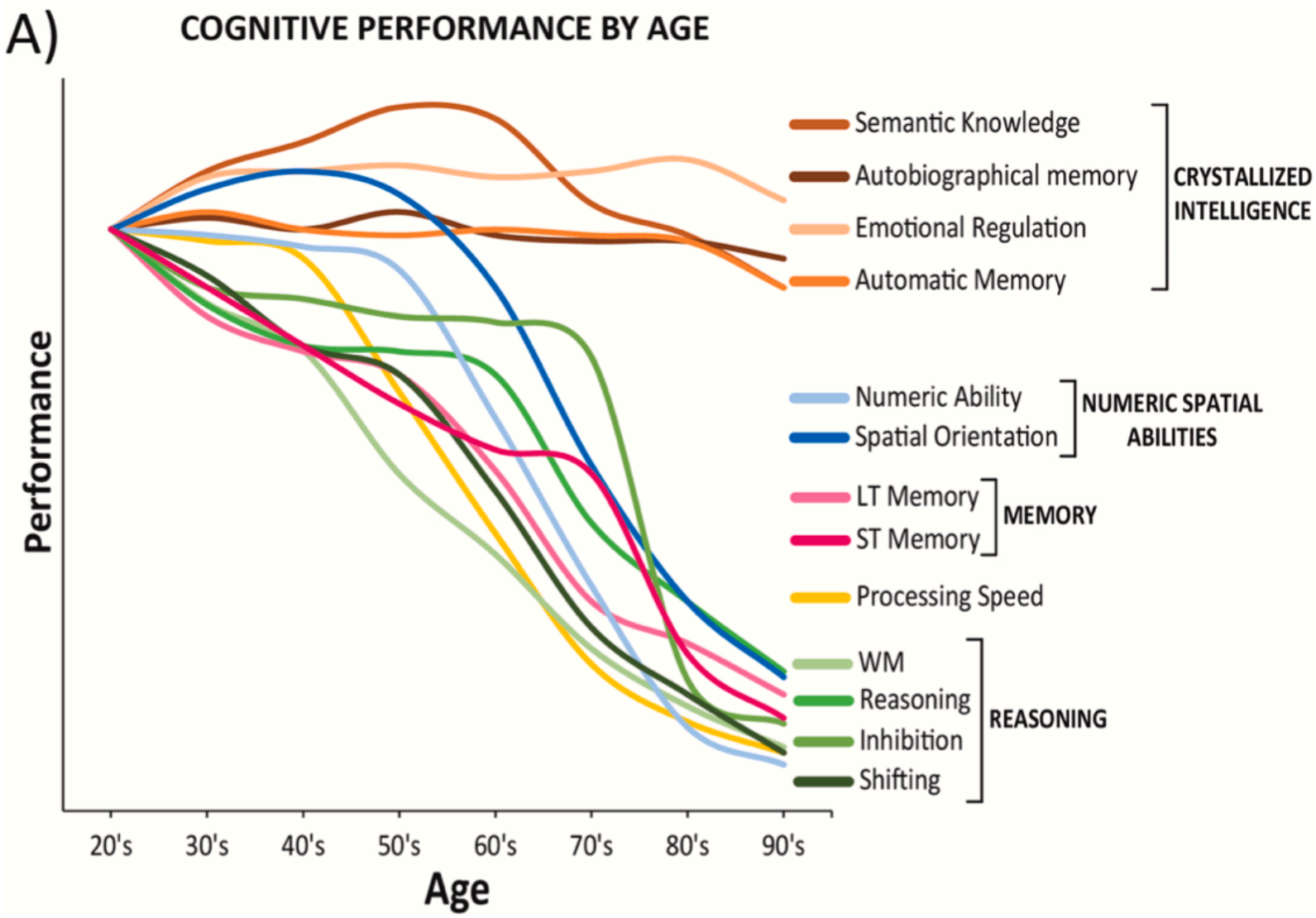
Use it or lose it

Tommy Wood, BM BCh, PhD
Associate Professor, University of Washington
Chair, Food the the Brain Research Group
Head Scientist for Motorsport, Hintsa Performance

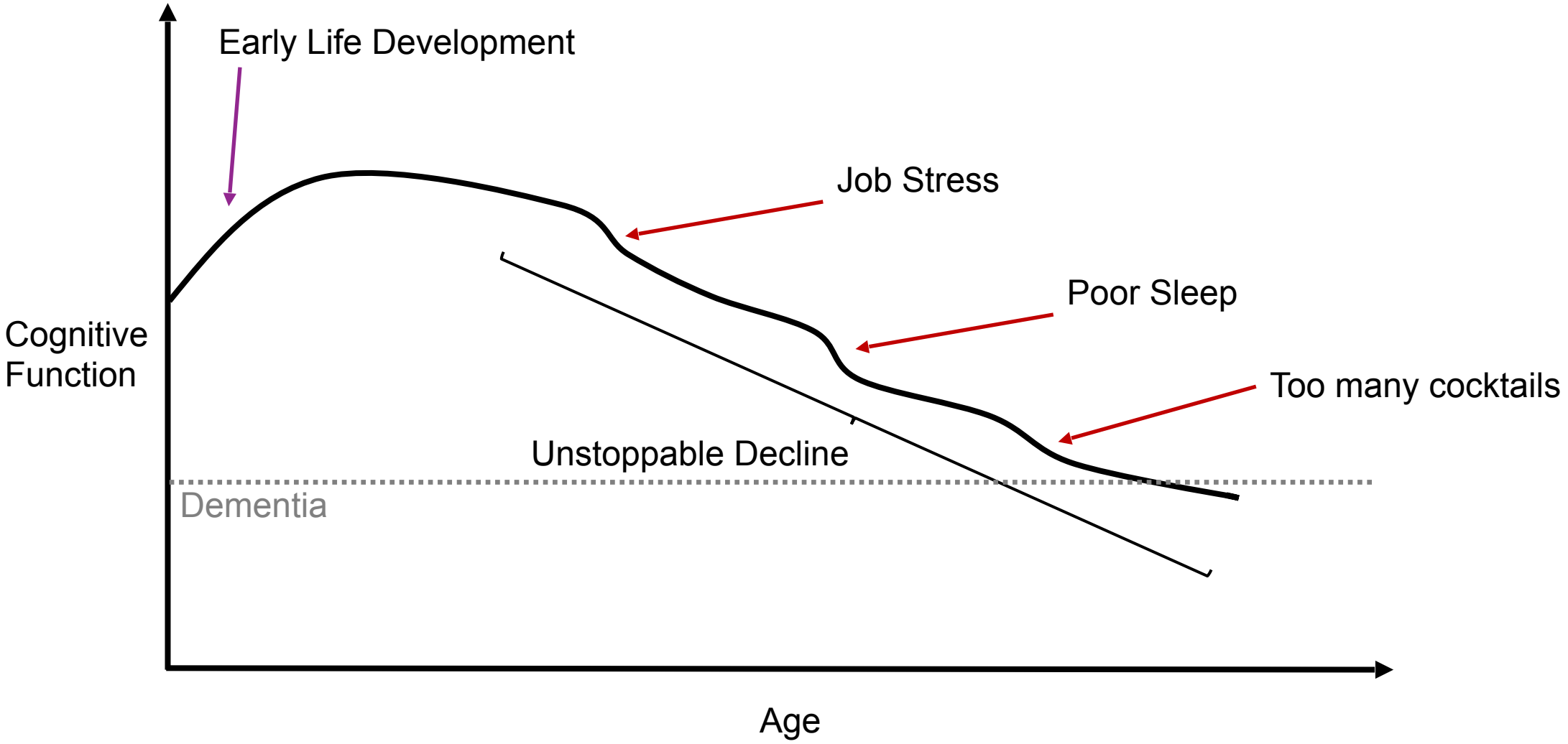
ALZHEIMER'S PREVENTION: NEW FRONTIERS

Cognitive function across the lifespan

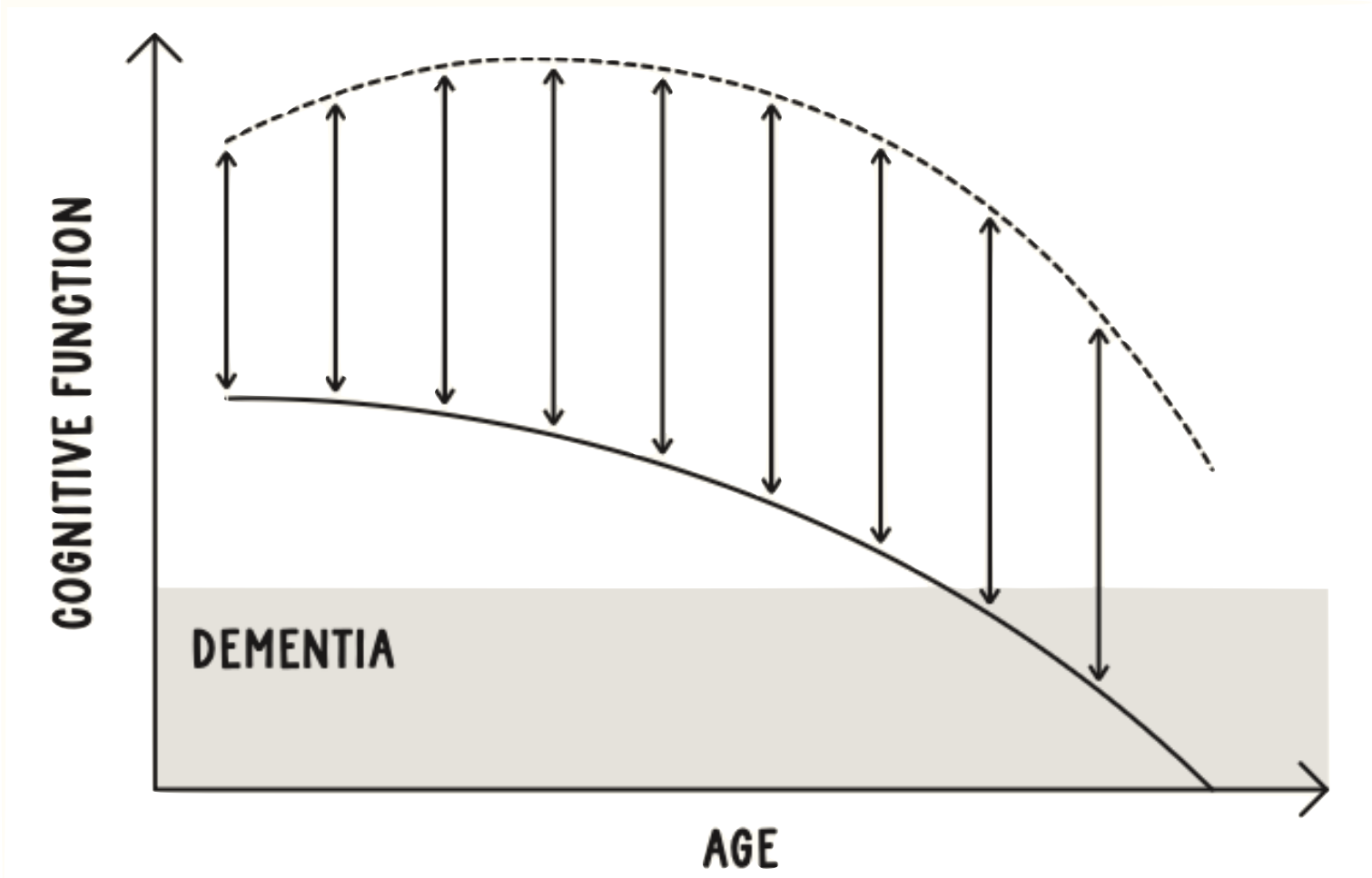


Turrini et al., Ageing Research Reviews 2023

How we think about our brains



The reality - a wide range of modifiable function



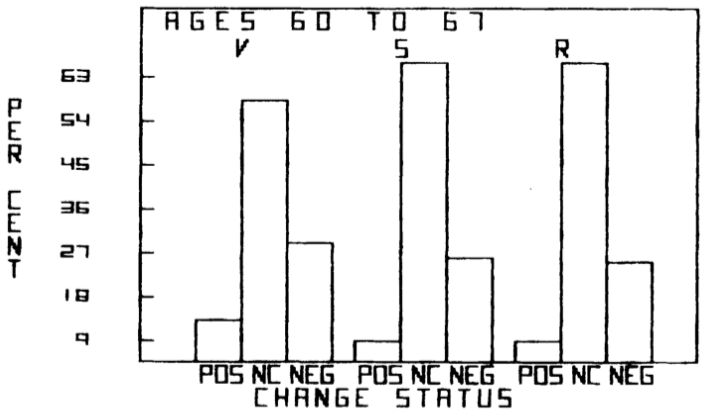
Hertzog et al., Psych Sci Pub Int 2009
From *The Stimulated Mind* (Penguin Random House, 2026)

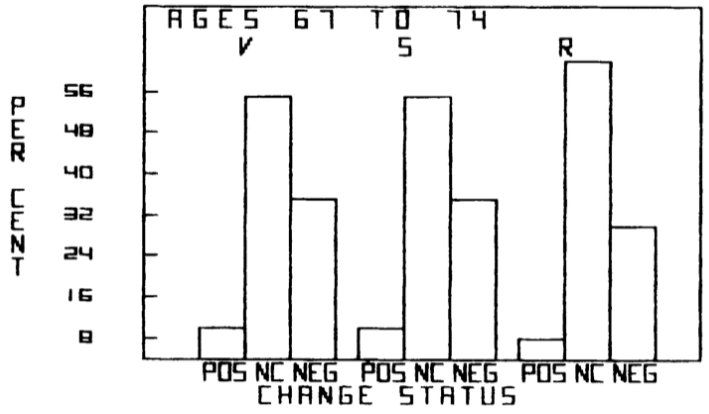
Decline is not inevitable

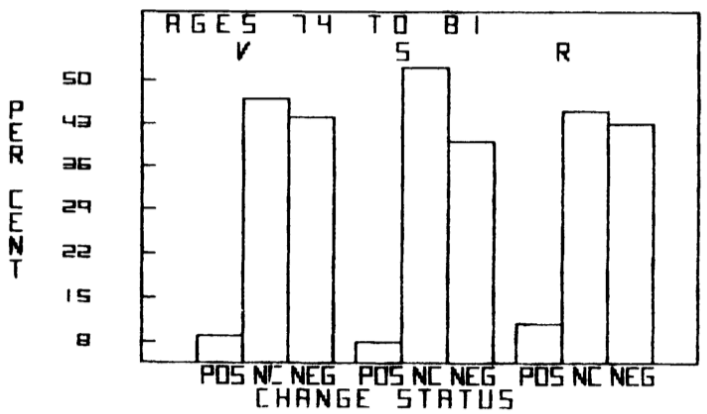
- Seattle Longitudinal Study
  - Majority of people remained stable until their 80s
    - Related to ”complexity” of lifestyle

Decline from peak performance level in standard deviation units.

Age	*N*	Verbal meaning	Spatial orientation	Inductive reasoning	Number	Word fluency
60	275	0.03	0.04	0.03	0.14	0.16
67	231	0.23	0.21	0.22	0.39	0.35
74	181	0.54	0.44	0.49	0.65	0.60
81	88	0.89	0.69	0.70	1.07	0.94

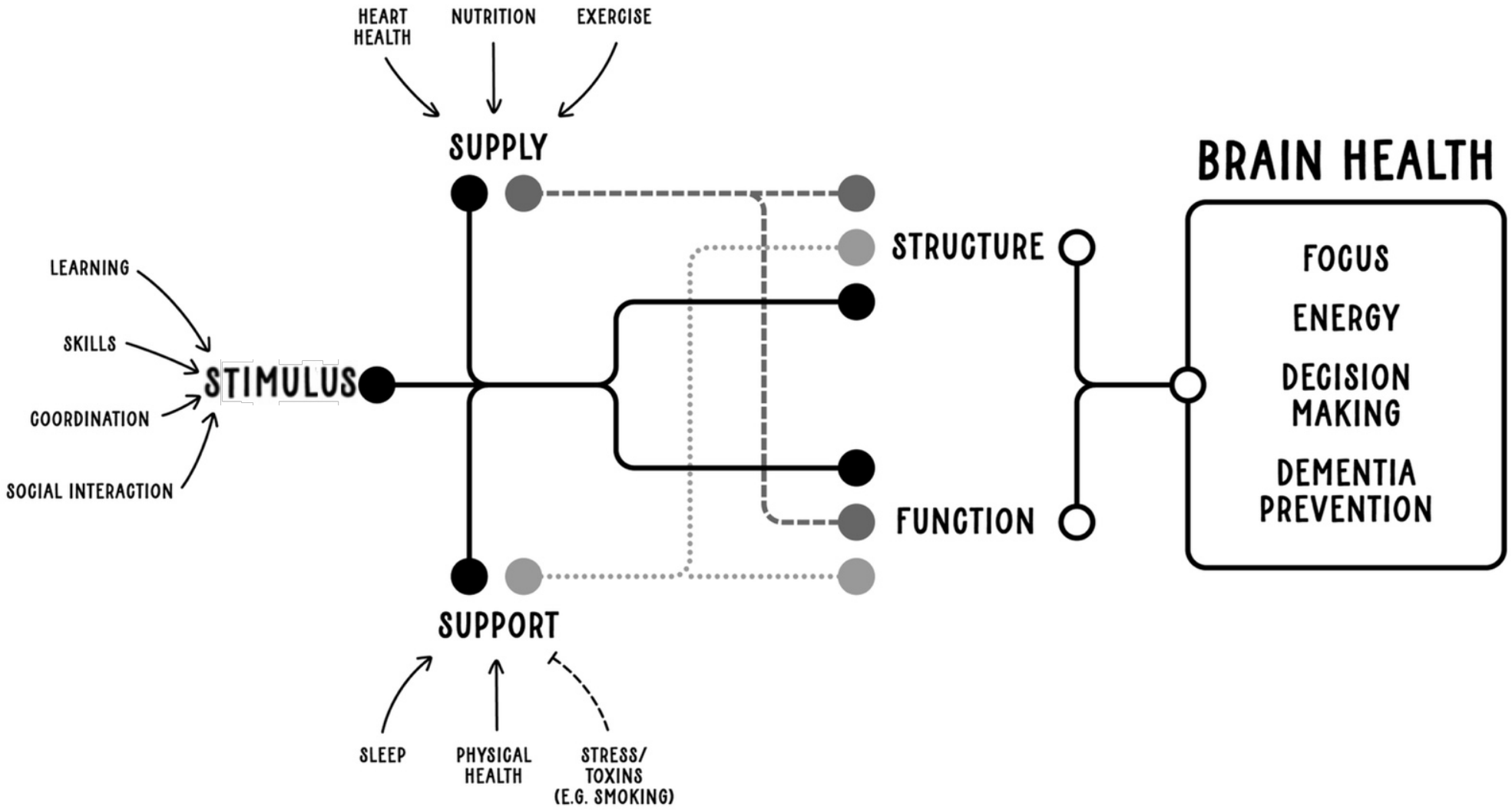






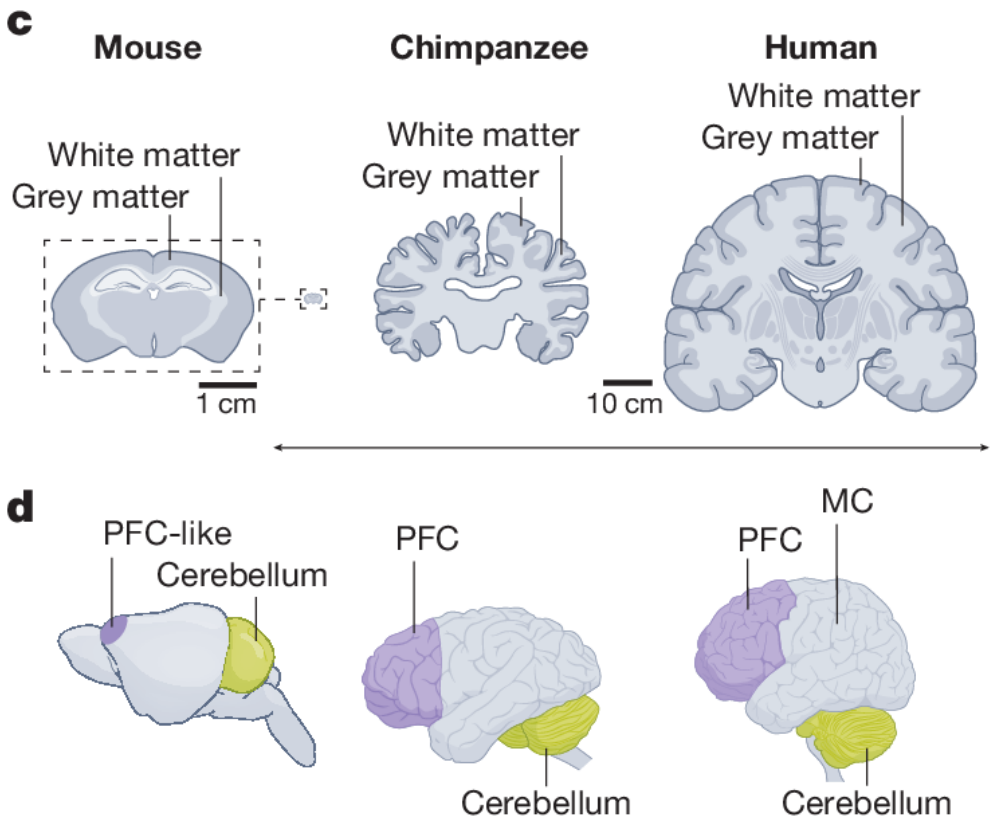
Schaie, Int J Behav Dev 1984; Gribbin et al., J Soc Iss 1980

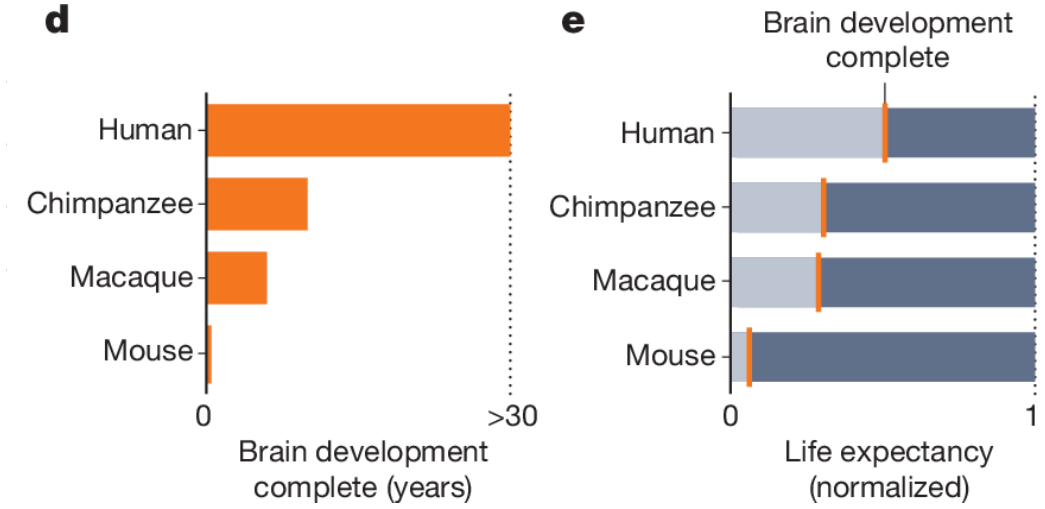
The 3 S model of brain function

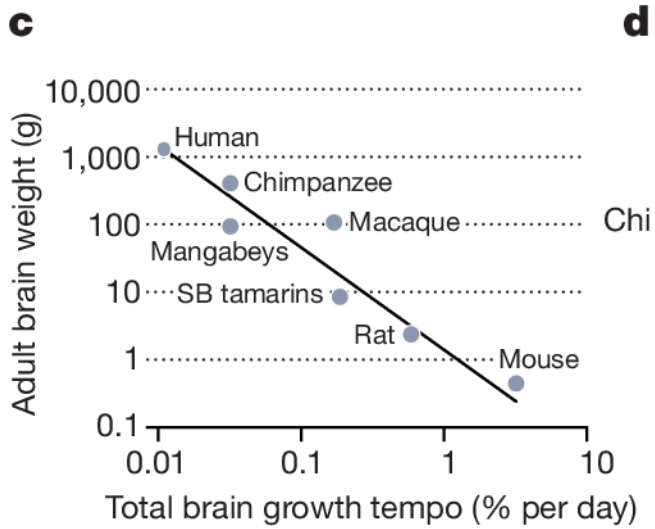


Turknett and Wood, Cells 2022
From *The Stimulated Mind* (Penguin Random House, 2026)

The human brain is uniquely shaped by the environment



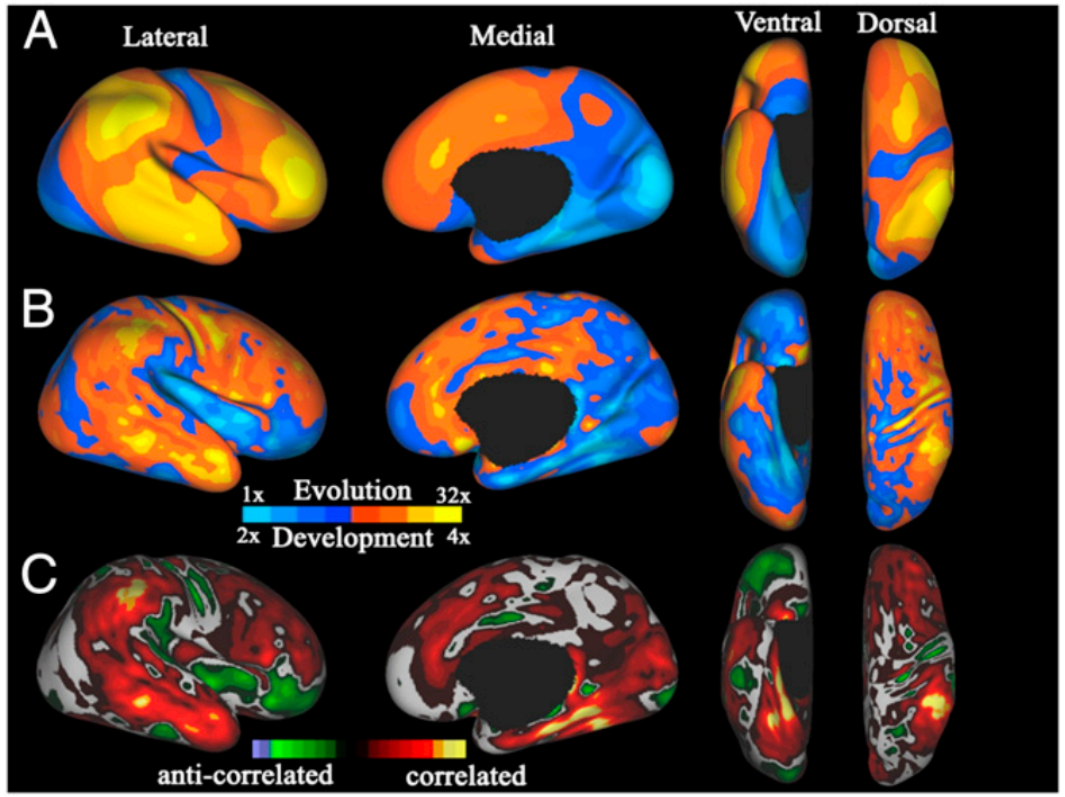


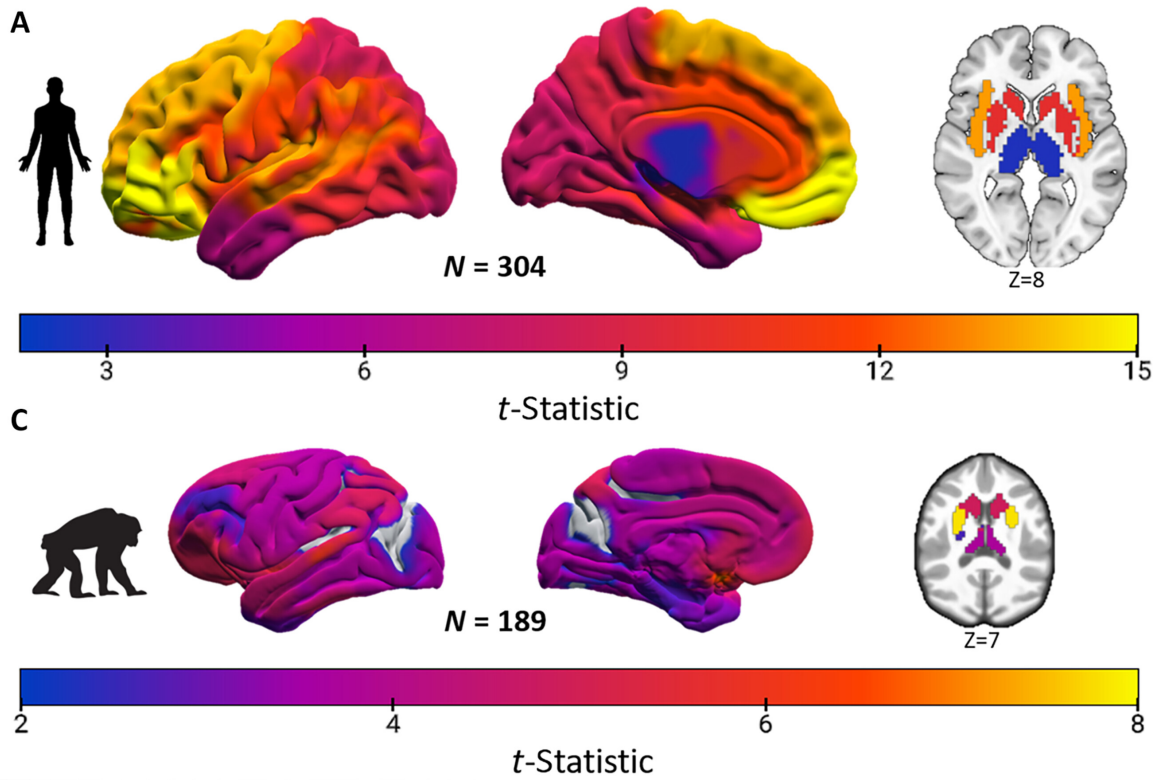


Lindhout et al., Nature 2024

The human brain is uniquely shaped by the environment

- Most recently evolved structures mature the slowest
  - Responsible for the most complex cognitive functions
- The same regions are more susceptible to effects of aging
  - Lack of ongoing stimulus?

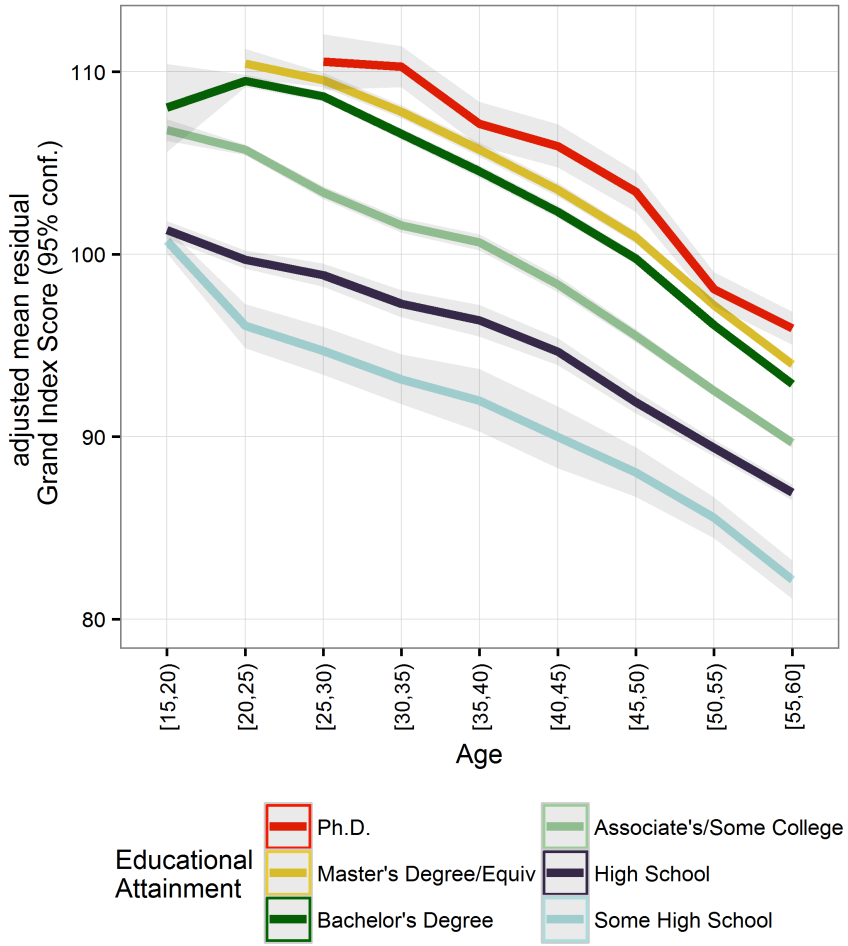




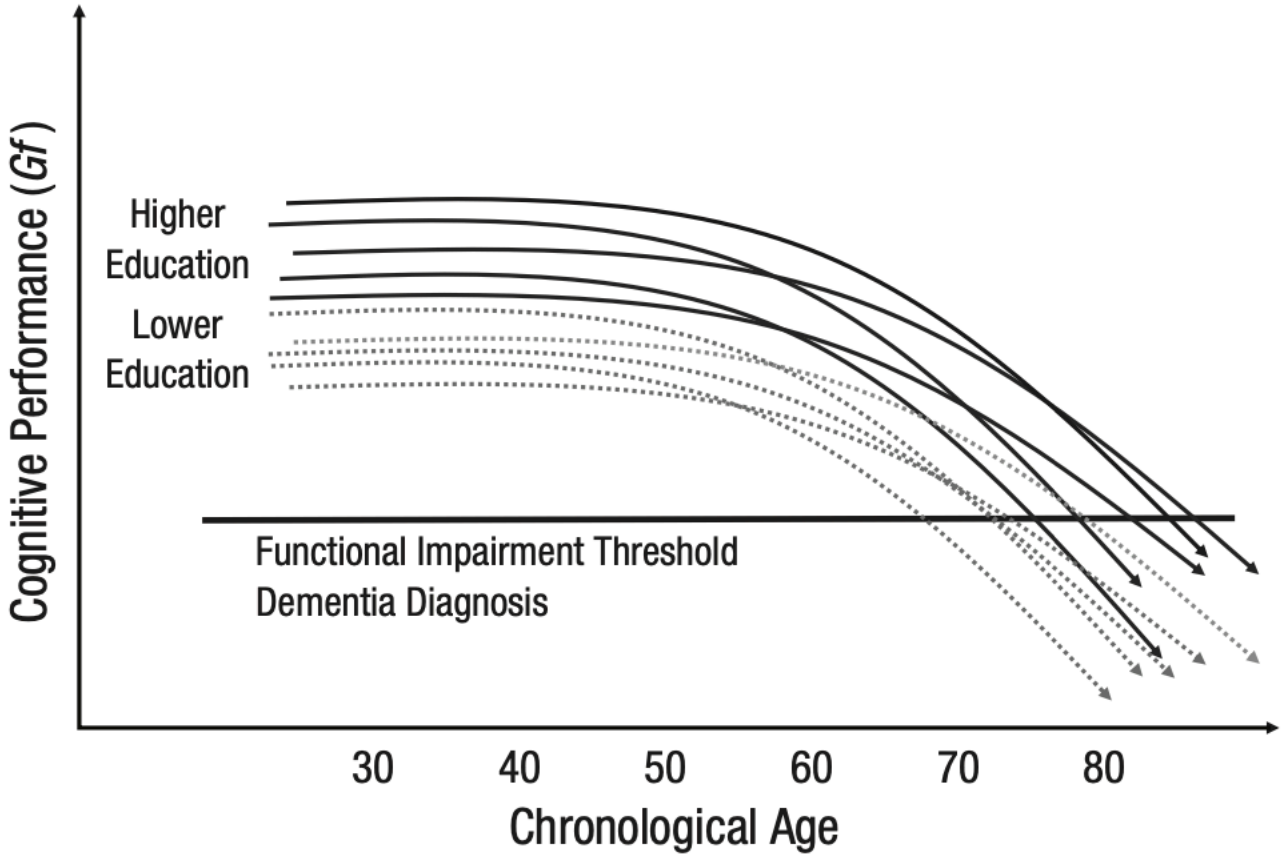
Hill et al., PNAS 2010; Vickery et al., Science Advances 2024

Early stimulation builds capacity

- Education and cognitive stimulus are the commonest proxies of cognitive reserve (and also increase cognitive resilience)



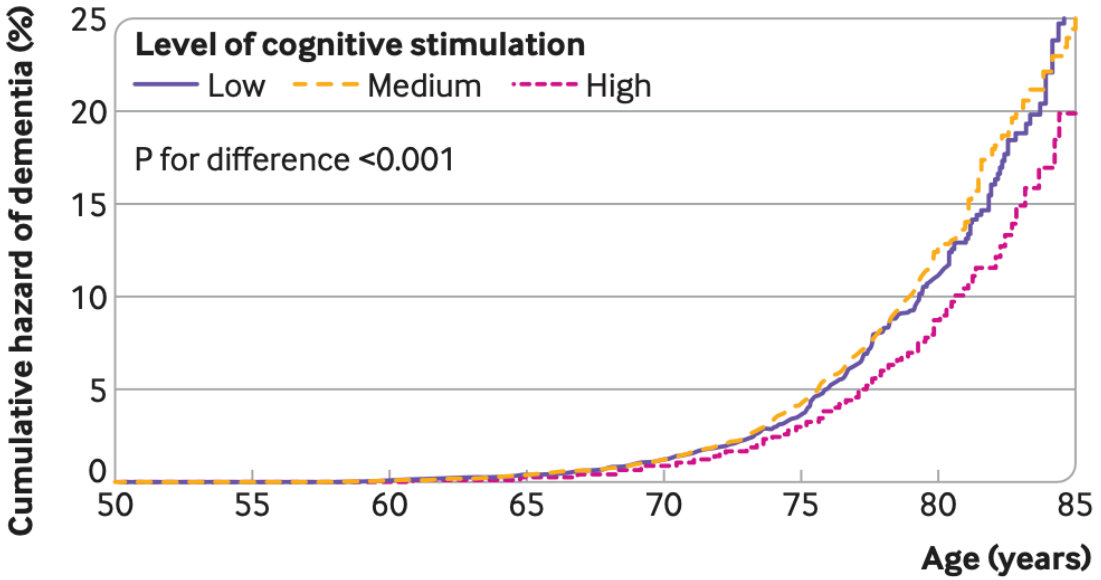
Guerra-Carrillo *et al.*, PLoS One 2017



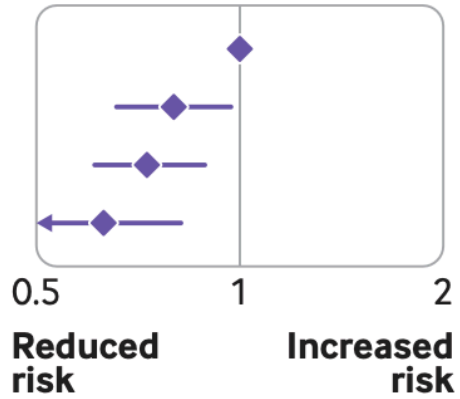
Lövdén *et al.*, Psych Sci Pub Int 2020

Later life stimulus slows decline

- Meta-analysis of ~110,000 people from seven cohorts
  - Cognitive stimulus from work predicts later dementia
  - Highly stimulating work overcomes the risk from lower education



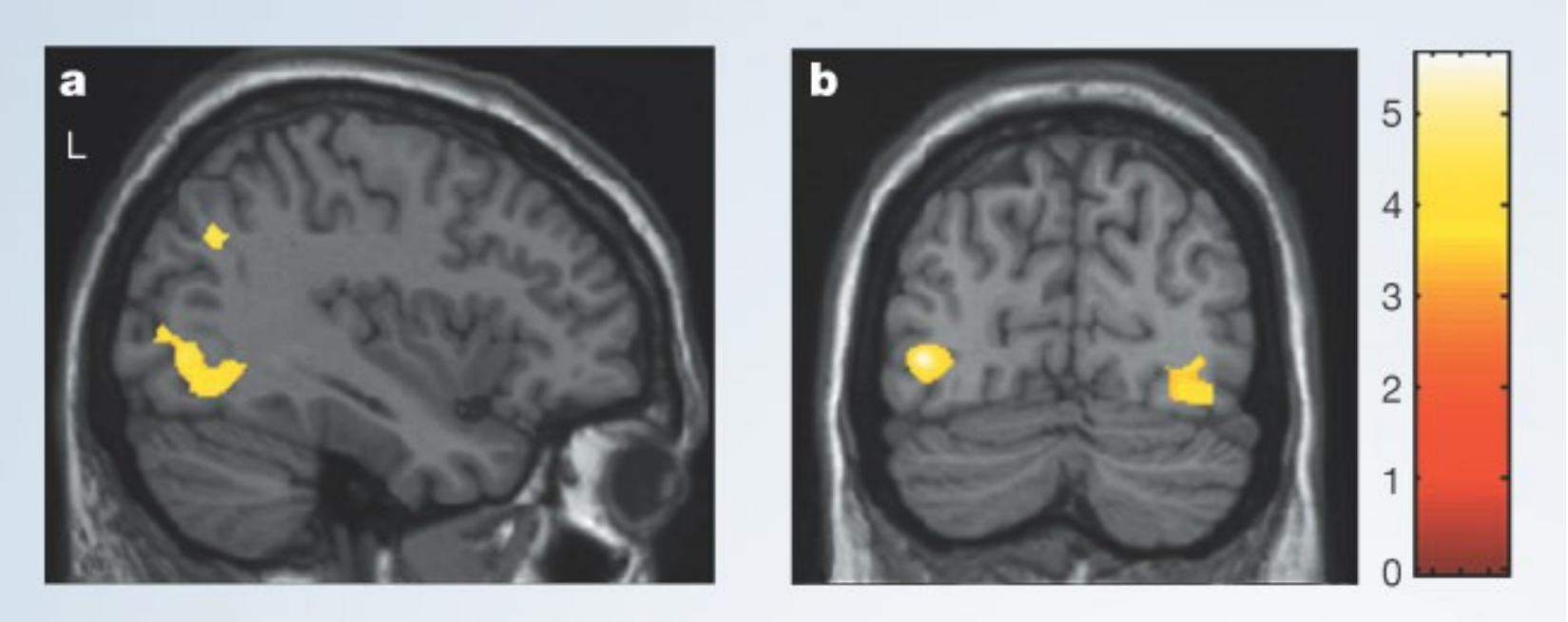
Cognitive stimulation		Total No	Dementia No	Incidence per 10 000 person years	Hazard ratio (95% CI)
Education	At work				
Low	Low	55 540	768	8.1	
Low	High	14 005	138	5.9	
High	Low	24 984	162	4.1	
High	High	13 367	75	3.5	

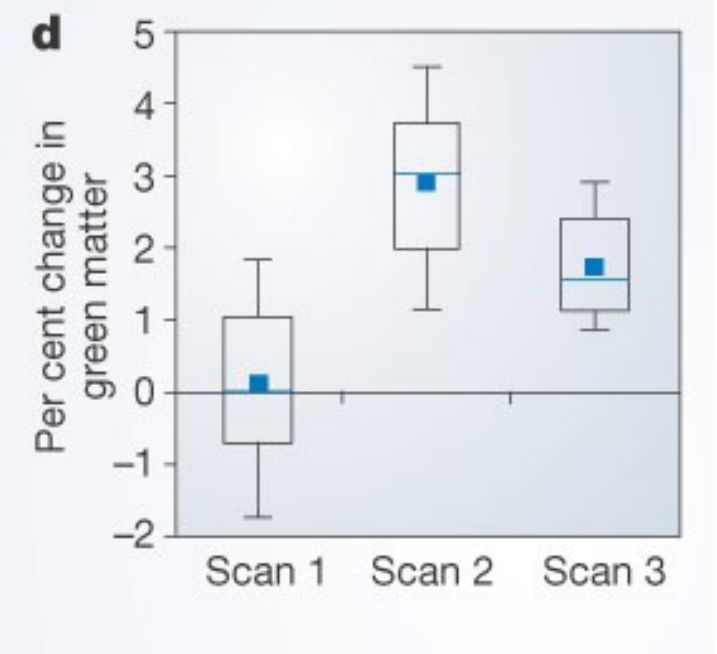


Kivimäki et al., BMJ 2021

Function-specific adaptations

- 3 months of juggling training stimulates the visual cortex
  - Yellow = changes compared to non-juggling controls (scan 2)
  - After 3 months without juggling, changes start to reverse (scan 3)

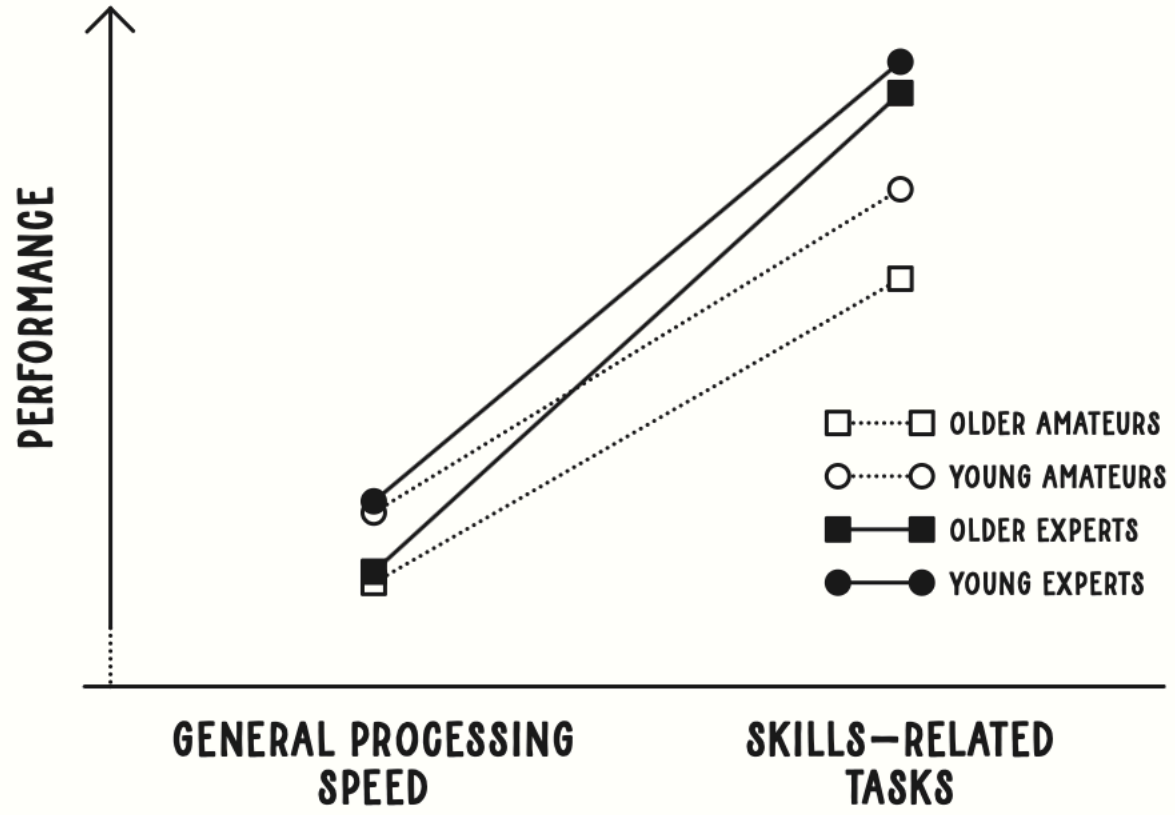




Draganski et al., Nature 2004

Practice maintains function

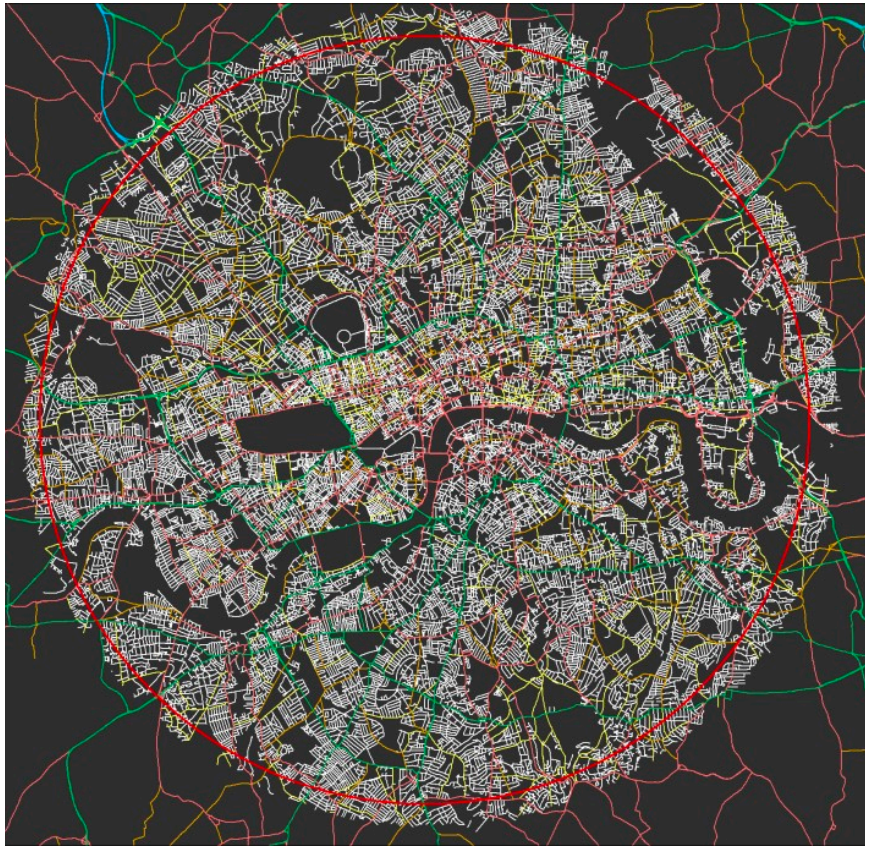
- Young (20s-30s) vs Older (50s-60s) Amateur vs Expert Pianists
  - Older experts had no loss in piano skills compared to younger experts
  - Piano skills in older pianists best predicted by recent practice

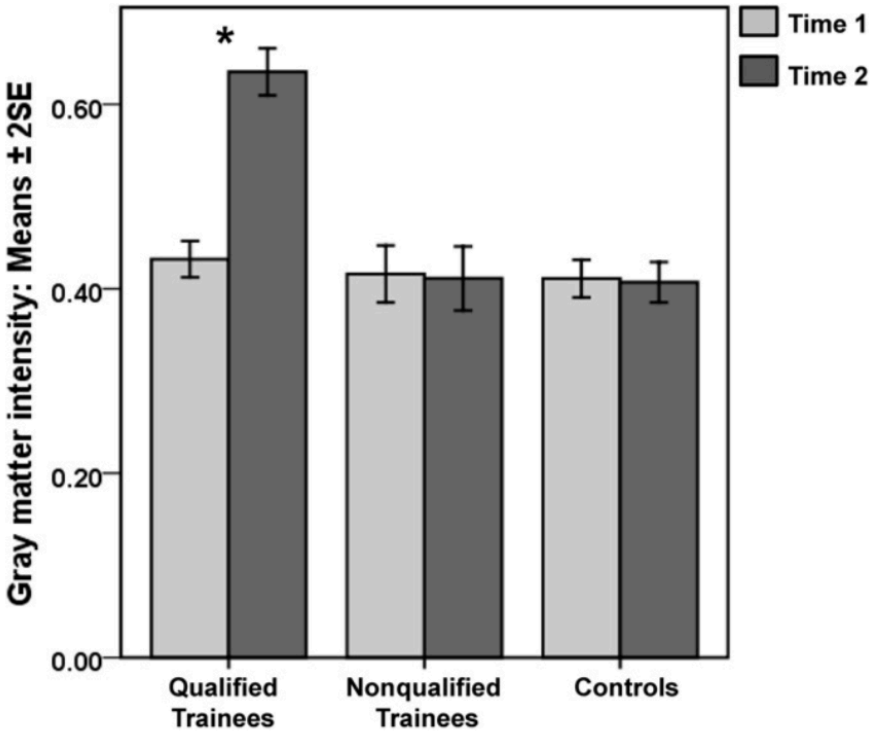


Adapted from: Krampe et al., J Exp Psychol Gen. 1996

Learning “The Knowledge” stimulates the hippocampus

- Spatial navigation/learning improves hippocampus function
  - Taxi and ambulance drivers have a lower risk of dementia

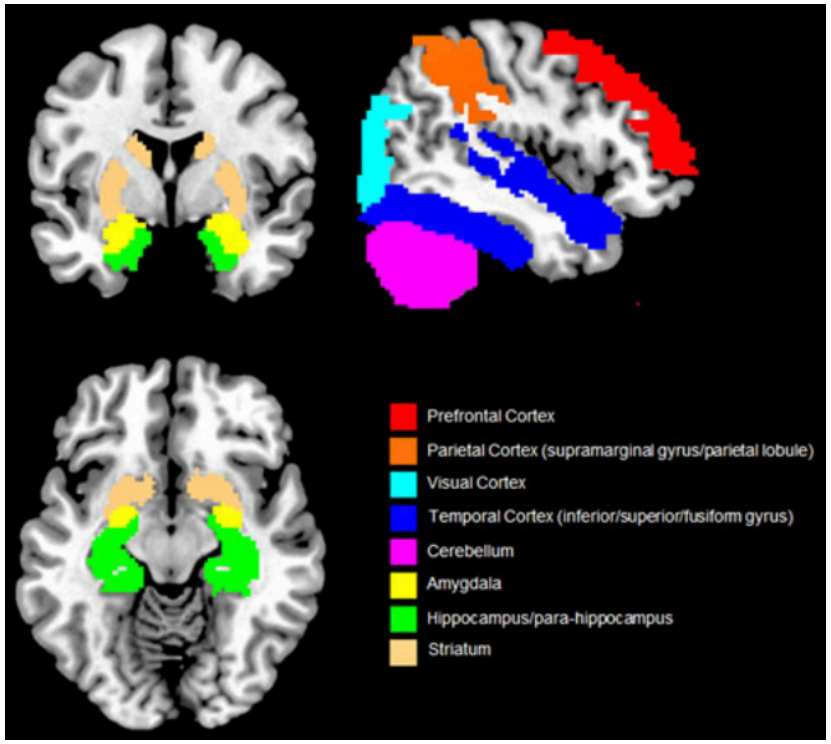


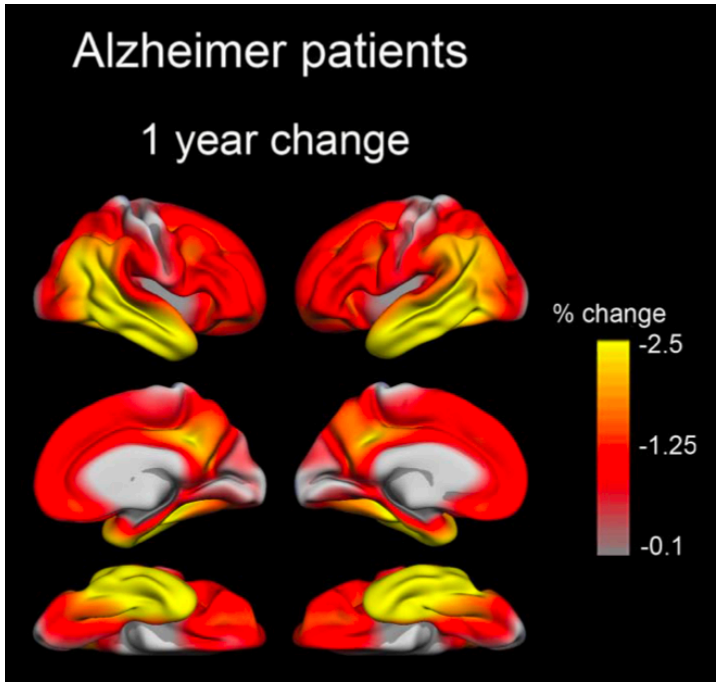


Woollett and Maguire. Current Biology, 2011; Patel et al., BMJ 2024.

Stimulus removal mimics aging-related brain atrophy

- Poor social engagement increases dementia risk
  - Living alone, limited social network, poor social support
- Regional functional and morphological brain changes associated with social isolation are very similar to Alzheimer's disease





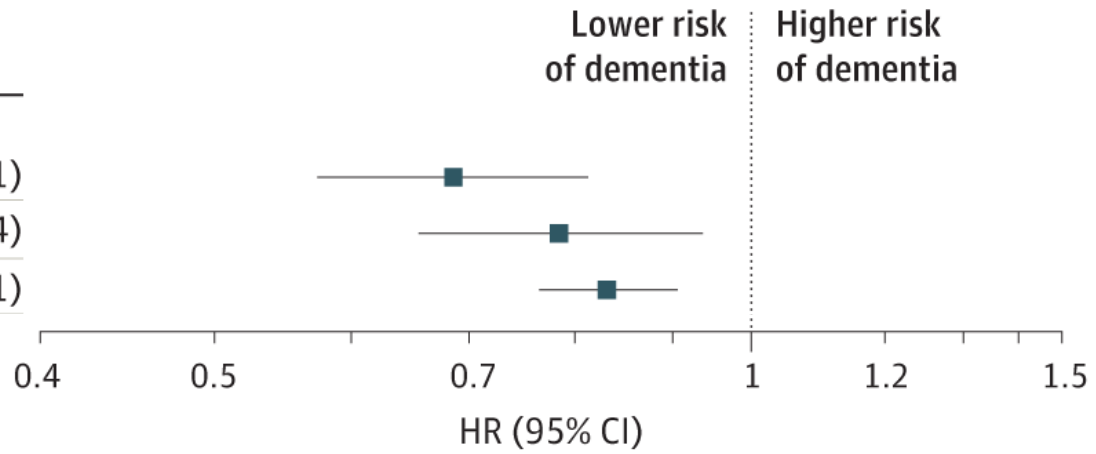
Penninkilampi et al., J Alz Dis 2018; Zovetti *et al.,* Epidemiology and Psychiatric Sciences 2021; Fjell et al., J Neurosci 2009

Loss of inputs increases cognitive decline

- Increased risk of dementia in those that lose a sense
  - Sight (e.g., cataracts), hearing, smell
  - Risk is reversed if sense is restored (especially if high risk)

B Alzheimer disease dementia

Variable	HR (95% CI)
Years since cataract surgery	
0-5	0.68 (0.57-0.81)
>5	0.78 (0.65-0.94)
Additional education, 4 y	0.83 (0.76-0.91)



- Cognitive decline accelerates at retirement

Lee *et al.*, JAMA Internal Med 2021; Turknett and Wood, Cells 2022;
Hale *et al.*, SSM Pop Health, 2021; Sundström et al., Ger Psych 2019

Engagement drives network-specific activity

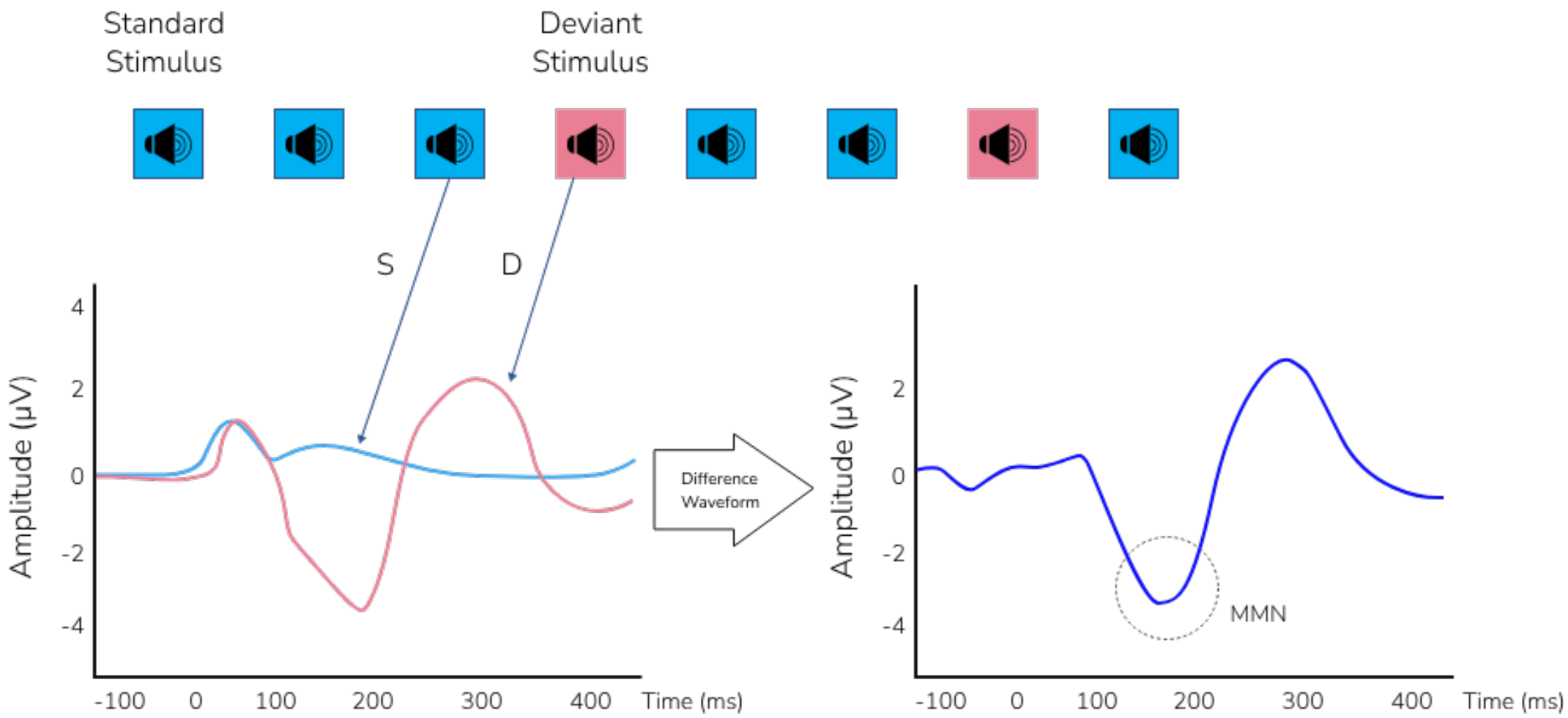
- “Your Brain on ChatGPT”
  - Recent study of 54 students
  - Three essay conditions: brain-only, search engine, LLM
- Work-related connectivity decreased with tool complexity
  - Lower ownership of work
  - Worse recall
- This is the brain working as expected
  - Different connectivity based on use
  - Lower engagement if offloading work

Kosmyna *et al*. arXiv 2025

Trying (and failing) is key

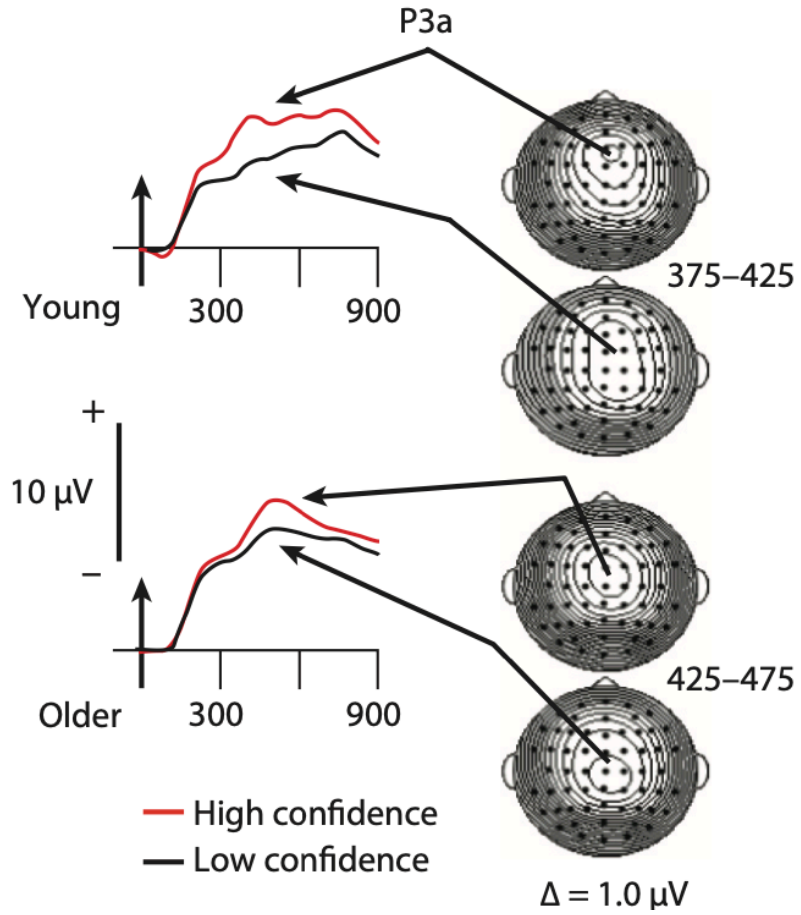
- Errors and failure are basic elements of learning
- Errors while learning were traditionally considered detrimental
  - Interference Theory - errors compete with the correct answer
  - Led to a preference for errorless learning in educational settings
- In general, adults tend to avoid errors
  - Embarrassment or concern about perceived lack of competence
- An increasing body of evidence suggests that experiencing errors during learning enhances subsequent memory retrieval

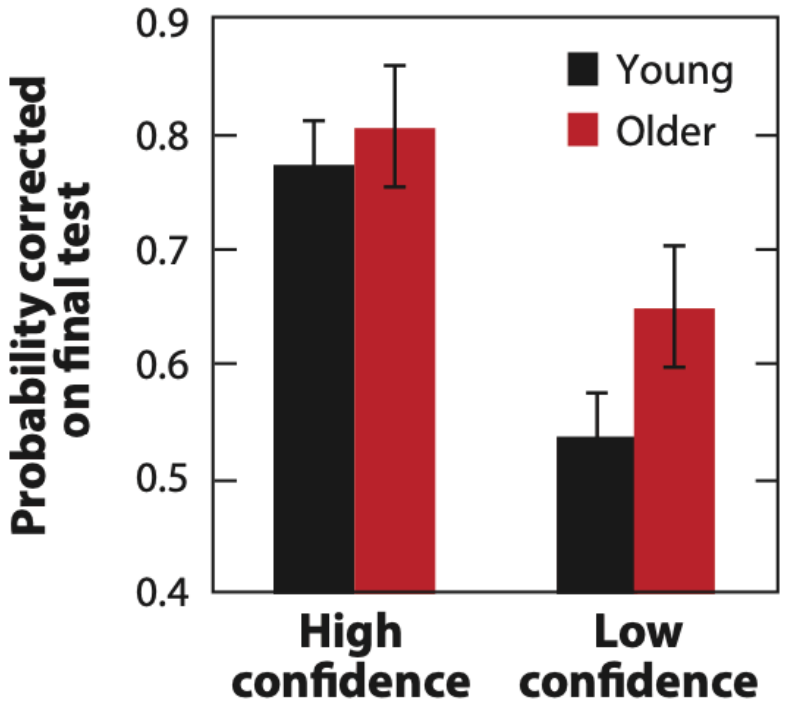
The brain is constantly monitoring for prediction errors



The bigger the error, the bigger the learning

- The more confident you are in your error, the more you learn

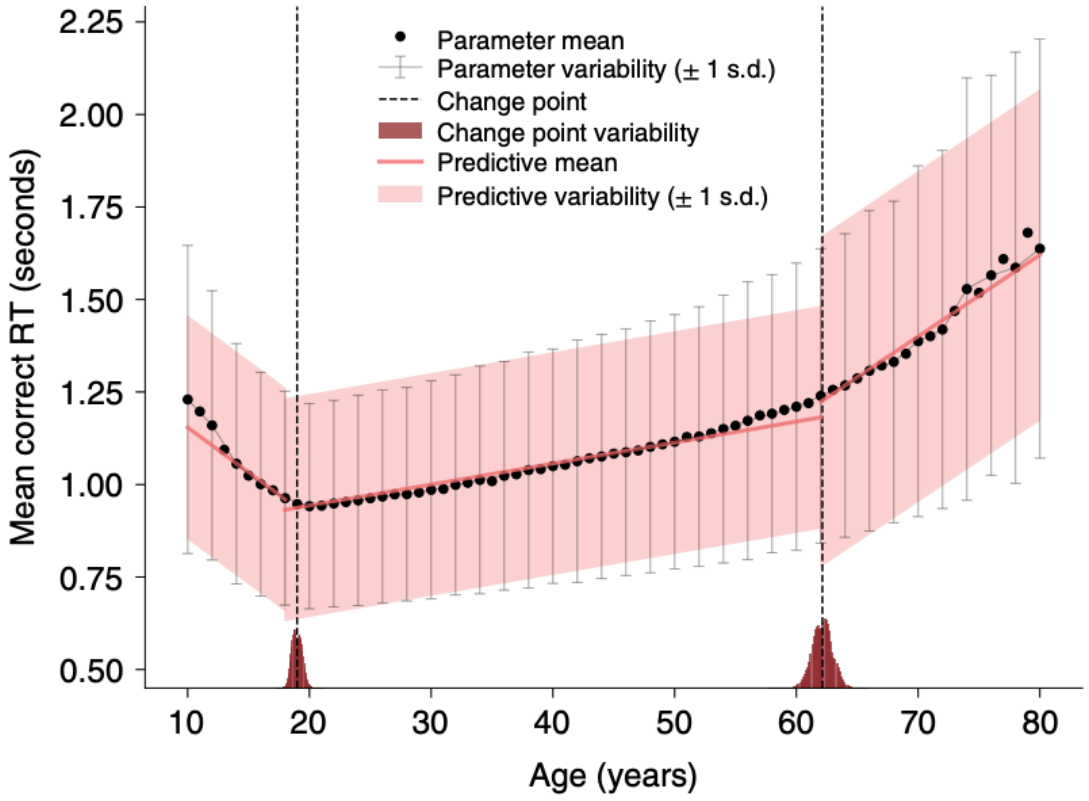


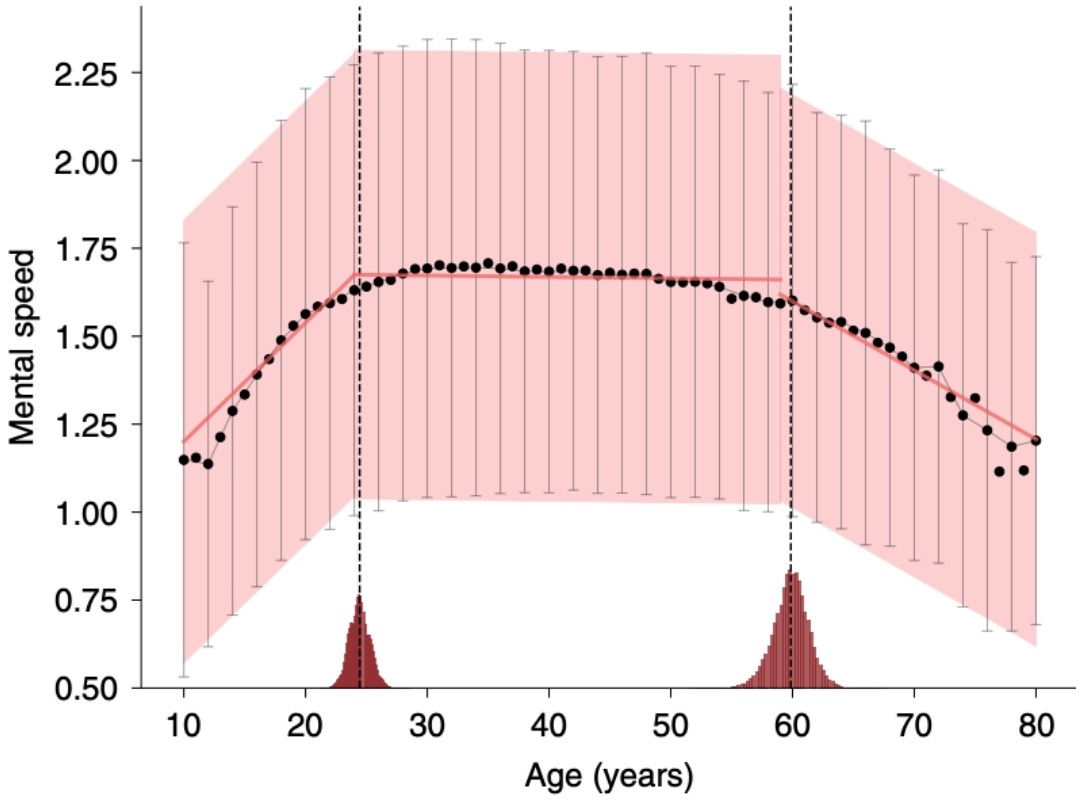


Metcalfe, Annual Review of Psychology, 2016

You can train functions that decline with age

- Reaction time and processing speed in 1.2 million people
  - Processing speed starts to decline around age 60





Krause et al., Nat Hum Behav 2022

Training processing speed lowers dementia risk

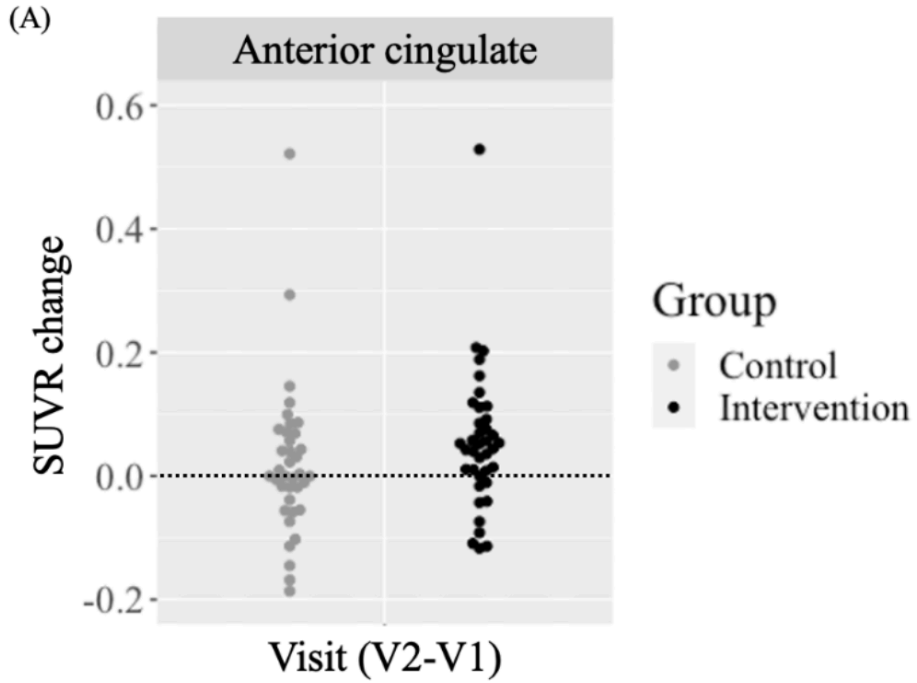
- Advanced Cognitive Training for Independent and Vital Elderly
  - 2,832 people aged 65-94
  - Processing speed group with booster sessions had lower dementia risk

Group	Intervention	Ever diagnosed dementia	Unadjusted analysis Hazard ratio (95%)	Adjusted analysis[g] Hazard ratio (95% CI)	Within-treatment difference with booster training[h] Hazard ratio (95% CI)
Booster-eligible subgroup[c]		594/1370 (43.40)			
	Memory + Booster	123/271 (45.39)	0.87 (0.70,1.08)	0.86 (0.68,1.07)	0.95 (0.78,1.15)[d]
	Memory without booster	79/185 (42.7)	0.85 (0.68,1.07)	0.84 (0.66,1.06)	
	Speed + Booster	105/264 (39.77)	0.74 (0.59,0.93)	0.75 (0.59,0.95)	0.81 (0.66,1.00)[e]
	Speed without booster	92/201 (45.77)	0.97 (0.78,1.21)	1.01 (0.81,1.27)	
	Reasoning + Booster	119/264 (45.08)	0.79 (0.63,0.98)	0.83(0.66,1.04)	0.91 (0.75,1.11)[f]
	Reasoning without booster	76/185 (41.08)	0.97 (0.77,1.23)	0.96 (0.76,1.21)	

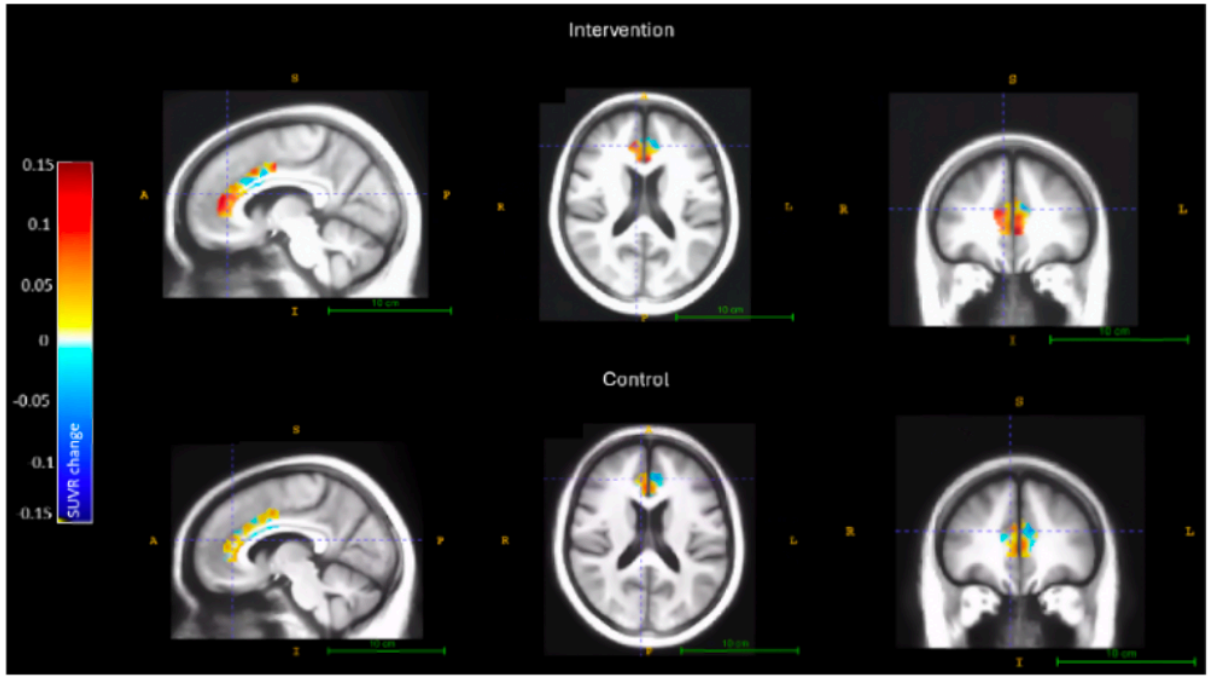
Coe et al., Alzheimer's Dement 2026

Training boosts cholinergic signaling

- 92 adults in the 60s/70s
  - Signaling changes compared to solitaire group

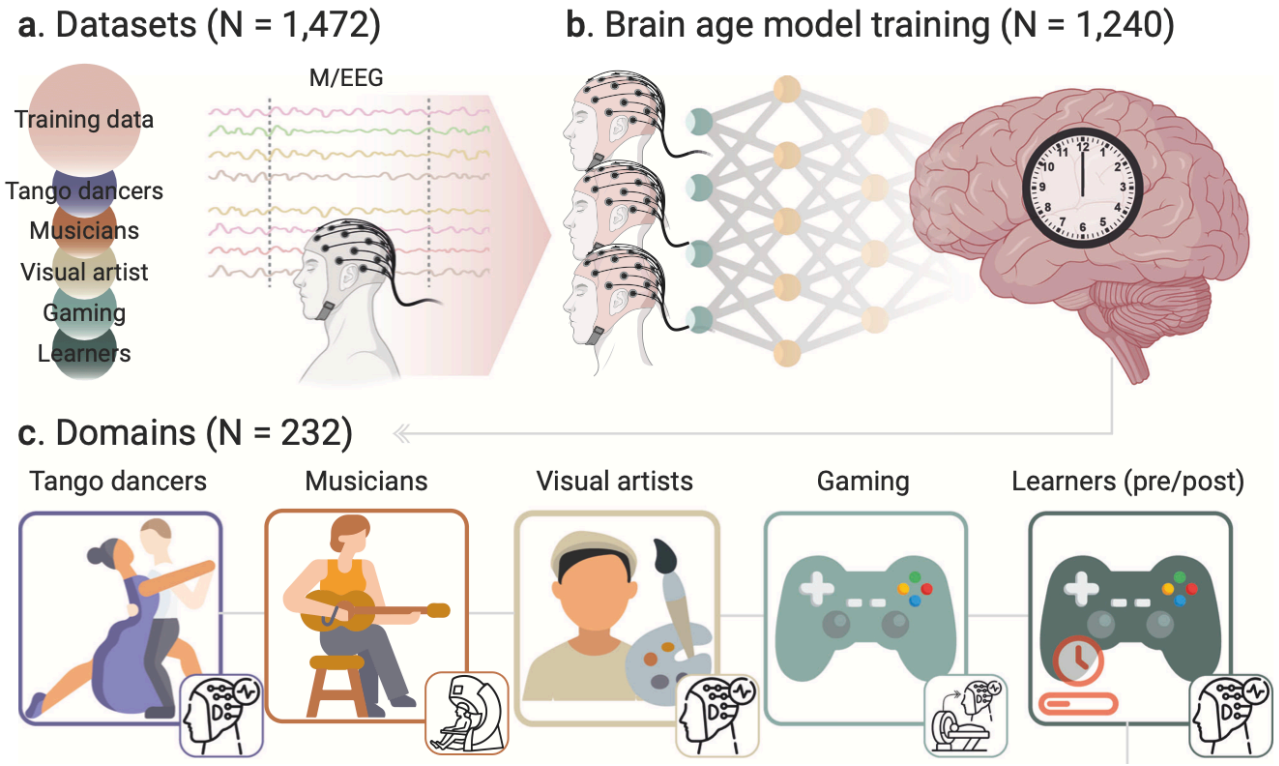


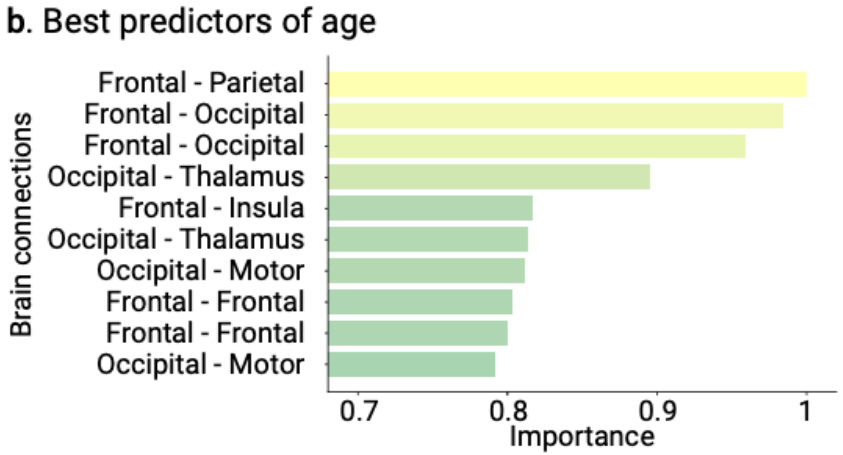
Intervention (V2-V1)
increase +0.044, significant P=.03, medium effect size ω^2=0.09
Control (V2-V1)
increase +0.014, nonsignificant P=.50, effect size ω^2<0.01

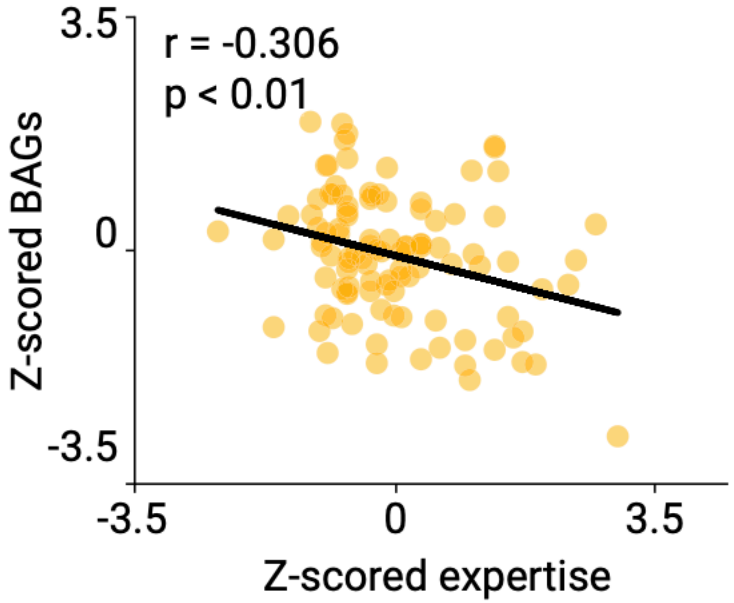


Attarha et al., JMIR Serious Games 2025

Mastery in creative skills maintains network function







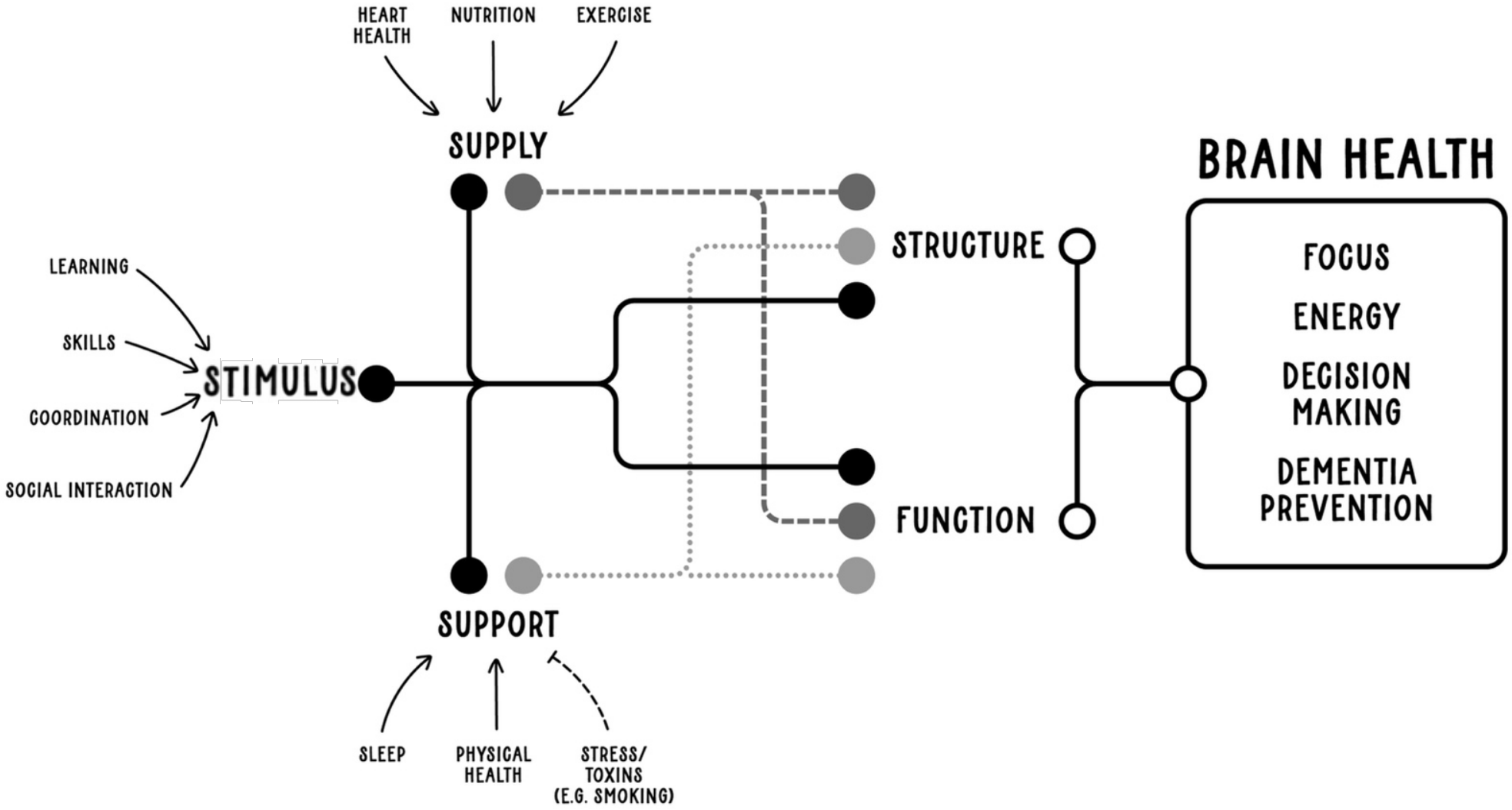
Coronel-Oliveros et al., Nat Comm 2025

Summary - the brain is like a muscle

- How you use it determines its function:
  - Do more of what you want your brain to be good at
  - Gainz are driven by challenge and occasional failure
  - Supported by other aspects of lifestyle and the environment

- Learn new skills (do things you're bad at)
  - Language, Music, Teaching
  - Interventions for sensory loss (cataract surgery, hearing aids etc)
  - Coordinative sports and challenges
  - Don't retire?
  - Build social networks
    - Volunteer, do activities with a group

When in doubt, start with the 3-S model



Turknett and Wood, Cells 2022
From *The Stimulated Mind* (Penguin Random House, 2026)

Use it or lose it

Tommy Wood, BM BCh, PhD
Associate Professor, University of Washington
Chair, Food the the Brain Research Group
Head Scientist for Motorsport, Hintsa Performance

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