

Using The Virtual Brain to trace trajectories of brain health in ageing

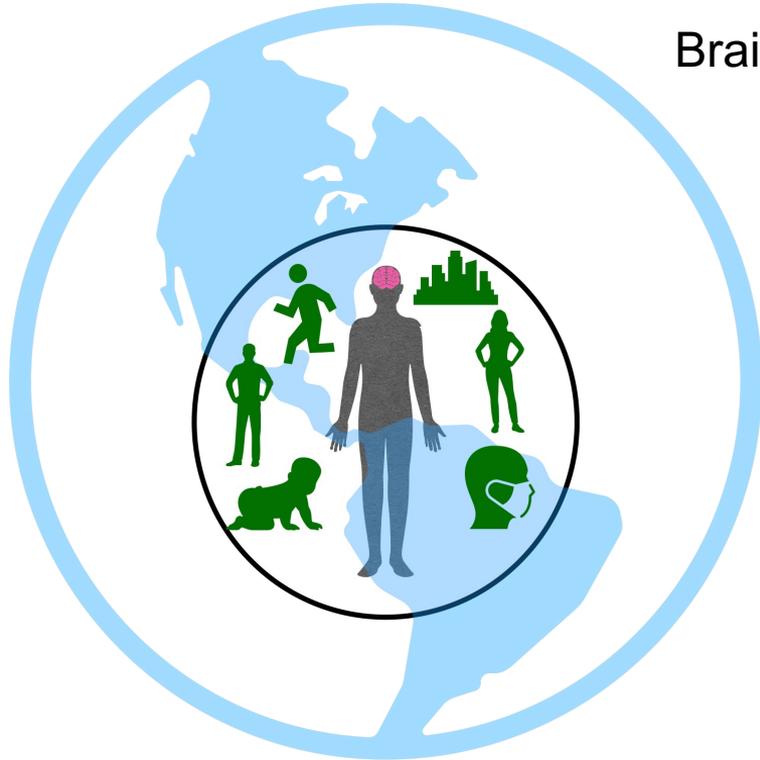
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Our key focus
What makes our brain resilient?

- Recover from stroke
 - Resist dementia
- Overcome head injury
- Adapt to developmental disabilities

What makes our brain resilient?



Brain resilience is determined by many factors

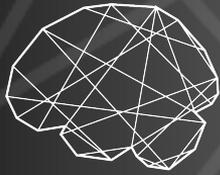
- *Biological*
- *Psychological*
- *Social*
- *Environment*

The interaction of these factors
may hold the key to
understanding

But

Studying such interactions is an
enormously complicated matter.

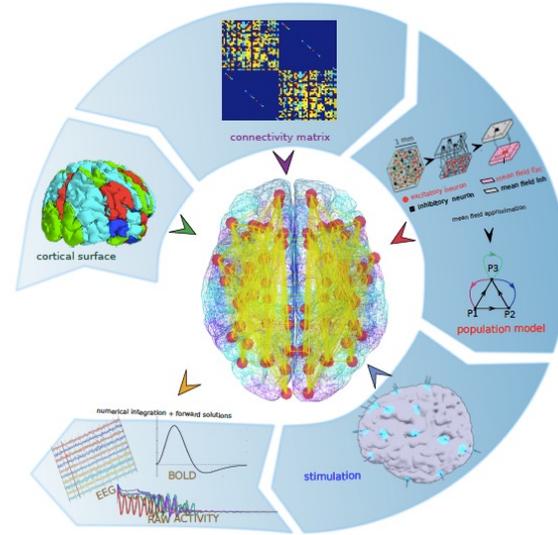
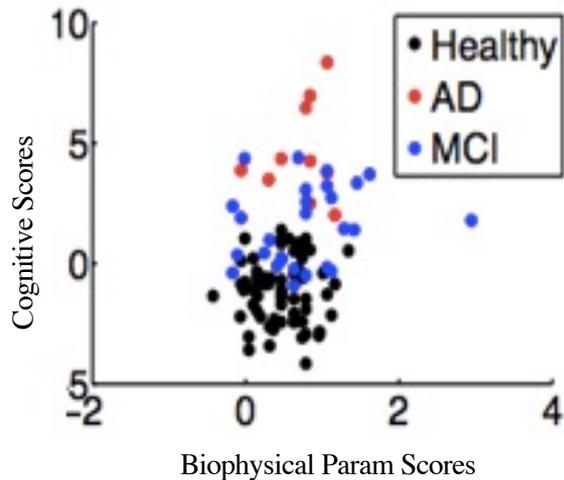
Computational modeling can help.



TVB model of Dementia

AGING & DEMENTIA

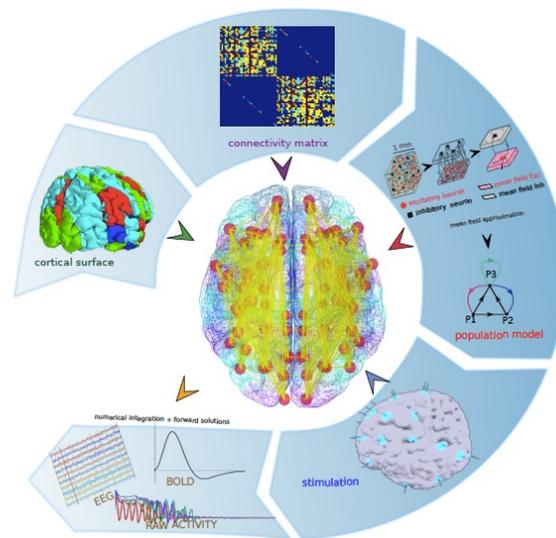
Biophysical model parameters correlate with behavioural changes in neurodegenerative diseases.



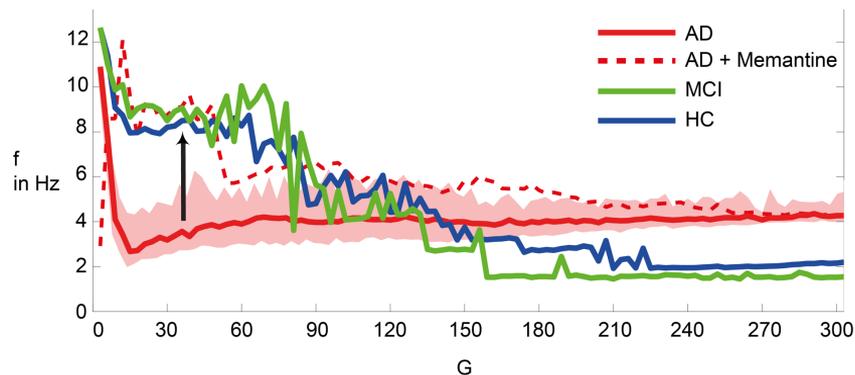
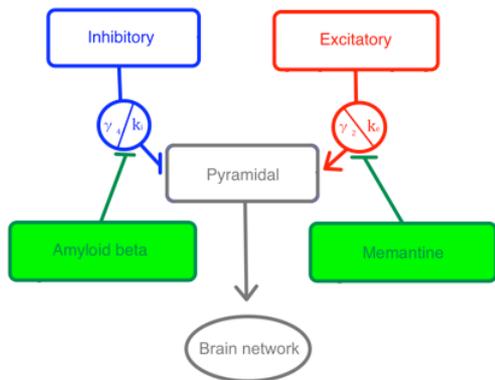
Replication and extension underway using ADNI, PPMI and Sydney MAS data sets.

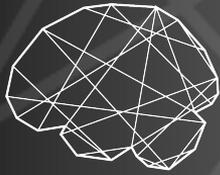
AGING & DEMENTIA

Simulated Drug Therapy: Can simulate drug effects on local and global brain dynamics
“Virtual memantine” treatment re-establishes frequency distributions of AD closer to controls



Stefanovski et al. 2019
Frontiers Neurosci

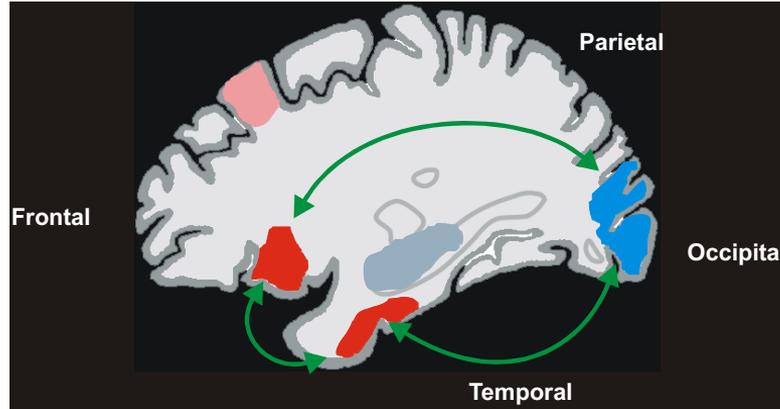




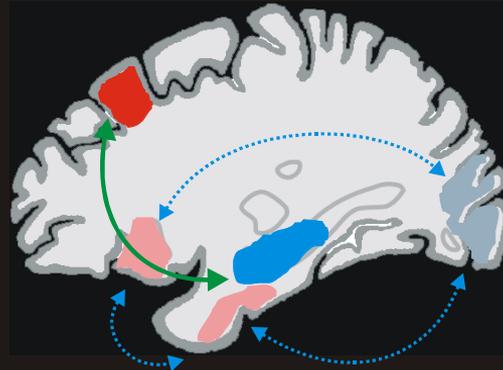
**But what happens in
“healthy” aging?**

Early clues on brain resilience

Young



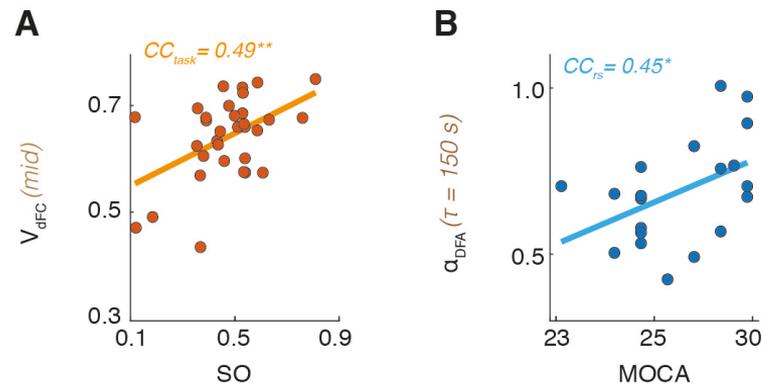
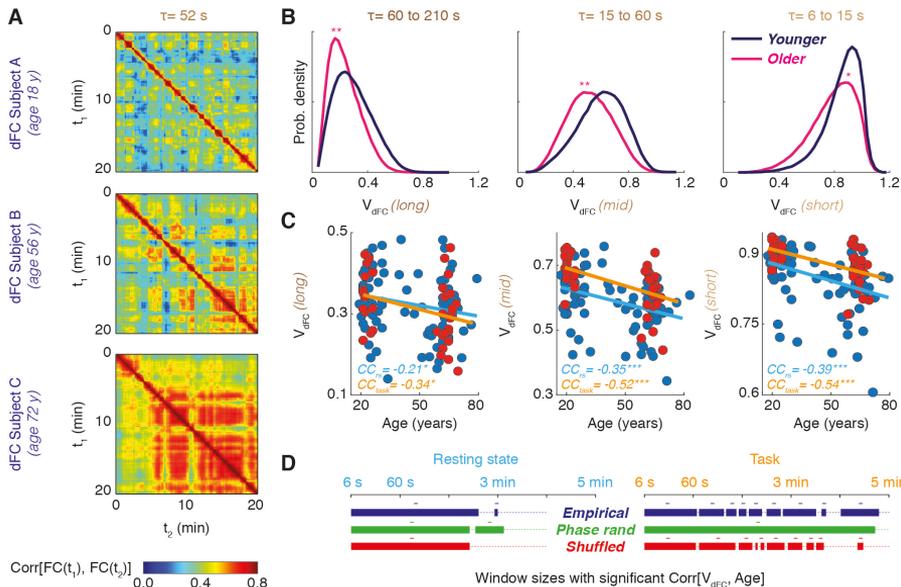
Old



Common observation that aging brings changes in functional architecture that may preserve cognitive function

Dynamic Functional Connectivity between order and randomness and its evolution across the human adult lifespan

Demian Battaglia^{a,*,} Thomas Boudou^{a, b,} Enrique C.A. Hansen^{a, c,} Diego Lombardo^{a,} Sabrina Chettouf^{d, e, f,} Andreas Daffertshofer^{f,} Anthony R. McIntosh^{g,} Joelle Zimmermann^{d, g,} Petra Ritter^{d, e, 1,} Viktor Jirsa^{a, 1}



Aging brings a shift in network dynamics.
Characteristics of the shift correlates with cognition

How often network states change

OPEN

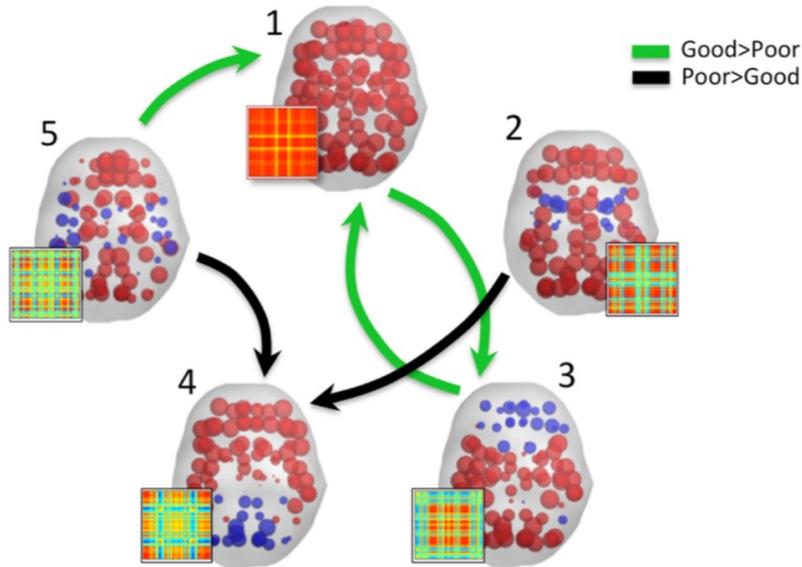
Cognitive performance in healthy older adults relates to spontaneous switching between states of functional connectivity during rest

Received: 19 December 2016

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Published online: 11 July 2017

Joana Cabral^{1,2}, Diego Vidaurre³, Paulo Marques^{4,5,6}, Ricardo Magalhães^{4,5,6}, Pedro Silva Moreira^{4,5,6}, José Miguel Soares^{4,5,6}, Gustavo Deco^{7,8,9,10}, Nuno Sousa^{4,5,6} & Morten L. Kringelbach^{1,2,11}



Aging brings a shift in network dynamics.
Characteristics of the shift correlates with cognition

Progression between network states

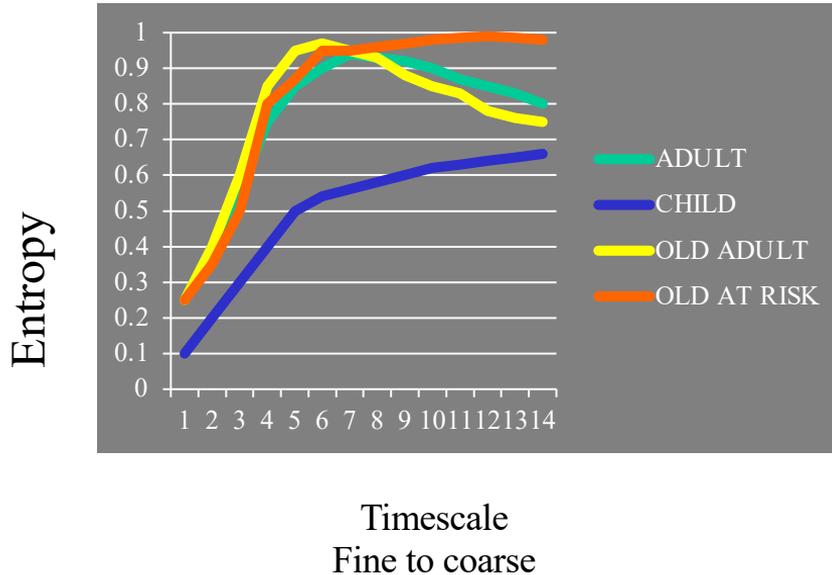
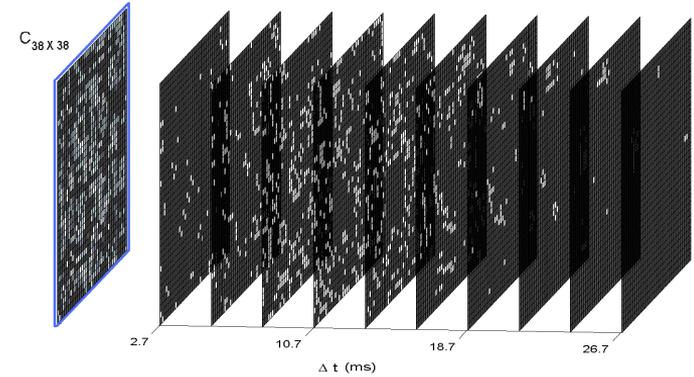
Oxford Research Encyclopedia of Psychology

Neurocognitive Aging and Brain Signal Complexity

Anthony Randal McIntosh

Subject: Cognitive Psychology/Neuroscience, Neuropsychology

Online Publication Date: Feb 2019 DOI: 10.1093/acrefore/9780190236557.013.386

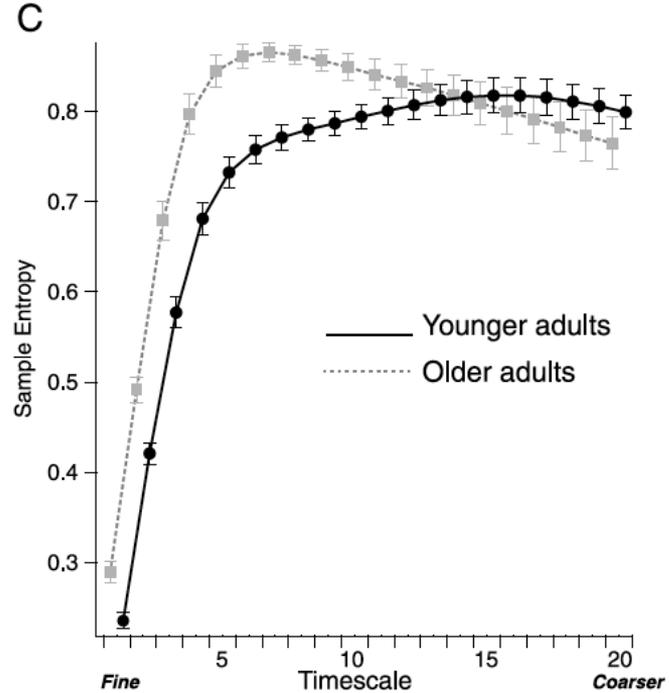
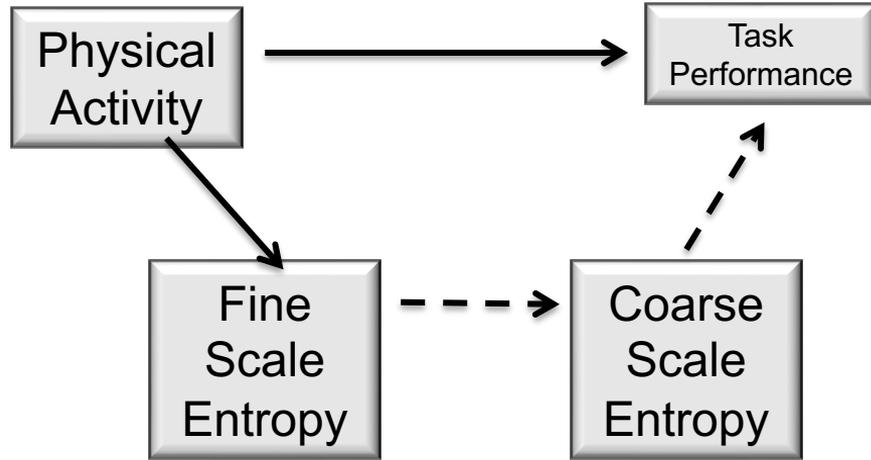


Aging brings a shift in network dynamics.
Characteristics of the shift correlates with cognition

*Entropy as a function of time scale (space-time structure).
The curve morphology relates to cognitive status*

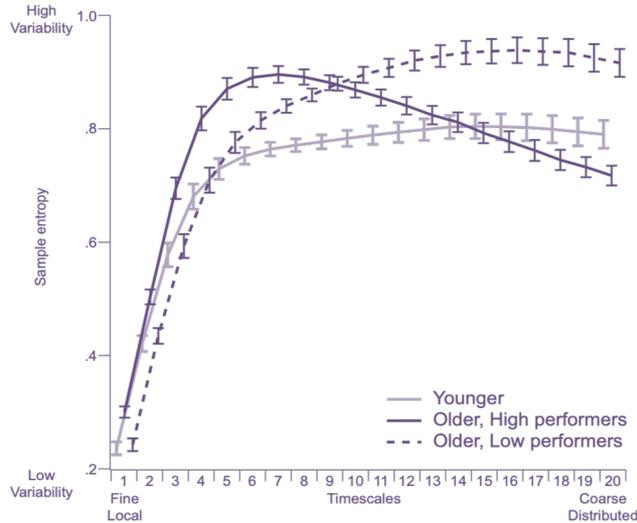
Age-related Shift in Neural Complexity Related to Task Performance and Physical Activity

Jennifer J. Heisz¹, Michelle Gould², and Anthony R. McIntosh²

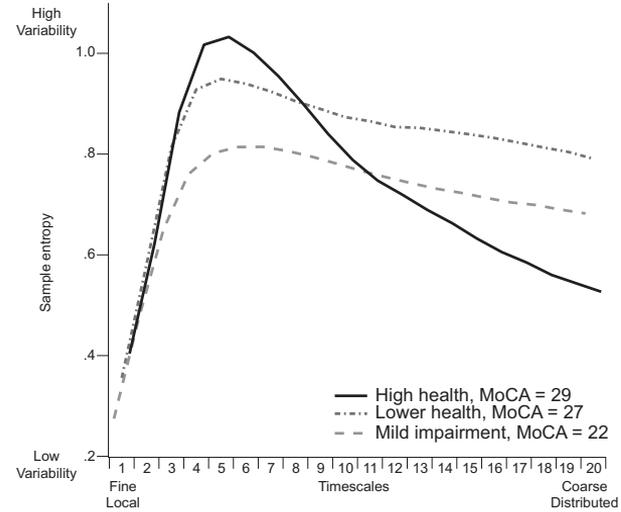


Entropy and Brain Health

A metric for risk?

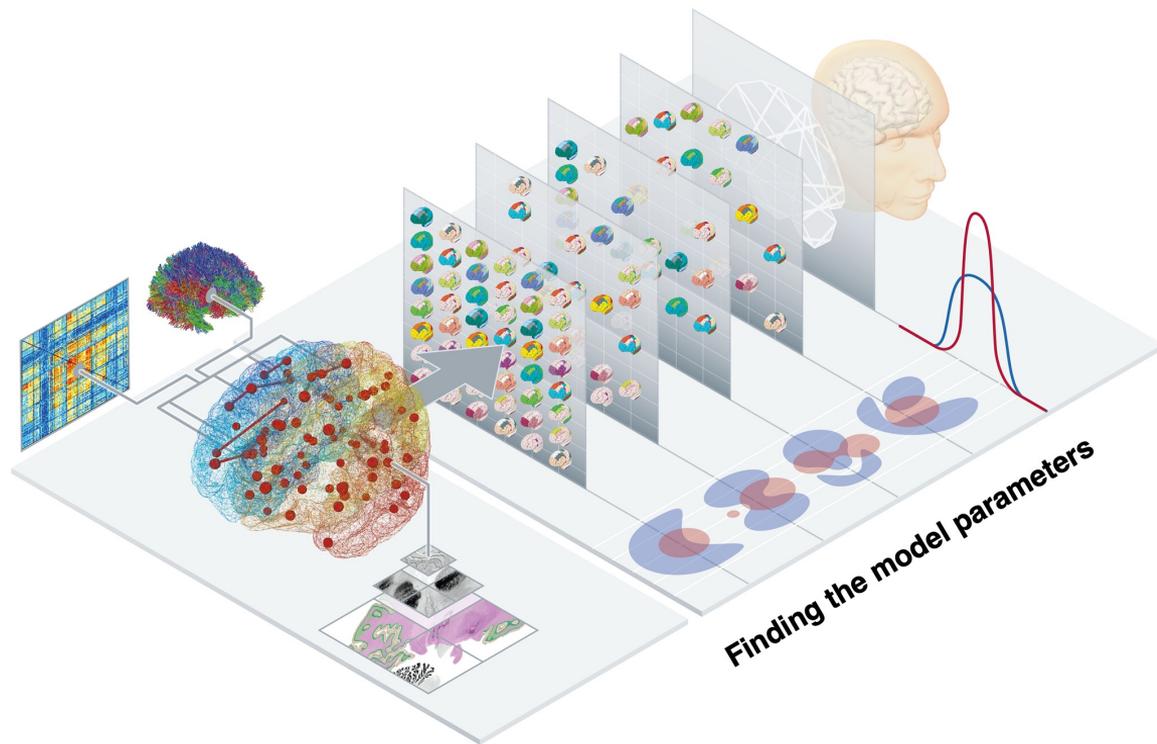


Age-related increase in fine scales with aging preserves performance



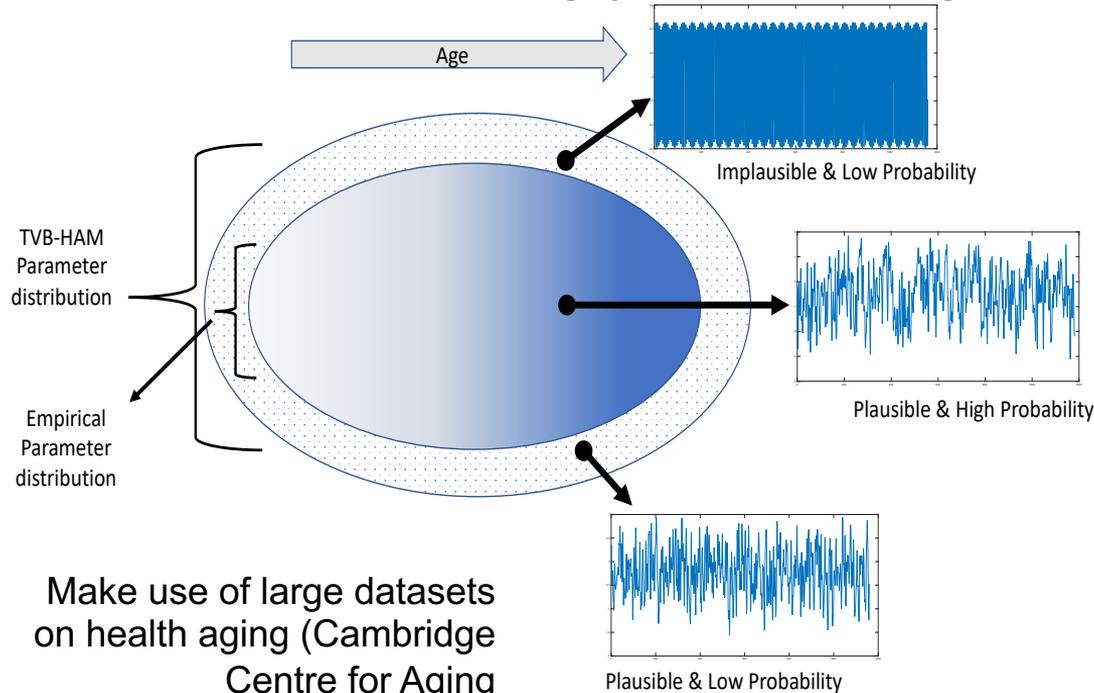
Higher entropy fine scales related to better cognitive status in aging

Modeling the age-related changes to better understand the trajectories

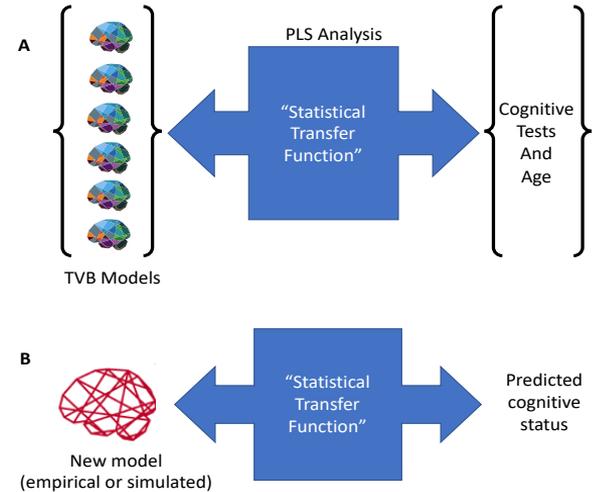


TVB Healthy Aging Model (TVB-HAM)

A distribution of possible trajectories in brain health

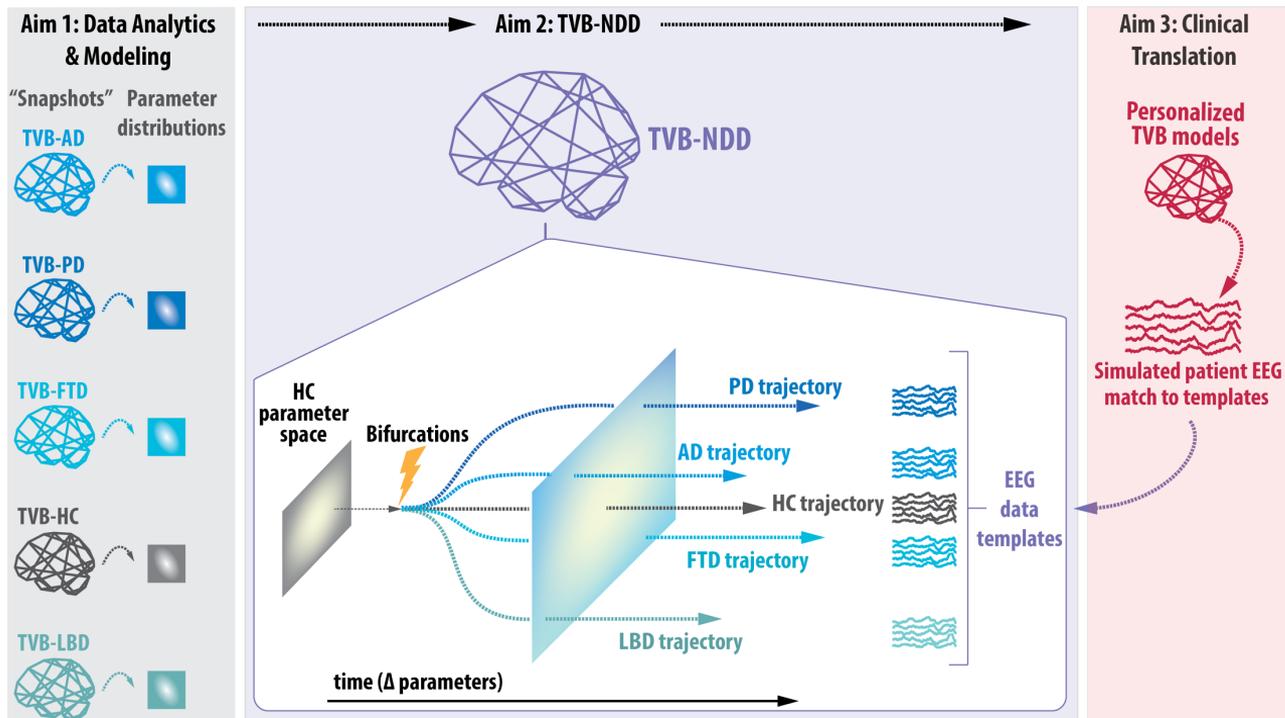


Make use of large datasets on health aging (Cambridge Centre for Aging Neuroscience) to establish a distribution of healthy aging brain networks



(A) Relate individual model dynamics to cognitive status and (B) Validate statistical mapping with new data

TVB NEURODEGENERATIVE DISORDERS (TVB-NDD) FLOWING FROM THE HEALTHY TRAJECTORY



Clinical Decision Support:

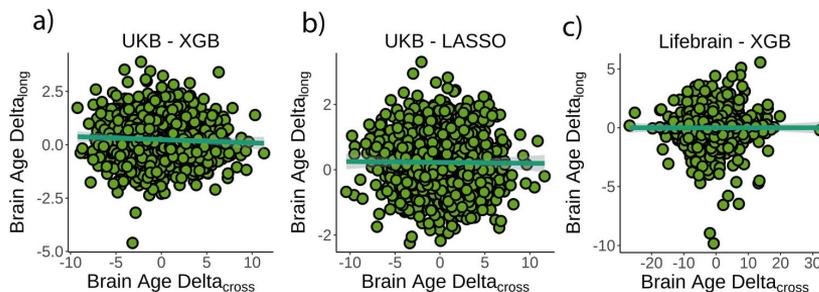
The TVB-NDD distribution can be used to map a single person's brain to determine if they are at risk

NB: this being evaluated in epilepsy (EPINOV)

TVB-NDD takes off from the healthy aging distribution to identify qualitative changes in dynamics that predict decline

Individual variations in 'brain age' relate to early-life factors more than to longitudinal brain change

Didac Vidal-Pineiro [✉], Yunpeng Wang, Stine K Krogsrud, Inge K Amlien, William FC Baaré, David Bartres-Faz, Lars Bertram, Andreas M Brandmaier, Christian A Drevon [see all »](#)



“The results showed no association between cross-sectional brain age and the rate of brain change measured longitudinally.

Rather, brain age in adulthood was associated with the congenital factors of birth weight and polygenic scores of brain age, assumed to reflect a constant, lifelong influence on brain structure from early life.

The results call for nuanced interpretations of cross-sectional indices of the aging brain and question their validity as markers of ongoing within-person changes of the aging brain.

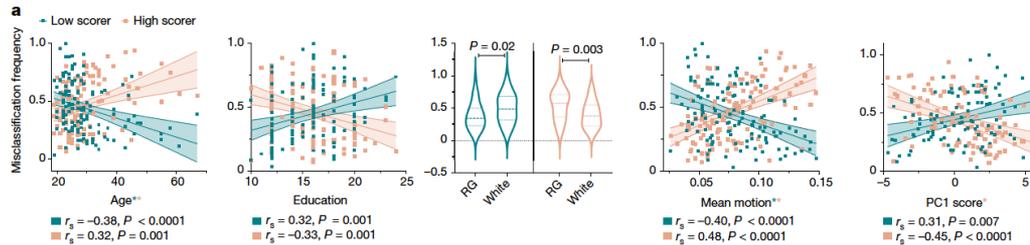
Longitudinal imaging data should be preferred whenever the goal is to understand individual change trajectories of brain and cognition in aging.”

CAUTION

Brain–phenotype models fail for individuals who defy sample stereotypes

[Abigail S. Greene](#) ✉, [Xilin Shen](#), [Stephanie Noble](#), [Corey Horien](#), [C. Alice Hahn](#), [Jagriti Arora](#), [Fuyuze Tokoglu](#), [Marisa N. Spann](#), [Carmen I. Carrión](#), [Daniel S. Barron](#), [Gerard Sanacora](#), [Vinod H. Srihari](#), [Scott W. Woods](#), [Dustin Scheinost](#) & [R. Todd Constable](#) ✉

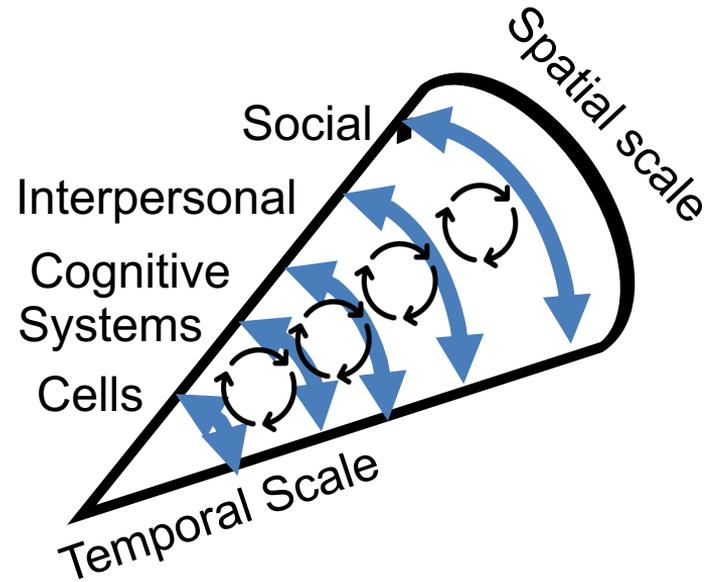
[Nature](#) (2022) | [Cite this article](#)



CAUTION

...Together, these results highlight the pitfalls of a one-size-fits-all modelling approach and the effect of biased phenotypic measures on the interpretation and utility of resulting brain–phenotype models.

*We can now use a platform like
TheVirtualBrain to model the links between
factors associated with brain resilience*



The simulations can tell us where to target our efforts in research, translation, and policy to help make our brain more resilient.

Final thoughts

- Building TVB models for healthy aging
 - There is a wealth of existing data, just needs a robust workflow
- We need to be very mindful of the data used
 - Cross-sectional may not be the best for trajectory estimation
- Great potential for personalization and monitoring
 - Mobile device to measure key indicators (e.g., entropy)
- Need to consider psychosocial factors seriously