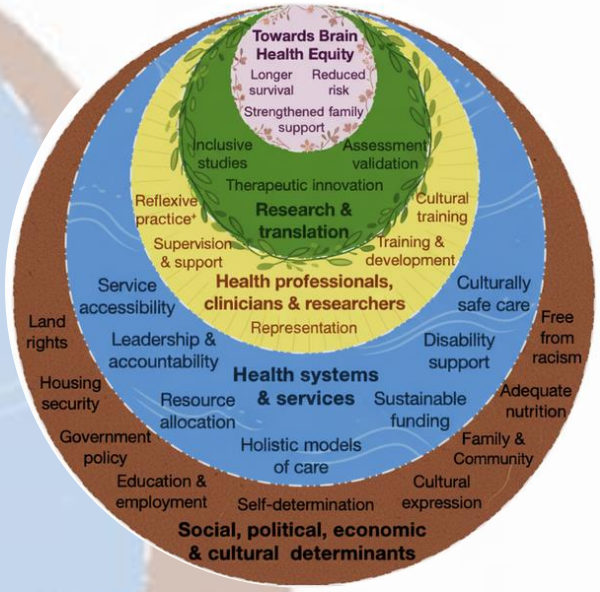
- no difference in brain volume between exercise groups[1]
- however, those in the CRX had faster speed of processing, and better executive and global cognitive function than those in the balance and stretching[1]
- similar findings in sedentary middle-aged adults comparing HIIT and MICT[2]
- similar benefits seen in yoga intervention in stroke survivors[3]

[1] Brodtmann, et al., *JAMA Network Open*, 2025; Broatch, et al., IN SUBMISSION 2026; [2]Thayabaranathan, *Neurol Int*, 2021



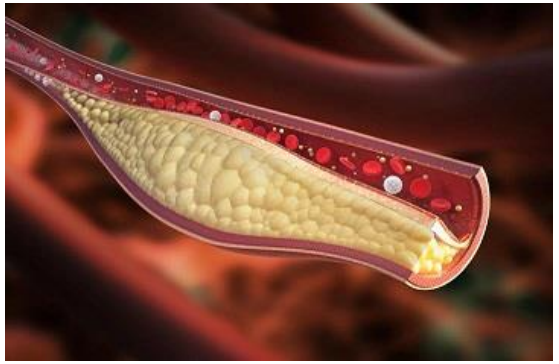


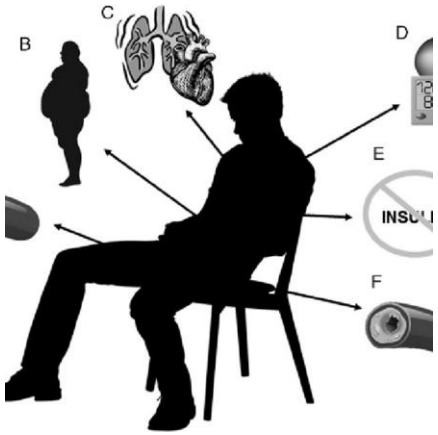




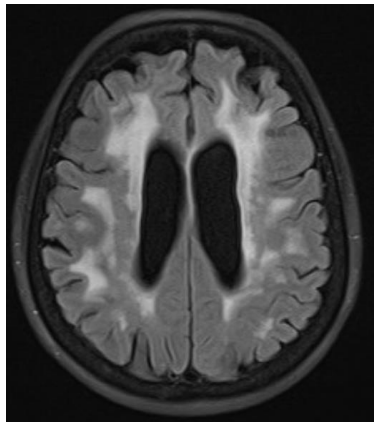
The future of brain health? Biomarkers, exercise, advocacy

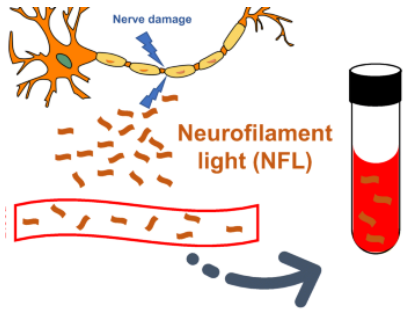
RISK MEASURES



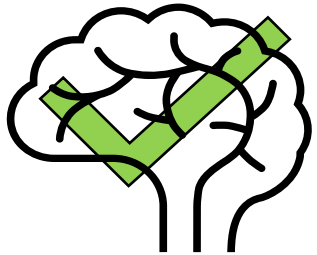


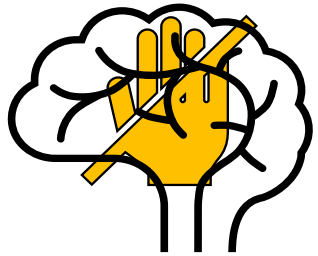
BRAIN HEALTH METRICS

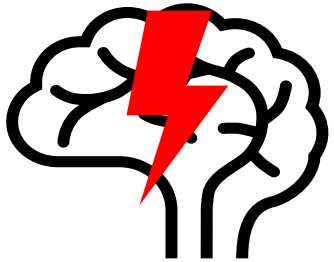




RISK ASSIGNMENT





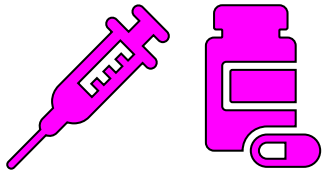


TARGETED PRESCRIPTIONS

BRAIN HEALTH OPTIMISATION

BRAIN HEALTH EXERCISE PRESCRIPTIONS

ROBUST RISK FACTOR CONTROL



DISEASE SPECIFIC PRESCRIPTION

TRIAL PARTICIPATION

Ed Whitlock, 3:41 marathon, 2013, aged 82

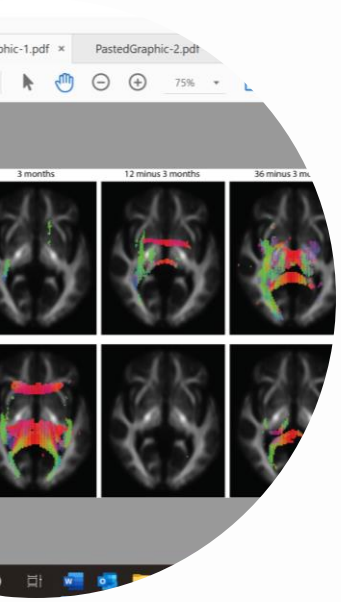
Harriette Thompson, 7:07 marathon, 2014, aged 91

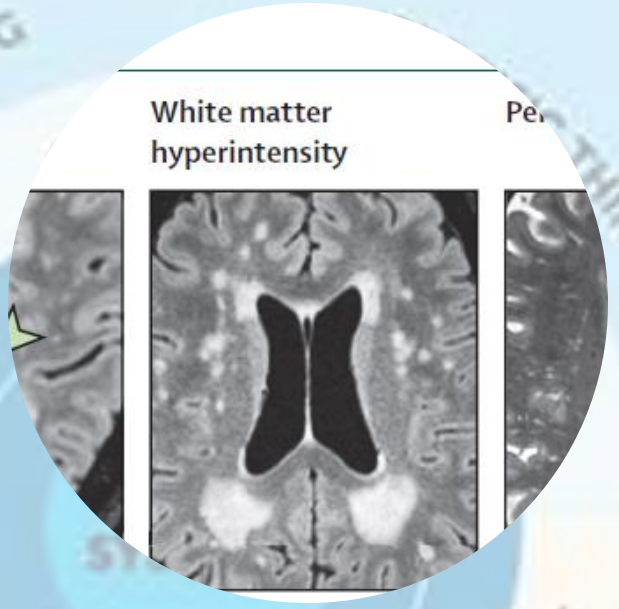

HOBBIES

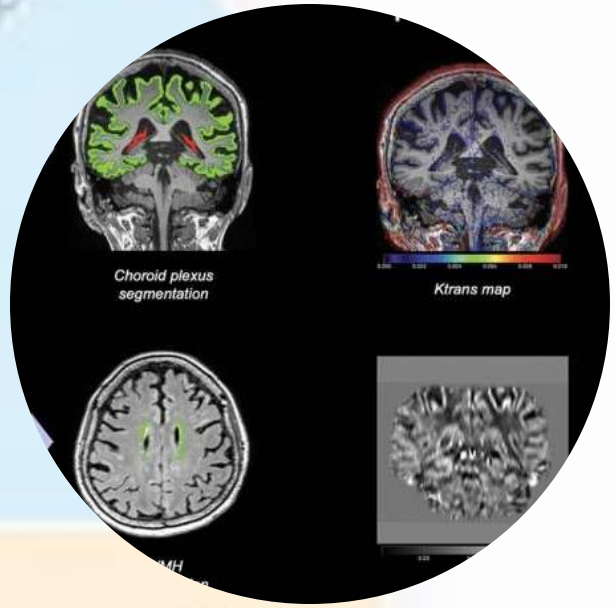
Summary

- vascular health = brain health from mid-to-late life
- vascular risk increases over and after the menopause, but risks can be managed
- HRT does not affect your brain health risk – good news for those who need it and those who cannot take it
- stretching, balance, resistance exercise, yoga, Tai Chi, all demonstrate brain benefits so do what moves you and your patients
- consider exercise prescriptions
- we need to rethink our models of care and what is best suited to our medical systems, community and cultures
- we need to be brain health champions and ambassadors!!
- looking forward to the launch of Women's Brain Care Clinics at JH

SO, MOVE!!





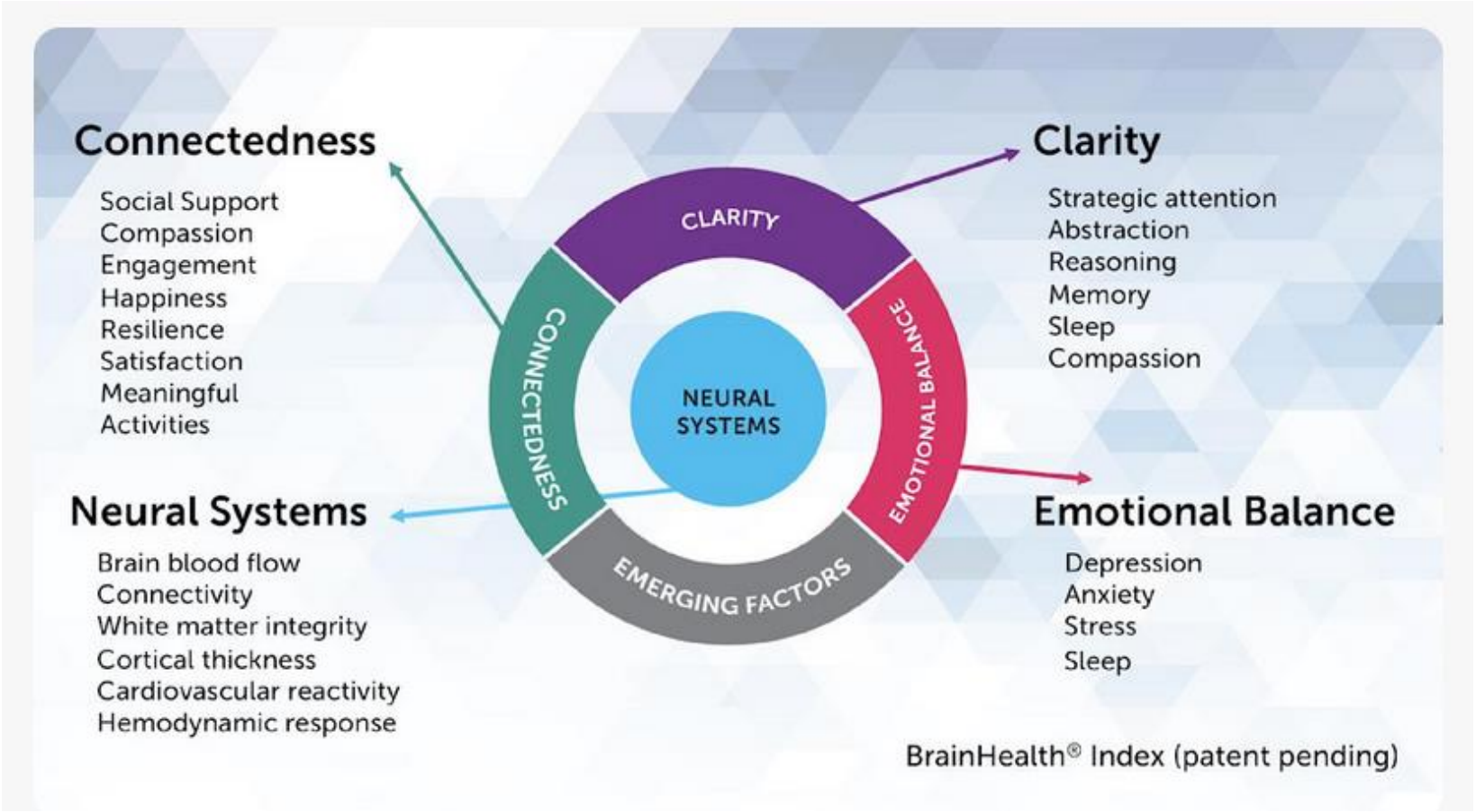


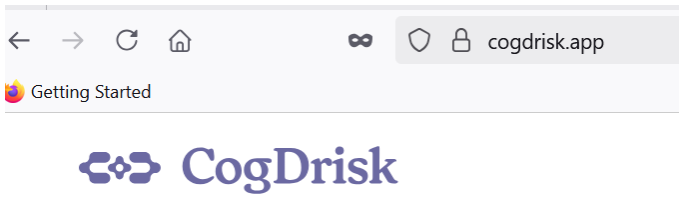
How do we measure brain health?
Disease risk versus brain health metrics

New industry of brain health measures?

- currently many brain health or brain care scores and indices
- one of the first was the the LIfestyle for BRAin health risk score (LIBRA), a weighted score of modifiable components including unhealthy lifestyle, poor cardiometabolic health, renal dysfunction, and depression
- developed upon a systematic literature review and Delphi expert study (Deckers*, et al., Int J Ger Psych,* 2015)
- highly associated with dementia risk when applied in observational cohorts
- most leverage heart risk scores and include sleep, psychological well-being
- some include environmental (pesticide, CogDrisk) exposure but not pollution, essential for India and China
- some include stakeholder/consumer/LEAG input (e.g., McVance Brain Care Score), some based on WHO definitions (BrainHealth® Index)
- most validated in White or European, educated cohorts
- none developed for First Nations peoples, very few validated outside European and US populations

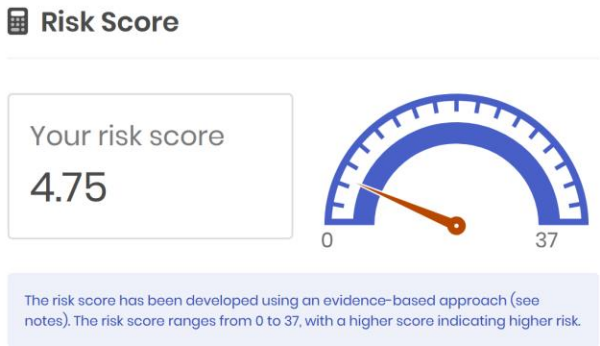
BrainHealth® Index at Center for Brain Health (U Texas) based on WHO definition and uses measures from Oxford Happiness Questionnaire and PSQI





Welcome to the CogDrisk Assessment

After completing the self-assessment you will be presented with a health profile and information on lifestyle and health behaviours that may improve your health and reduce the dementia risk.



PREVENTION

It's all about lifestyle and engagement: lower inflammation, increase physical activity, sleep better, be happy, eat really well (great microbiome), engage socially

"Our brains function best when we are happy, when our hearts are healthy, when we're with people, and when we're moving." Brodtmann 2023

The **National Institute on Aging has funded its Resilience-AD Program,** which began in 2017, with $40 million in an effort to identify genetic and other factors that keep Alzheimer's at bay even in people whose brains scream "Alzheimer's," and to somehow bottle that resilience.

News & Views | Published: 20 October 2023

Alzheimer disease

Could microbiota transfer between cohabitants influence Alzheimer disease risk?

Kristina Endres & Karl-Herbert Schäfer

Nature Reviews Neurology (2023) | Cite this article

212 Accesses | 12 Altmetric | Metrics

The underlying cause of sporadic Alzheimer disease (AD) remains enigmatic, but an increased risk among spouses of people with AD has led to speculation of transmissibility. A mouse study now suggests that the transfer of microbiota could underlie this potential transmissibility, but the findings leave many questions unanswered.

Refers to Zhang, Y. et al. Transmission of Alzheimer's disease-associated microbiota dysbiosis and its impact on cognitive function: evidence from mice and patients. *Mol. Psychiatry*,

https://doi.org/10.1038/s41380-023-02216-7 (2023)

Article | Open access | Published: 01 November 2023

Transcriptomic analyses reveal proinflammatory activation of human brain microvascular endothelial cells by aging-associated peptide medin and reversal by nanoliposomes

Yining Zhang, Nina Karamanova, Kaleb T. Morrow, Jillian Madine, Seth Truran, Maria Lozoya, Volkmar Weissig, Ming Li, Mehdi Nikkhah, Jin G. Park & Raymond Q. Migrino

Scientific Reports 13, Article number: 18802 (2023) | Cite this article

158 Accesses | 1 Altmetric | Metrics

Abstract

Medin is a common vascular amyloidogenic peptide recently implicated in Alzheimer's disease (AD) and vascular dementia and its pathology remains unknown. We aim to identify

Dementia News *November 5, 2*

Top Headlines

Strawberry Consumption May Reduce Dementia Risk for Middle-Aged Individuals

Nov. 1, 2023 — New research found that daily strawberry consumption could help reduce the risk of dementia for certain middle-aged populations. ...

Improving Deep Sleep May Prevent Dementia, Study Finds

Oct. 30, 2023 — As little as 1 per cent reduct in deep sleep per year for people over 60 yea of age translates into a 27 per cent increased risk of dementia, according to a study which gests that enhancing or maintaining deep sle also known as slow wave ...

New Atrial Fibrillation Diagnosis May Increase Risk of Memory Decline

Oct. 25, 2023 — Atrial fibrillation (AF) diagnosis was associated with a 45% increased risk of mild cognitive impairment (MCI) among a cohort of 4.3 million individuals in the UK, according to a new ...

Higher Levels of Triglycerides Linked to Lower Risk of Dementia

Oct. 25, 2023 — Older people who have high levels of triglycerides, a type of fat, may have lower risk of dementia and a slower cognitive cline over time compared to people who have lower levels, according to new research. Whi the study found a link, it ...

McVance Brain Care Score

McCANCE Brain Care Score™

MASSACHUSETTS GENERAL HOSPITAL
McCANCE CENTER FOR BRAIN HEALTH

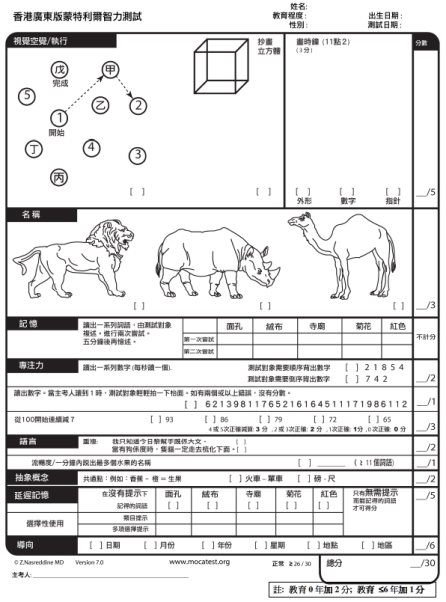
Category		Criteria / Description	Rank	Score
Physical	Blood Pressure	Resting blood pressure greater than 140/90, with or without treatment	0	
		Resting blood pressure 120-139/80-89, with or without treatment	2	
		Resting blood pressure less than 120/80	3	
	Blood Sugar	Hemoglobin A1c greater than 6.4	0	
		Hemoglobin A1c between 5.7 and 6.4	1	
		Hemoglobin A1c less than 5.7	2	
	Cholesterol	190 or higher	0	
		No treatment required or less than 190 mg/dL	1	
		If cardiovascular disease is present, LDL is in accordance to the latest CDC recommendations	1	
	BMI	Lower than 18.5 kg/m^2	1	
		18.5-25 kg/m^2	2	
		25-29.9 kg/m^2	1	
		Greater than 30 kg/m^2	0	
Lifestyle	Nutrition	Dietary habits: • 4.5 servings of fruit and vegetables per day; • 2 servings of lean protein per day • 3 or more servings of whole grains per day • Less than 1,500 mg of sodium per day • Less than 36 oz of sugar sweet beverages (soda, juice, etc.) per week		
		Typical weekly diet does not include at least 2 of the recommendations above	0	
		Typical weekly diet includes 2 or more of the recommendations above	1	
		Typical weekly diet includes 3 or more of the recommendations above	2	
	Alcohol	4 or more alcoholic drinks per week	0	
		2-3 alcoholic drinks per week	1	
		0-1 alcoholic drink per week	2	
	Smoking	Current smoker	0	
		Never smoked or quit more than a year ago	3	
	Aerobic Activities	Less than 150 minutes of moderate or 75 minutes of high intensity physical activity per week	0	
		At least 150 minutes of moderate physical activity (ex. walking) or 75 minutes of high intensity physical activity per week	1	
	Sleep	Untreated sleep disorder and/or sleeps <7hrs per night	0	
		Treated sleep disturbances and 7-8 hours of routine sleep per night	1	
Social Emotional	Stress	High level of stress that often makes it difficult to function	0	
		Moderate level of stress that occasionally makes it difficult to function	1	
		Manageable level of stress that rarely makes it difficult to function	2	
	Social Relationships	I have few or no close connections other than my spouse or children	0	
		I have at least two people, other than my spouse or children, that I feel close with and could talk about private matters or call upon for help	1	
	Meaning in Life	I often struggle to find value or purpose in my life	0	
		I generally feel that my life has meaning and/or purpose	1	

The components above reflect the latest, scientific based key contributors to brain health.
It is important to discuss your score with a healthcare professional.

Total Brain Care Score (0-21)

Building brain health metrics

CogDrisk


香港廣東版蒙特利爾智力測試

姓名:
教育程度:
性別:
出生日期:
測試日期:

視覺空間/執行 | 分數

名稱

記憶 | 面孔 | 絨布 | 寺廟 | 菊花 | 紅色

專注力

抽象概念 | 共通點：例如：香蕉 - 橙 = 生果

延遲記憶 | 在沒有提示下 | 只有無需提示

定向 | [ ]日期 [ ]月份 [ ]年份 [ ]星期 [ ]地點 [ ]地區

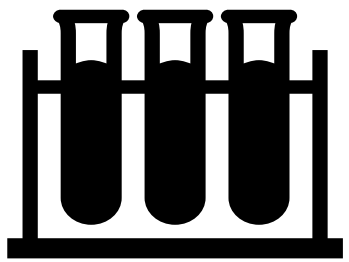
© Z Nasreddine MD Version 7.0 www.mocatest.org

總分 __/30

註: 教育 0 年加 2 分; 教育 ≤6 年加 1 分

+

+/-



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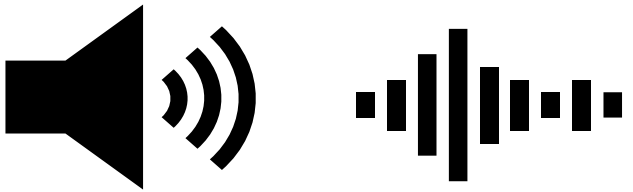
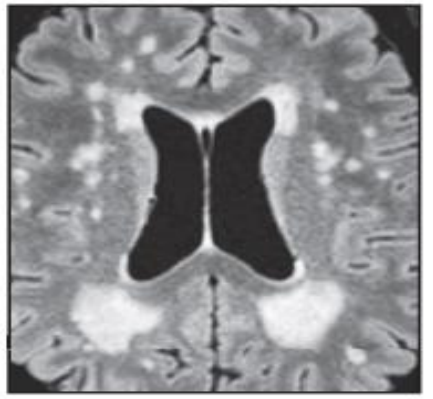
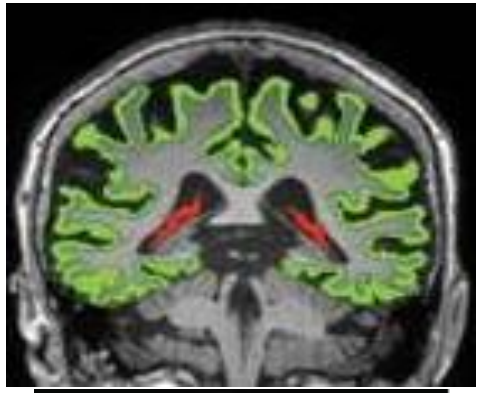
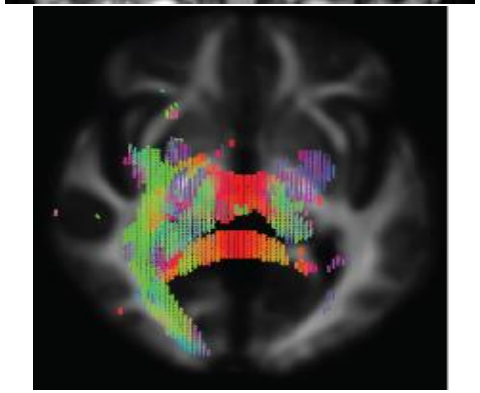


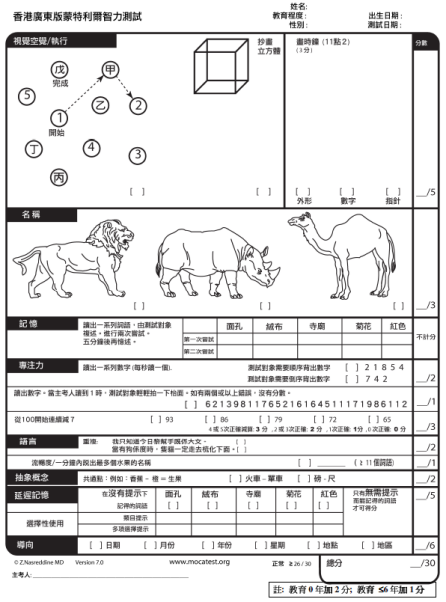






Building brain health metrics

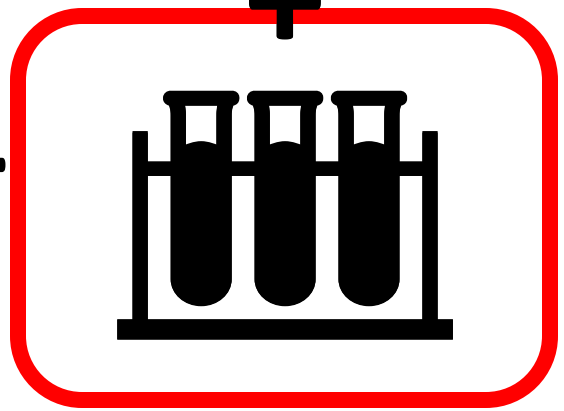
CogDrisk


香港廣東版蒙特利爾智力測試

姓名:
教育程度:
性別:
出生日期:
測試日期:

視覺空間/執行
名稱
記憶
專注力
語言
抽象概念
延遲記憶
定向
面孔
絨布
寺廟
菊花
紅色
總分
正: 教育 0 年加 2 分; 教育 ≤6 年加 1 分
© Z Nasreddine MD Version 7.0 www.mocatest.org

+/-



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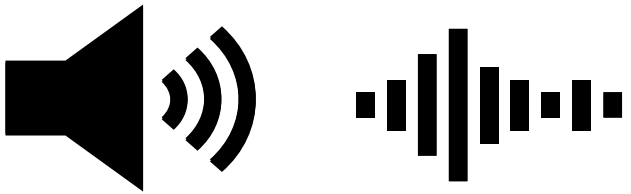
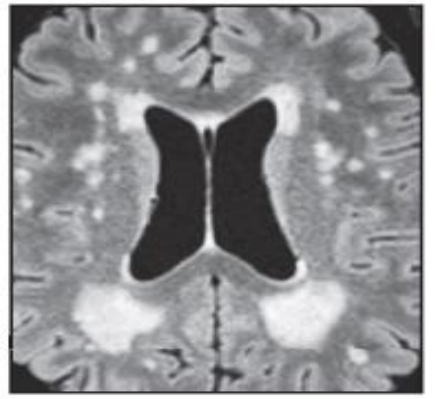
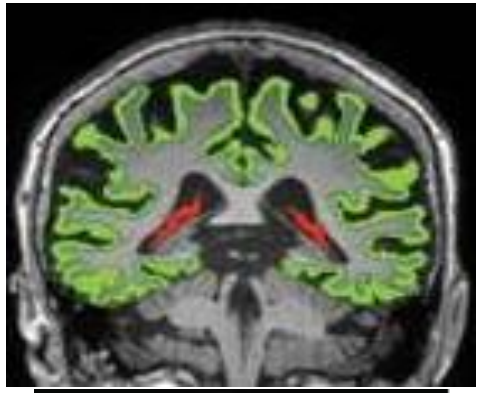
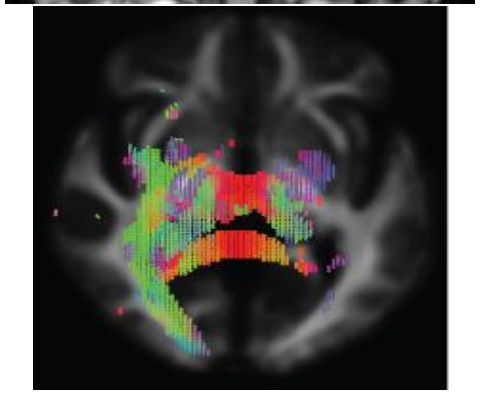




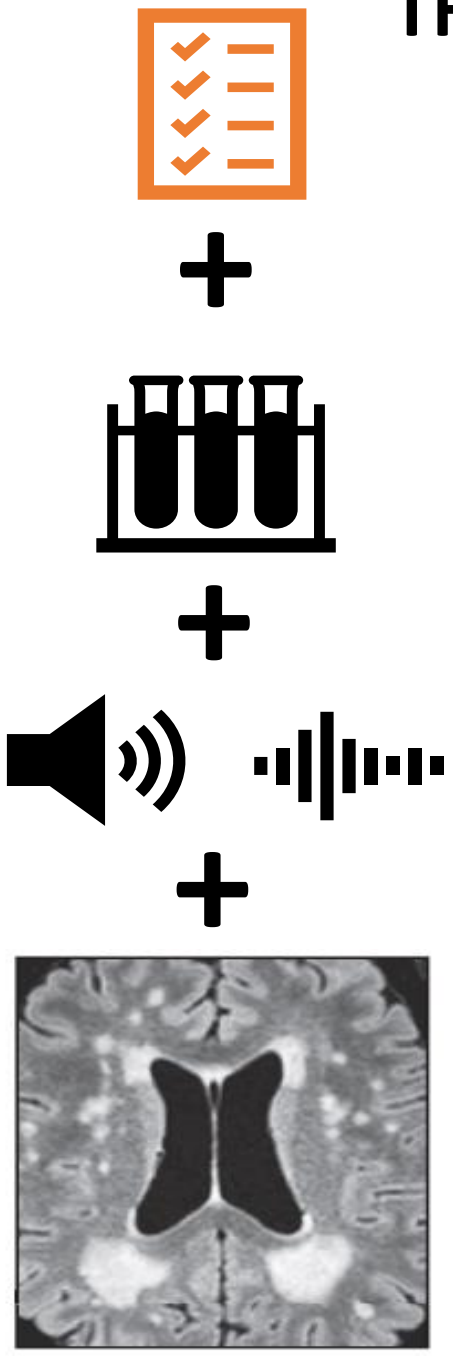




Blood biomarkers for brain health?

- We can now measure brain proteins in a peripheral blood sample
- Literally hundreds of proteins!
- most current BBM are used for detecting presence of Alzheimer's pathology – none of them tell you anything about a person's cognitive or functional state
- Current commercial one is p-tau181 but p-tau217 especially good correlation with presence of brain amyloid
- neurofilament light chain (NfL) non-specific marker of neuro-degeneration (axonal damage)
- GFAP correlates with astrocytic activation or level of inflammation in the brain

THE FUTURE OF BRAIN HEALTH MEASUREMENT?



CLINICAL TOOLS
current
screens/scans/tests

BLOOD BIOMARKERS
Utility
NfL/tau217/GFAP

MULTIMODAL SCORES
Imaging scales + blood + digital biomarkers

AI OPTIMISATION
Current tests + digital + blood biomarkers