Modelling Trajectories of Brain Health & Aging

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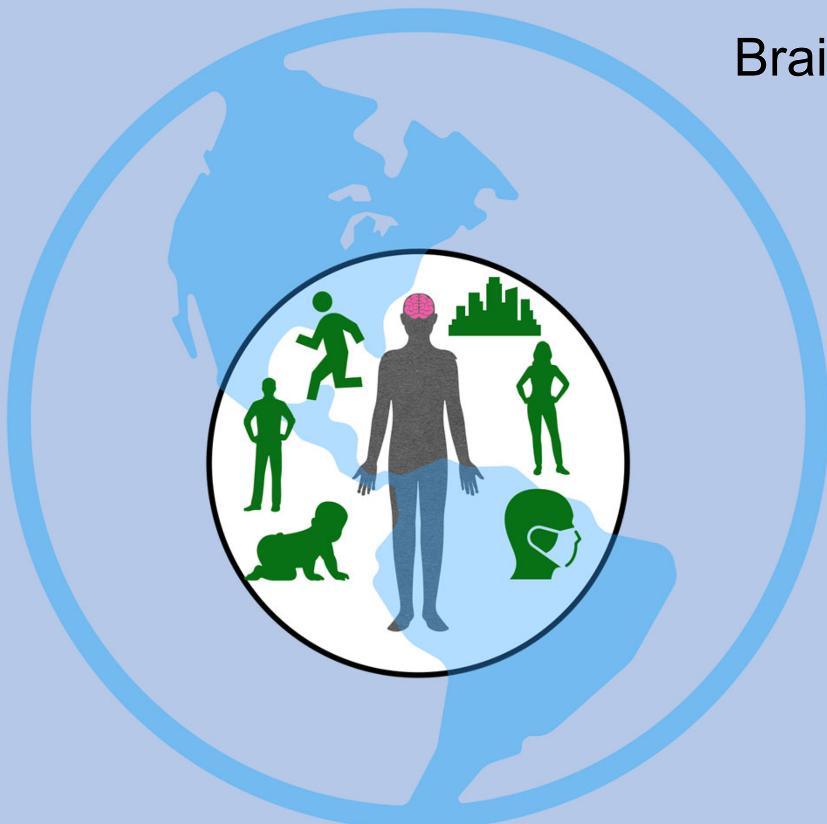
Our key focus

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.

NETWORK NEURO SCIENCE

Perspective

The hidden repertoire of brain dynamics and dysfunction

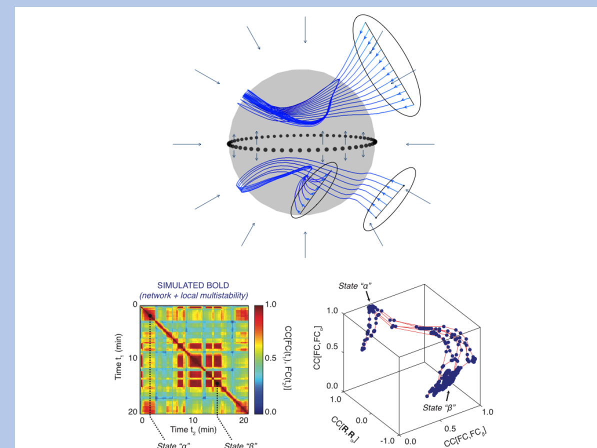
Anthony R. McIntosh[1] and Viktor K. Jirsa[2]

[1]Rotman Research Institute, Baycrest, University of Toronto, Toronto, Canada
[2]Institut de Neurosciences des Systemes, INSERM, Aix-Marseille Universite, Marseille, France

Keywords: Dynamical systems, Epilepsy, Cognition, Neuroimaging, Computational modeling

ABSTRACT

The purpose of this paper is to describe a framework for the understanding of rules that govern how neural system dynamics are coordinated to produce behavior. The framework, structured flows on manifolds (SFM), posits that neural processes are flows depicting system interactions that occur on relatively low-dimension manifolds, which constrain possible functional configurations. Although this is a general framework, we focus on the application to brain disorders. We first explain the Epileptor, a phenomenological computational model showing fast and slow dynamics, but also a hidden repertoire whose expression is similar to refractory status epilepticus. We suggest that epilepsy represents an innate brain state whose potential may be realized only under certain circumstances. Conversely, deficits from damage or disease processes, such as stroke or dementia, may reflect both the disease process per se and the adaptation of the brain. SFM uniquely captures both scenarios. Finally, we link neuromodulation effects and switches in functional network configurations to fast and slow dynamics that coordinate the expression of SFM in the context of cognition. The tools to measure and model SFM already exist, giving researchers access to the dynamics of neural processes that support the concomitant dynamics of the cognitive and behavioral processes.



Structured Flows on Manifolds: derive rules (manifolds) that constrain the evolution of system trajectories (flows).

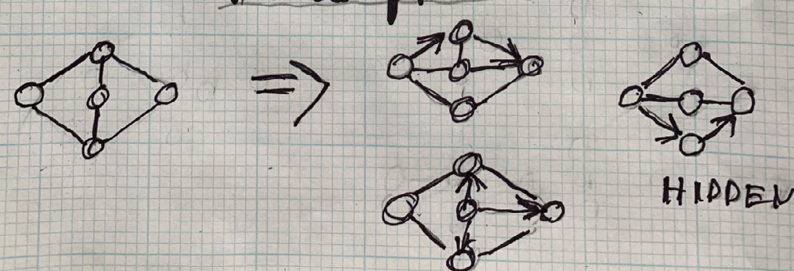
Move the emphasis from observing only what a system does in a given situation to deriving models that define not only that realization but also other possibilities (**dimensionality**).

Can we estimate the “full” repertoire of a brain?

①

Hidden Repertoires

- Arise when the distribution of parameters underlying state space enables configurations that are possible, but seldom actualized
- For the brain ⇒ functional configurations that are possible for a given architecture but seldom visited
  - redundant, inefficient or maladaptive

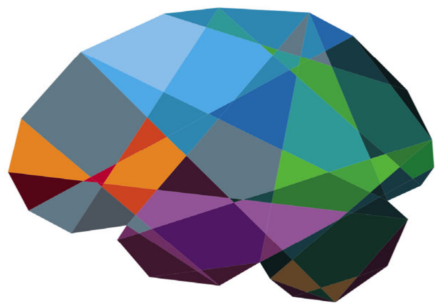


The TVB platform

The Virtual Brain Team

The Science
Randy McIntosh
Viktor Jirsa
Petra Ritter
Michael Breakspear
Gustavo Deco
Ana Solodkin
Olaf Sporns

The Technology
Jochen Mersmann
Lia Domide
Kelly Shen
Marmaduke Woodman



Try it, you'll like it.

www.thevirtualbrain.org

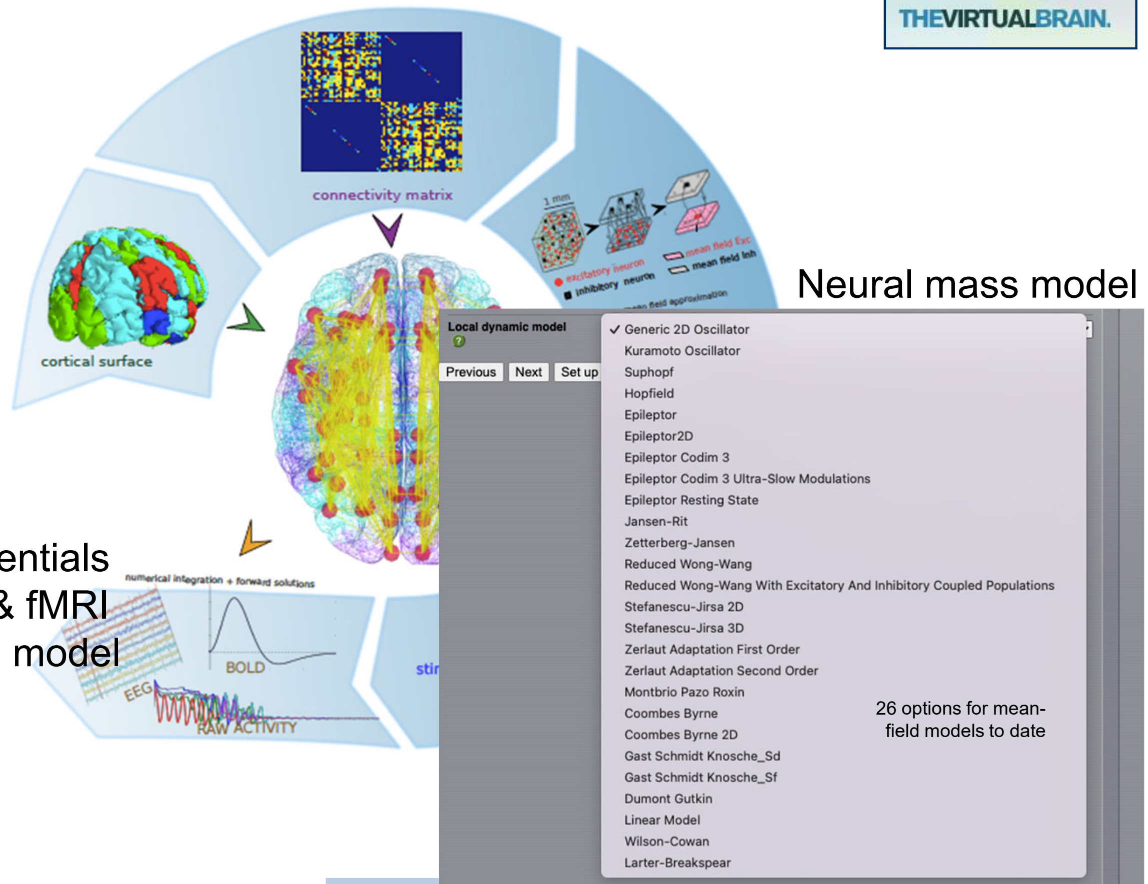
The Virtual Brain – Workflow

Individual tractography to estimate structural connections

Individual cortical geometry

Output local field potentials or EEG/MEG & fMRI thru forward model

Neural mass model



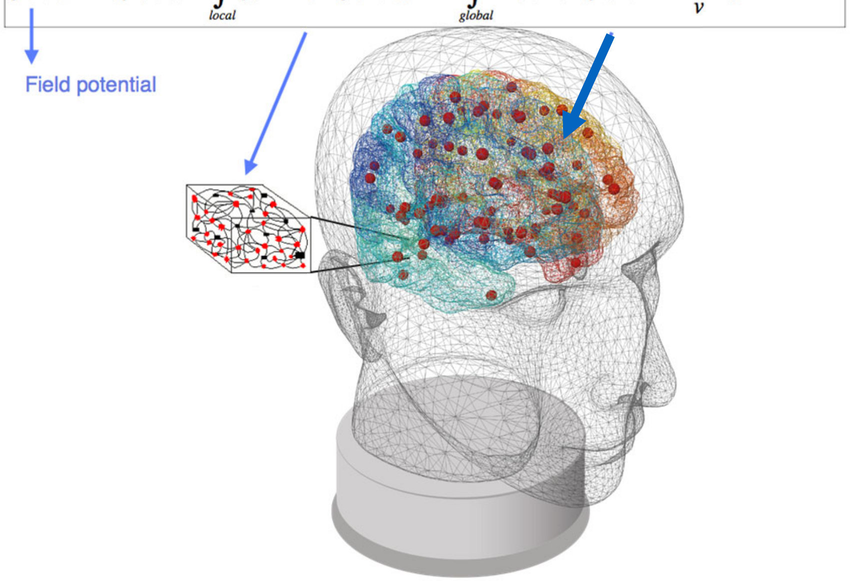
Sanz Leon et al Front Neuroinformatics 2013

The Virtual Brain

- Local and global network dynamics are integrated with forward solutions mapping source to sensor activity (e.g., fMRI, EEG).

Local dynamics   Global dynamics

$$\psi(x,t) = N(\psi(x,t)) + \int_{local} g(x-x')S(\psi(x',t))dx' + \int_{global} G(x,x')S(\psi(x',t-\frac{|x-x'|}{v}))dx' + \text{noise}$$



Deco, Jirsa, McIntosh Nature Rev Neurosci 2011

THEVIRTUALBRAIN.

TVB model of Dementia

AGING & DEMENTIA

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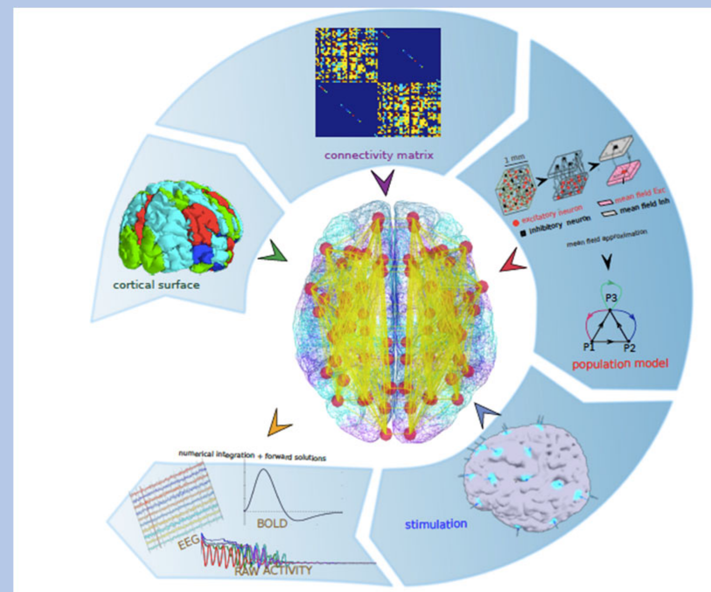

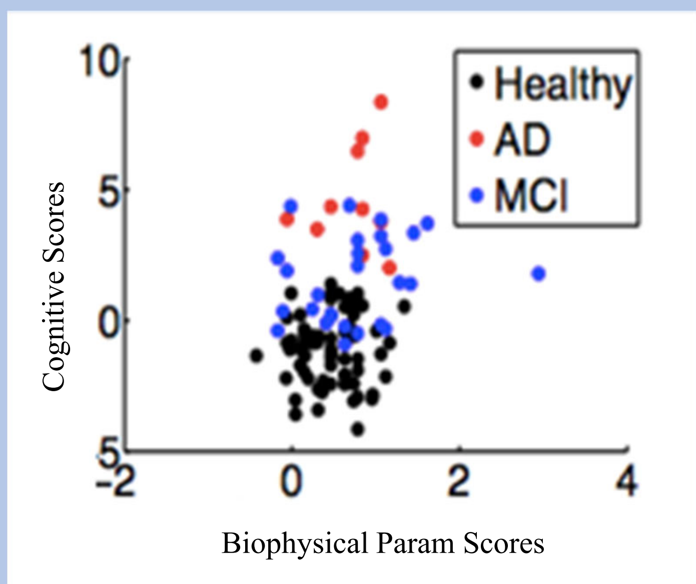

Replication and extension underway using ADNI, PPMI and Sydney MAS data sets.

Zimmermann et al. 2018
Neuroimage Clinical

AGING & DEMENTIA

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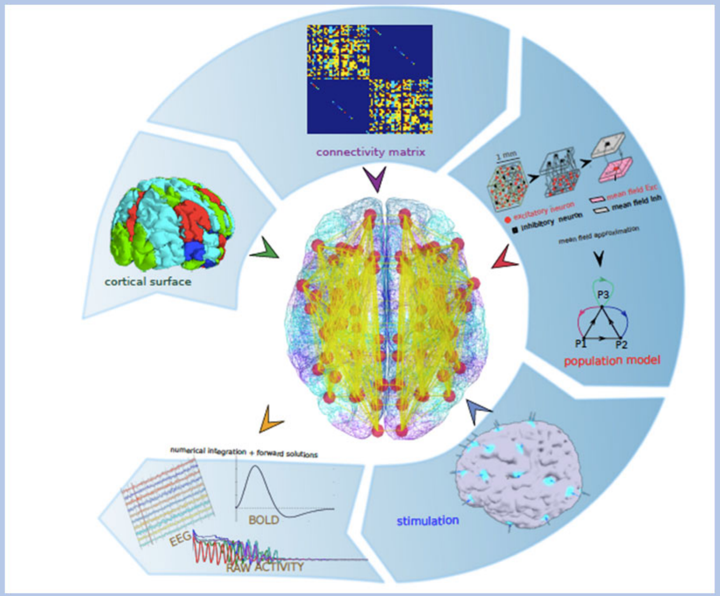
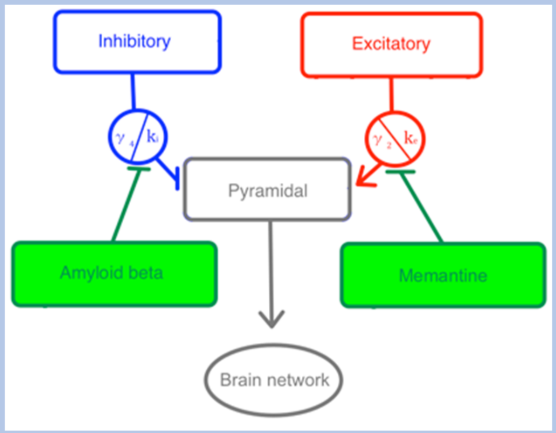
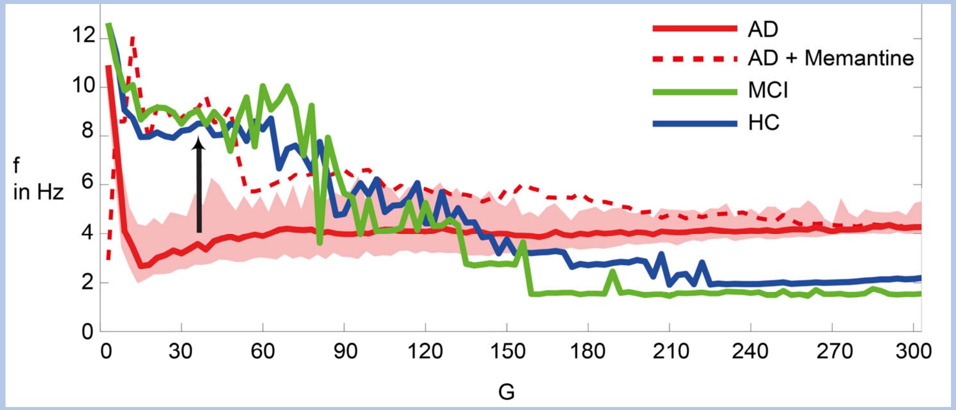


Stefanovski et al. 2019
Frontiers Neurosci





But what happens in “healthy” aging?

NETWORK NEUROSCIENCE

Perspective

The hidden repertoire of brain dynamics and dysfunction

Anthony R. McIntosh[1] and Viktor K. Jirsa[2]

[1]Rotman Research Institute, Baycrest, University of Toronto, Toronto, Canada
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Can we see hints of hidden repertoires in aging?

Aging and hidden repertoires

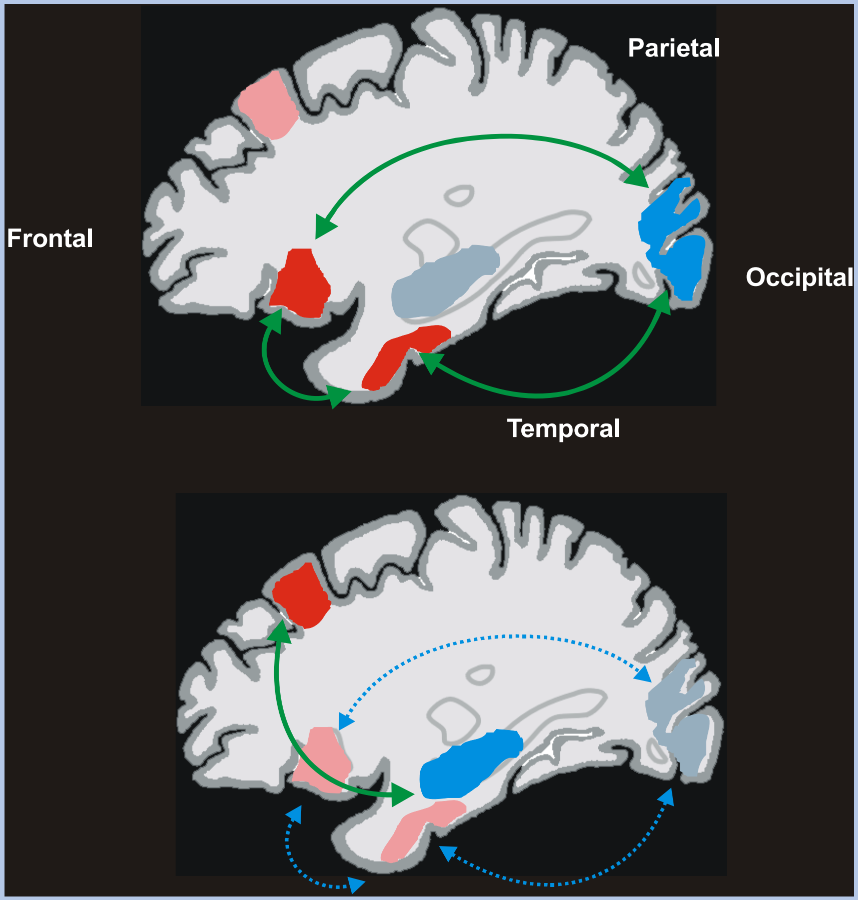
Young

Short-term visual memory task
Young (18-35yrs) and Old (65-80 yrs)

No difference in performance
Different functional networks that support behaviour

Old

McIntosh et al, Current Biol, 1999



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

Is it a hidden repertoire or an adaptation?

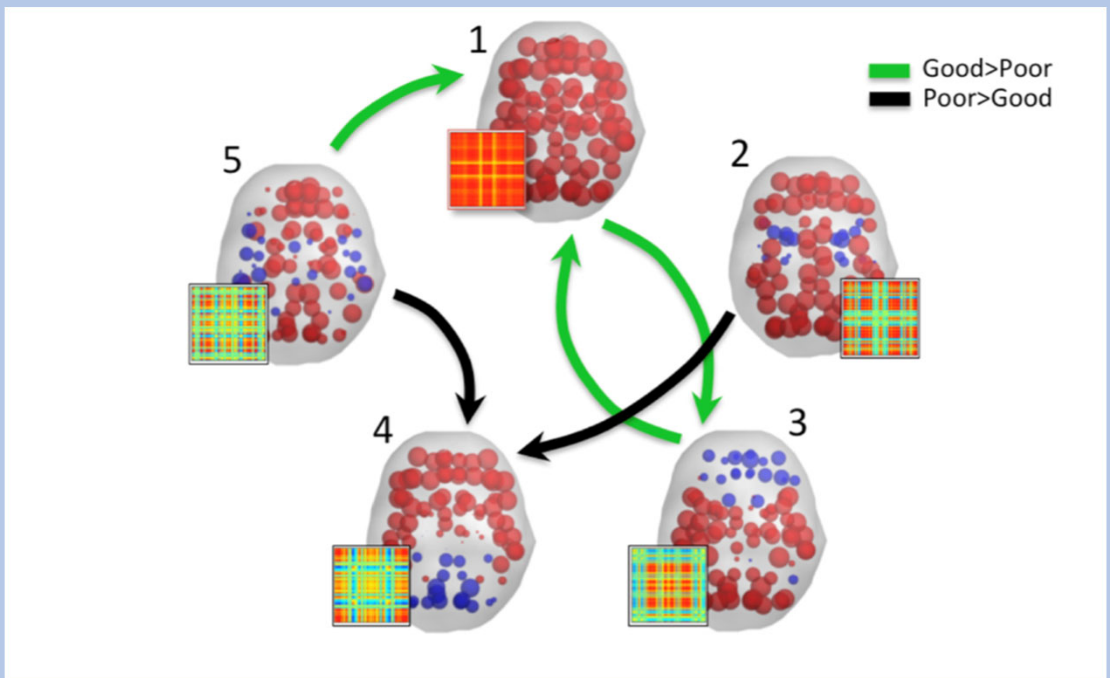
SCIENTIFIC REPORTS

OPEN

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

Received: 19 December 2016
Accepted: 30 May 2017
Published online: 11 July 2017

Joana Cabral[1,2], Diego Vidaurre[3], 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

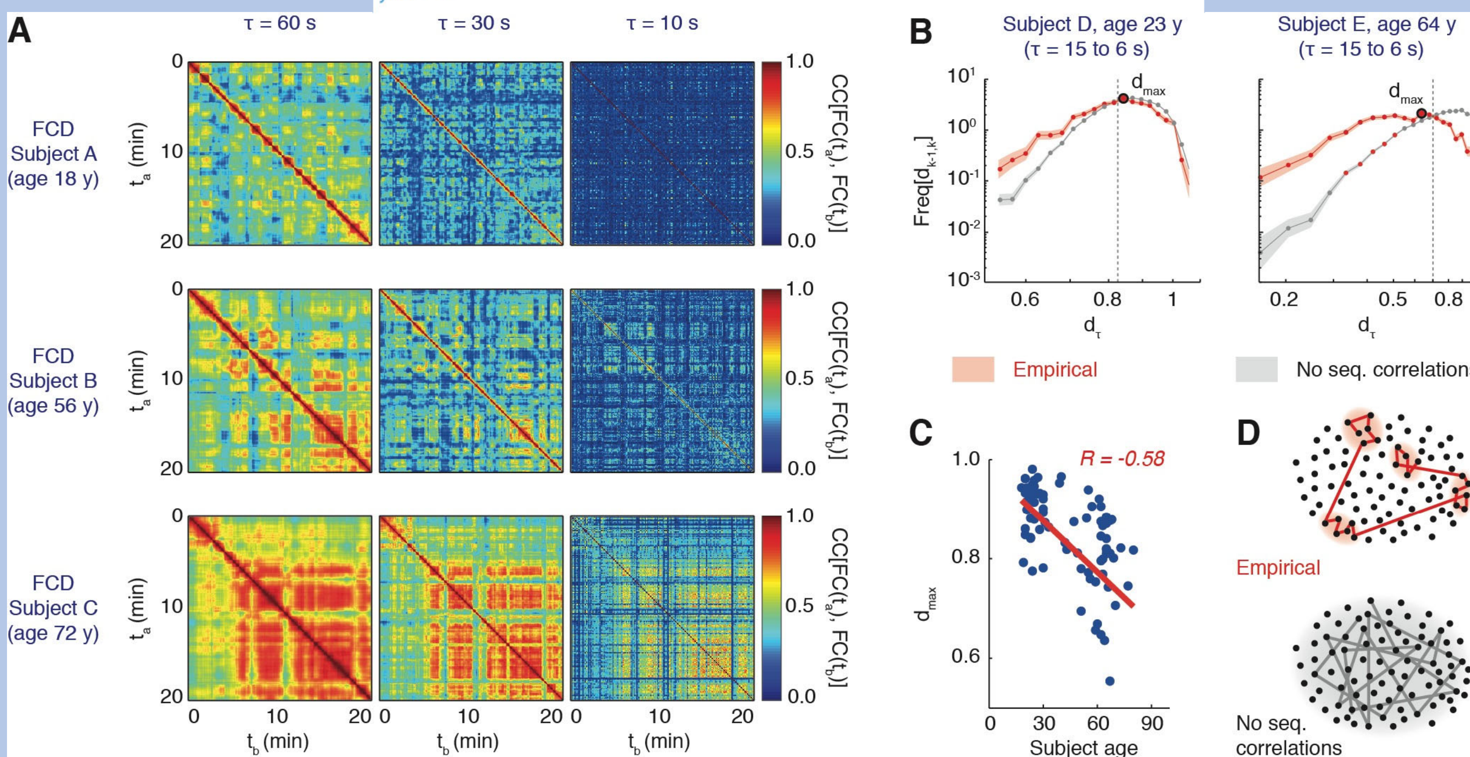
ELSEVIER

NeuroImage

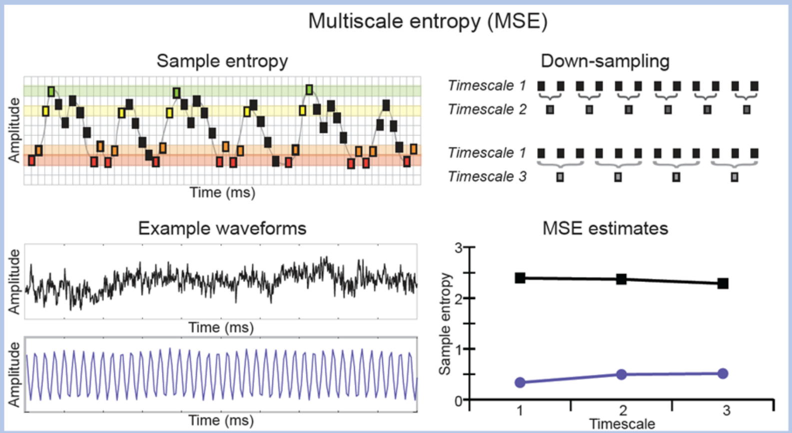
Volume 222, 15 November 2020, 117156

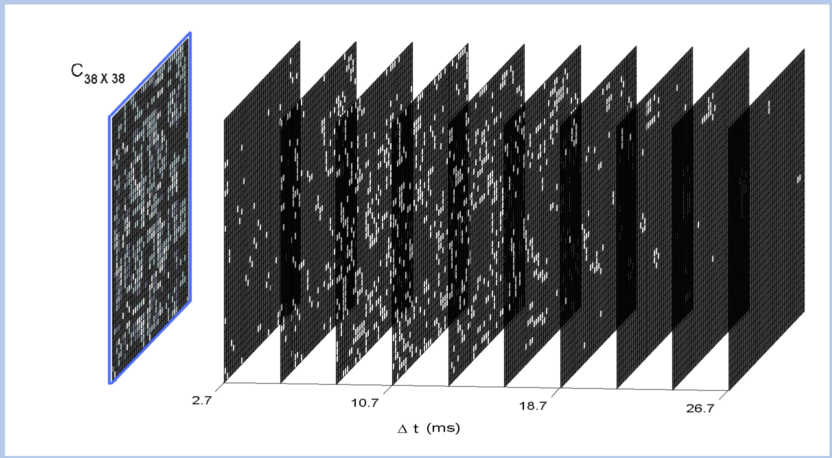
Dynamic Functional Connectivity between order and randomness and its evolution across the human adult lifespan

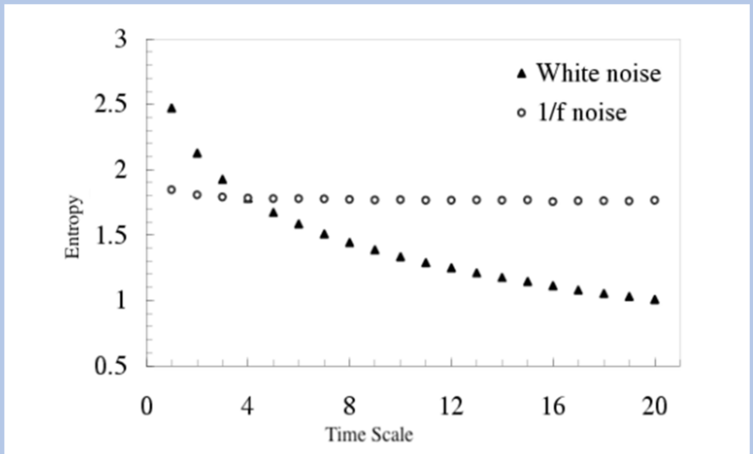
Demian Battaglia [a], Thomas Boudou [a, b], Enrique C.A. Hansen [a, c], Diego Lombardo [a], Sabrina Chettouf [d, e, f], Andreas Daffertshofer [f], Anthony R. McIntosh [g], Joelle Zimmermann [d, g], Petra Ritter [d, e, 1], Viktor Jirsa [a, 1]



How do we assess the efficacy of network dynamics?







Multiscale Entropy measure "information" as a function of timescale

Costa, Goldberger & Peng, Phys Rev Lett, 2002
http://www.physionet.org/physiotools/mse/tutorial/

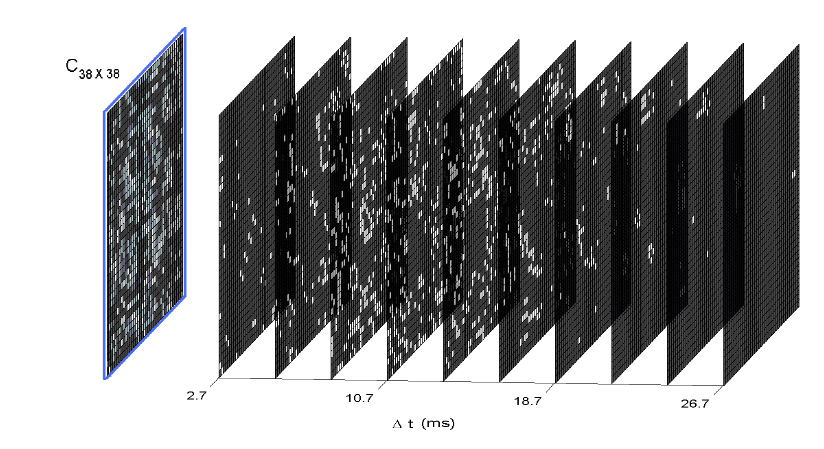
Oxford Research Encyclopedia of Psychology

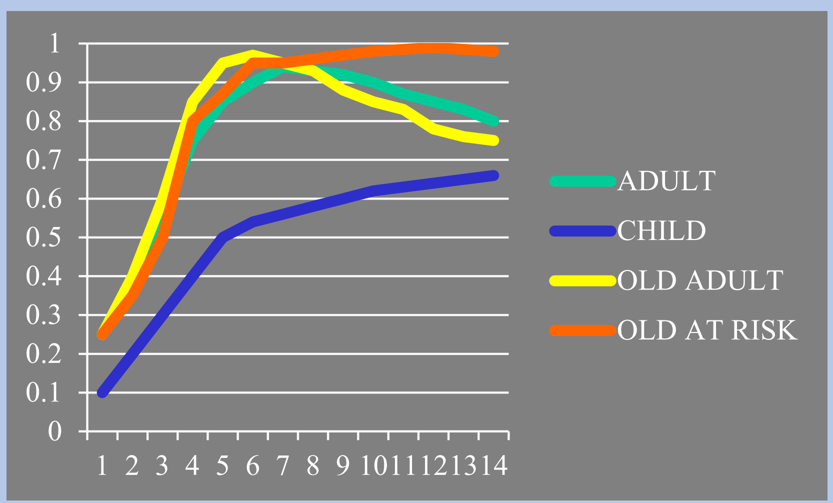
Neurocognitive Aging and Brain Signal Complexity

Anthony Randal McIntosh

Subject: Cognitive Psychology/Neuroscience, Neuropsychology

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





Entropy

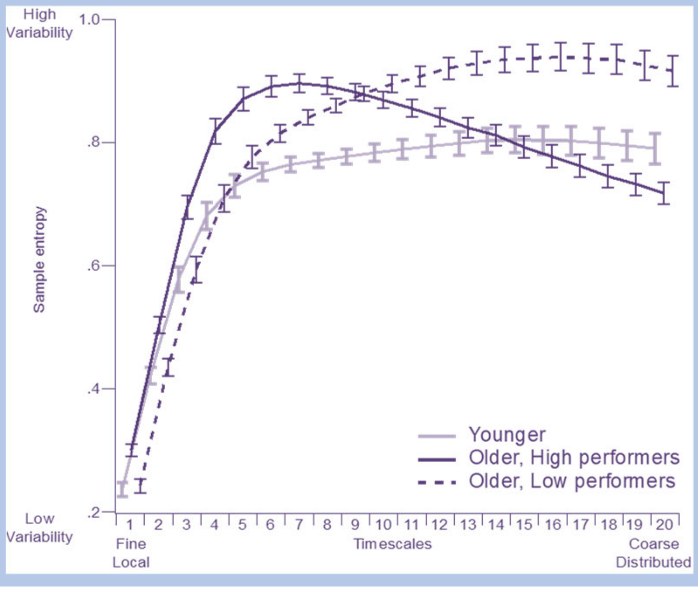
Timescale
Fine to coarse

Multiscale entropy: *Entropy as a function of time scale.*

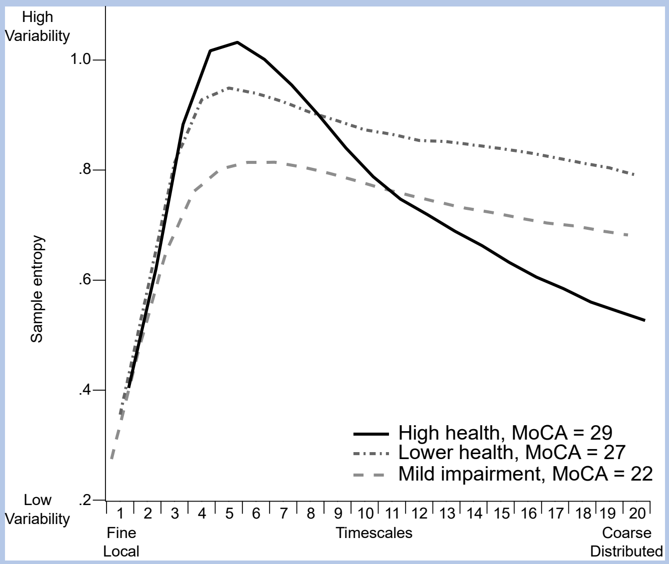
The curve morphology relates to cognitive status

A metric of network integrity?

Entropy and Brain Health
A metric for risk?



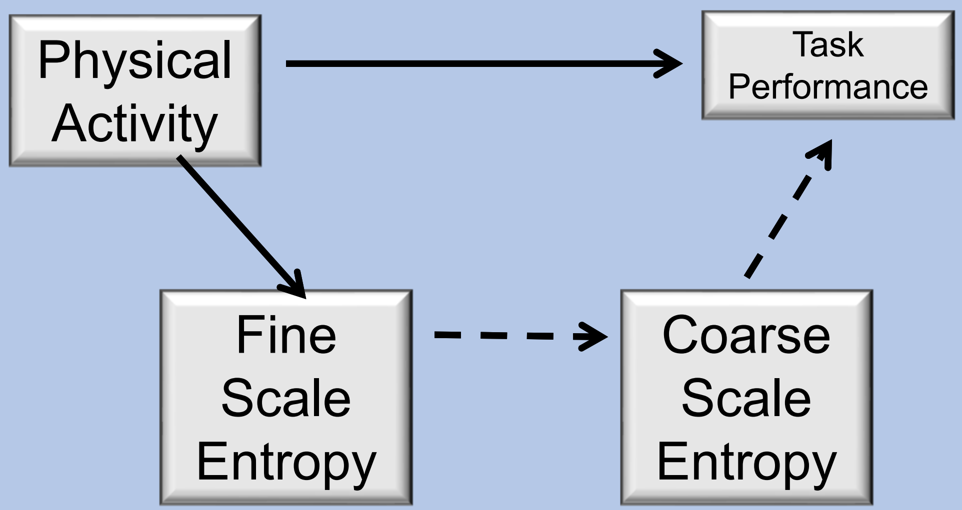
Age-related increase in fine scales with aging preserves performance

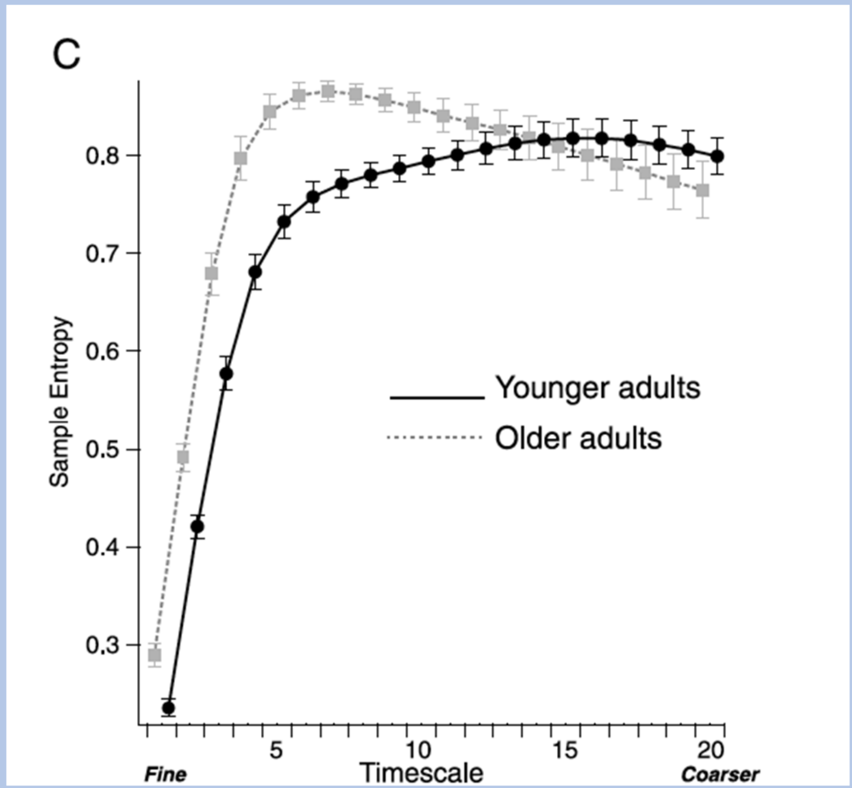


Higher entropy fine scales related to better cognitive status in aging

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

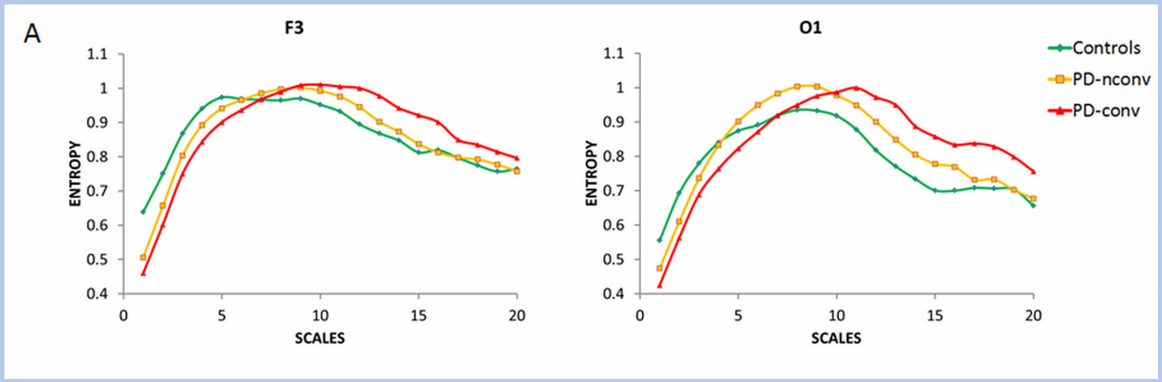
Jennifer J. Heisz[1], Michelle Gould[2], and Anthony R. McIntosh[2]



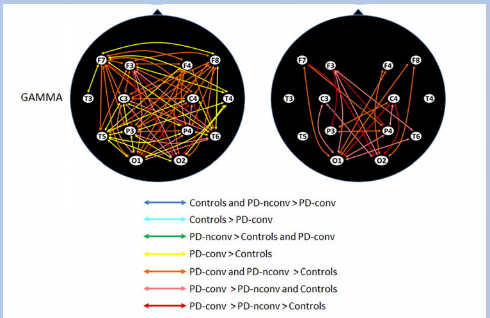


J Cogn Neurosci, 2015

Parkinson's Dementia

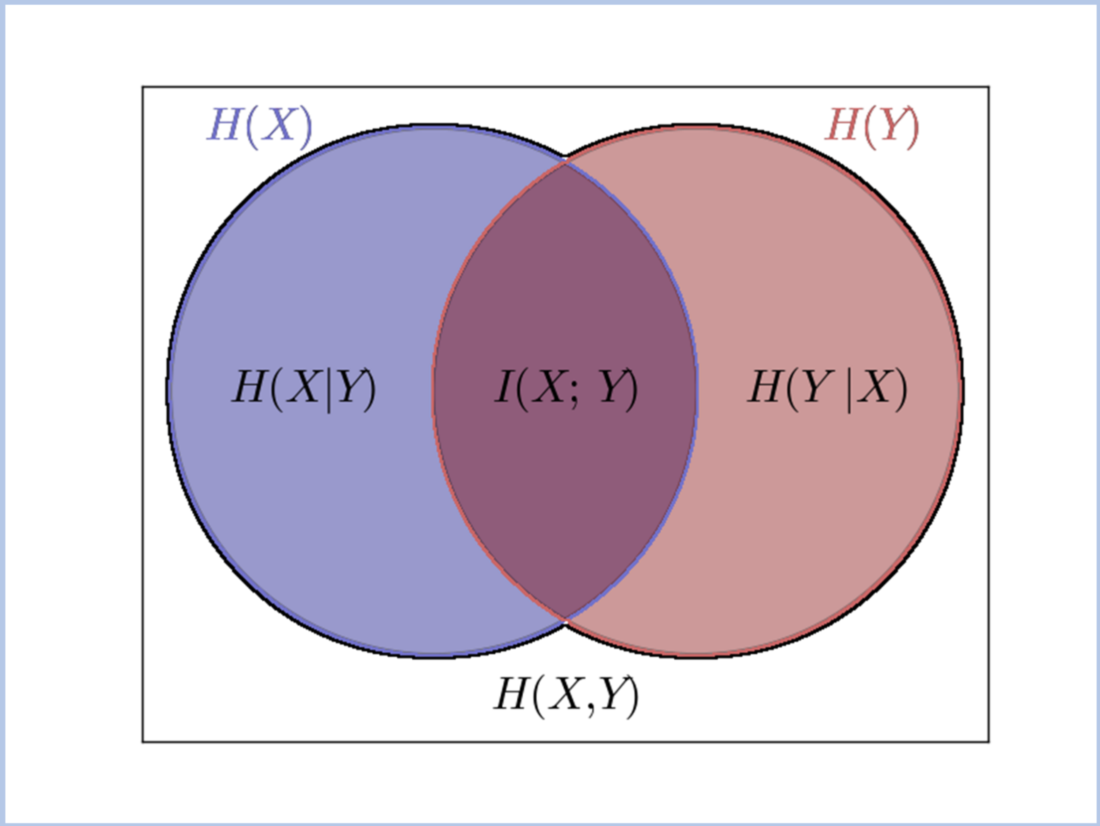


Parkinson's patients who will show dementia have lower fine scale entropy and high coarse scale entropy, along with hypersychrony in gamma <u>1 year prior to converting</u>



Bertrand, McIntosh, et al, 2016, Brain Connectivity

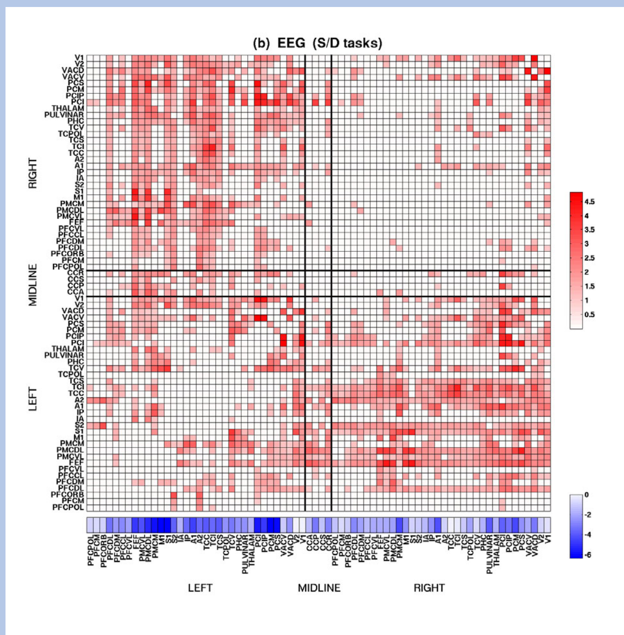
Can we parse entropy into local and distributed sources?



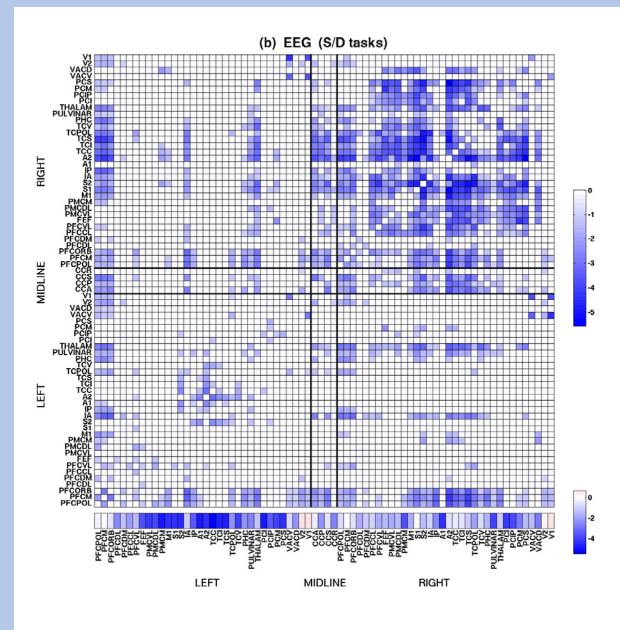
Vakorin, Lippe & McIntosh, J Neurosci, 2011

Local vs Distributed Entropy EEG Data

Distributed entropy decreases across hemispheres



Distributed entropy increases within hemispheres



Local entropy increases with age

McIntosh,et al; Cereb Cortex, 2013

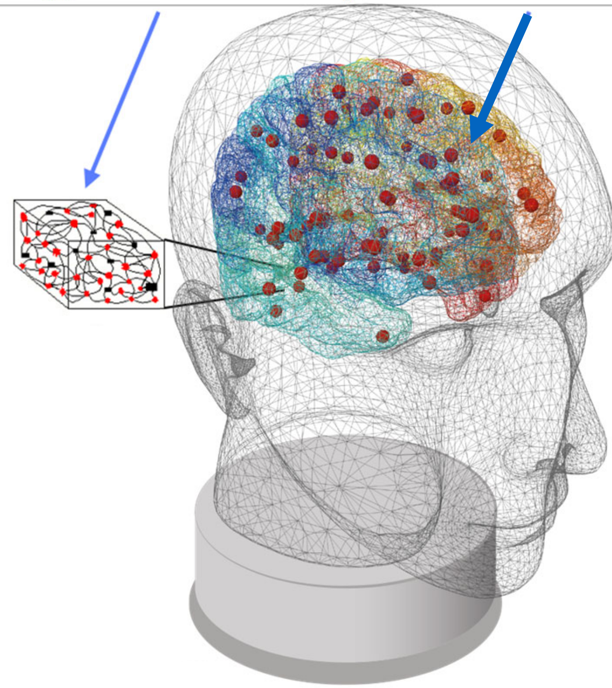
Modelling Functional Connectivity Dynamics in the Virtual Brain

Local dynamics

Global dynamics

$$\psi(x,t) = N(\psi(x,t)) + \int_{local} g(x-x')S(\psi(x',t))dx' + \int_{global} G(x,x')S\left(\psi\left(x',t-\frac{|x-x'|}{v}\right)\right)dx' + \text{noise}$$

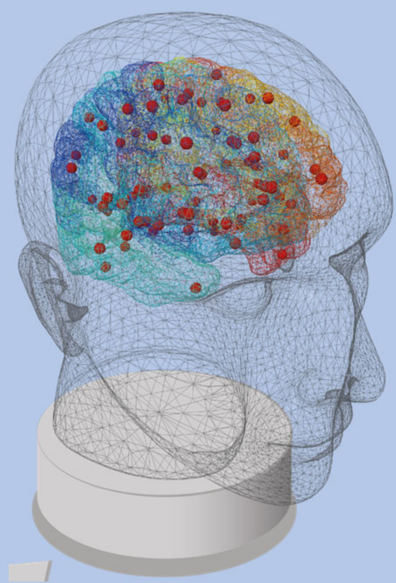
Field potential

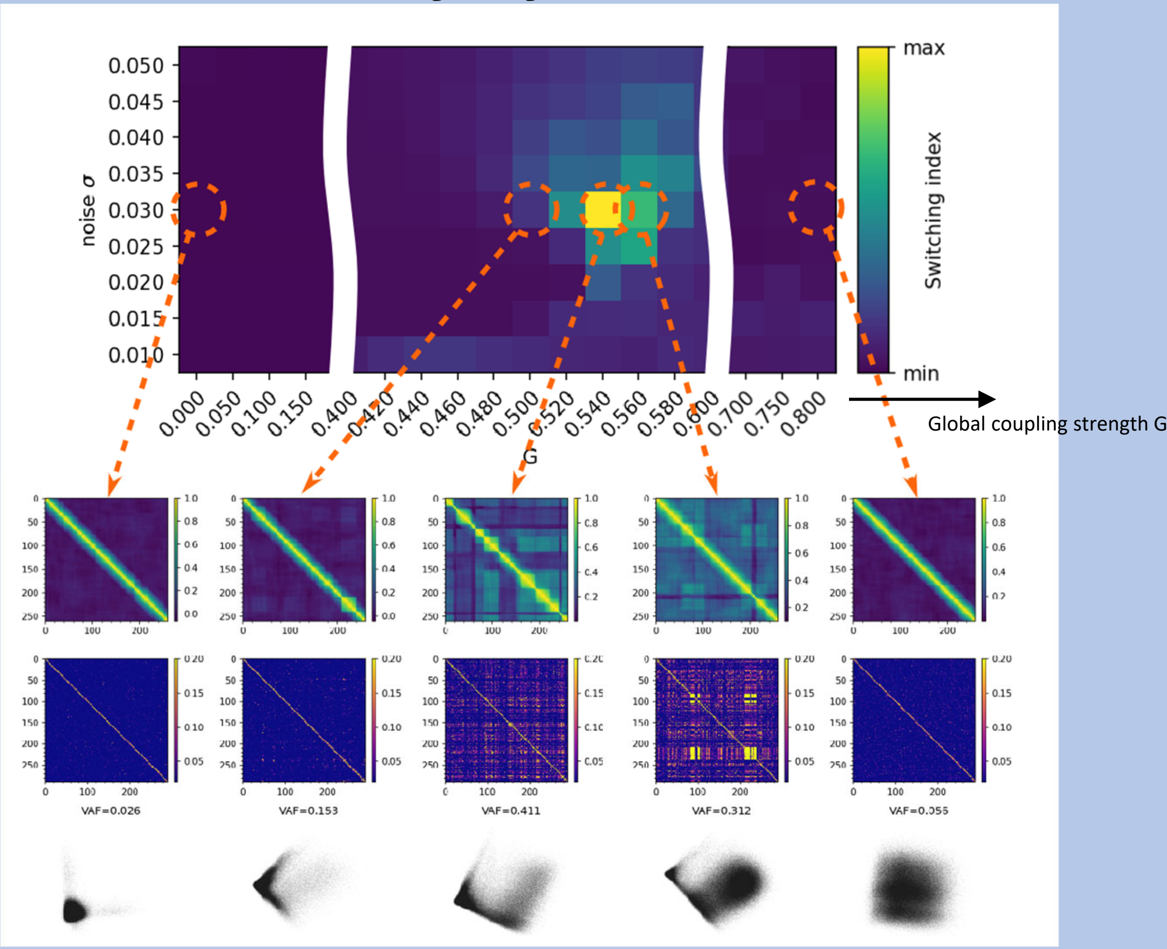


THEVIRTUALBRAIN.

Deco, Jirsa, McIntosh Nature Rev Neurosci 2011

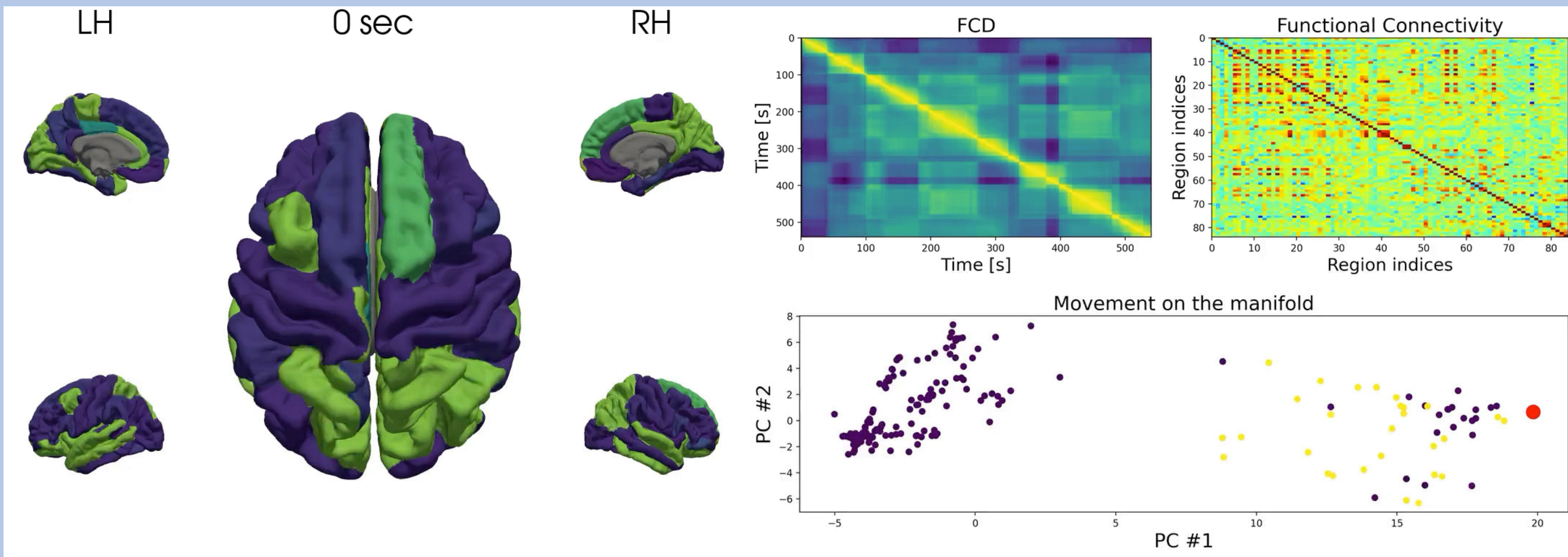
Modelling Functional Connectivity Dynamics in the Virtual Brain





Fousek et al (in preparation)

Modelling Functional Connectivity Dynamics in the Virtual Brain

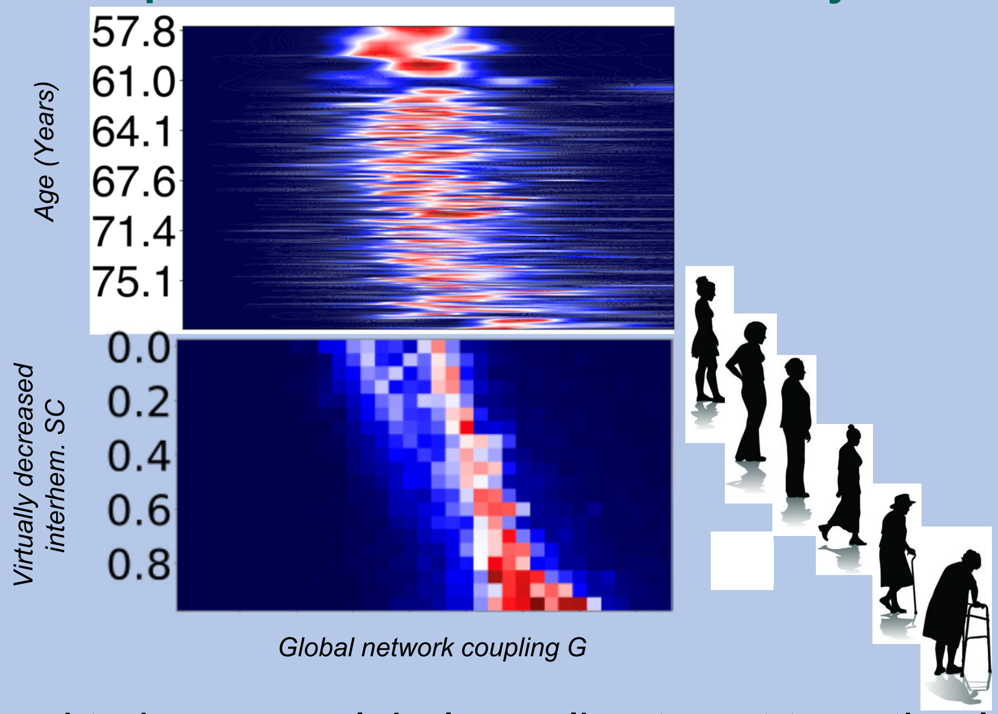


- FC invariant epochs correspond to local sub-manifolds
- combination of FCs in the epochs describe the overall evolution of the system better

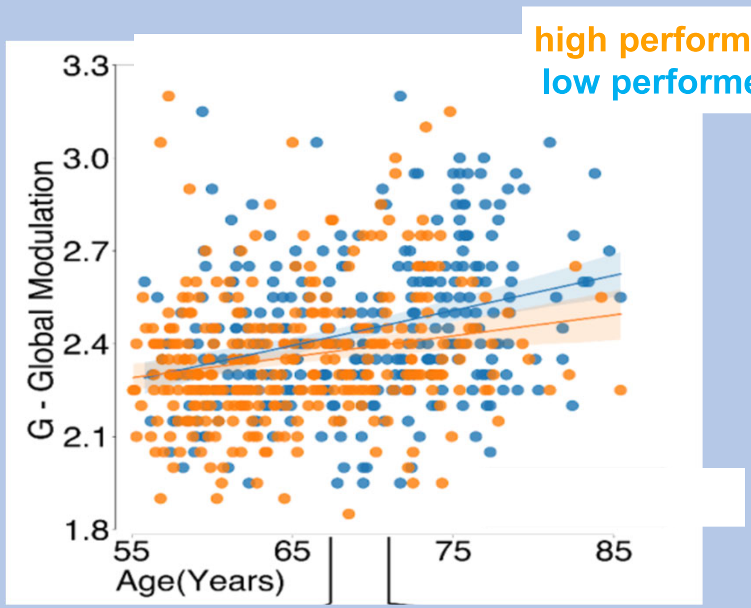
Fousek et al (in preparation)

Virtual aging - evidence for dedifferentiation?

Increased global coupling by manipulation of structural connectivity



Effects on cognition



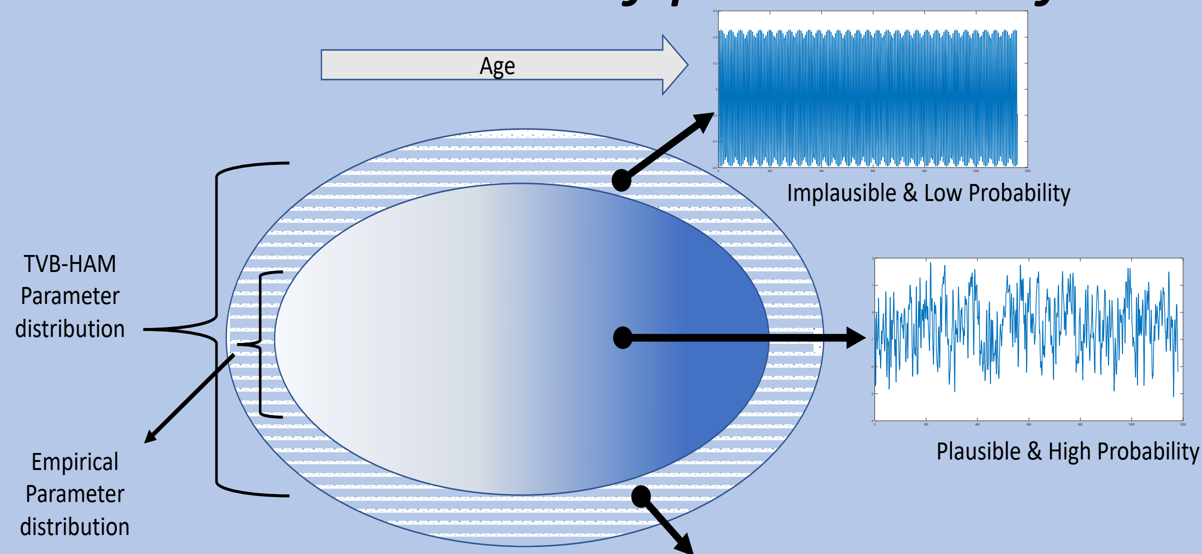
p=0.046

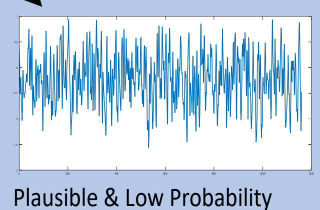
Need to increase global coupling to get to optimal working point in (simulated) aging

Lavanga et al bioRxiv 2022

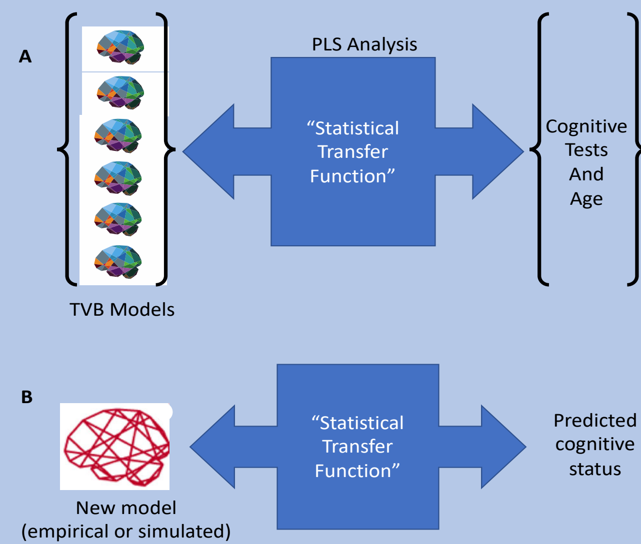
TVB Healthy Aging Model (TVB-HAM)

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

RM0

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., multiscale entropy)
- Need to consider psychosocial factors seriously

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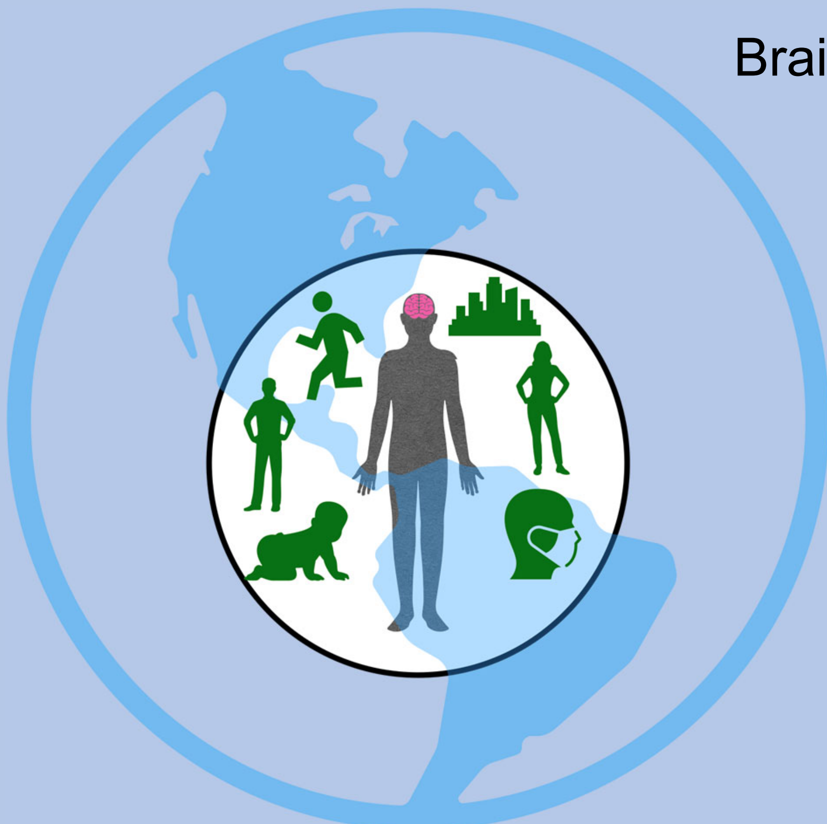
Slide 30

RM0 learn more when a model doesn’t work

Randy McIntosh, 2023-02-27T18:58:23.073

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.

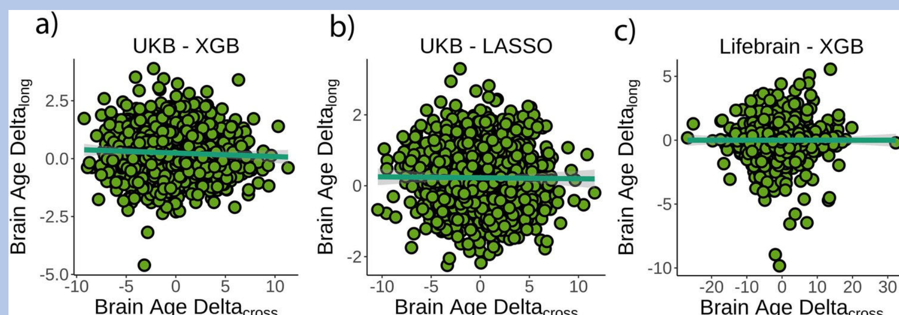
Computational modeling can help.

eLife

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 »

CAUTION



"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."

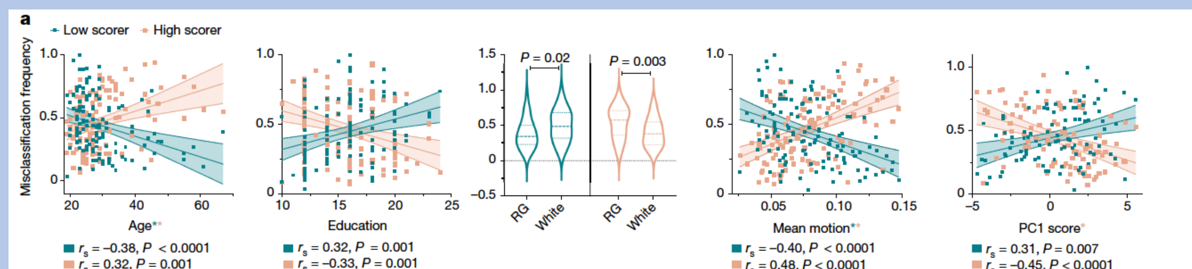
Article | Open Access | Published: 24 August 2022

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

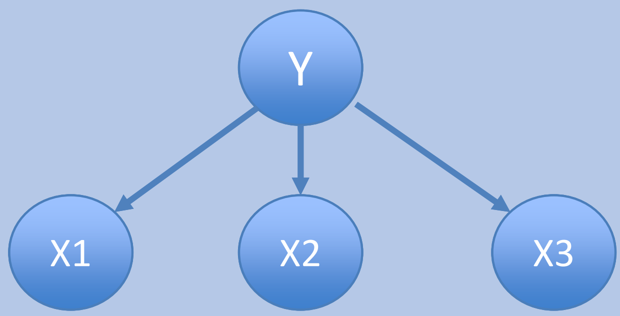
Nature (2022) | Cite this article

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.

Generative vs Predictive Models

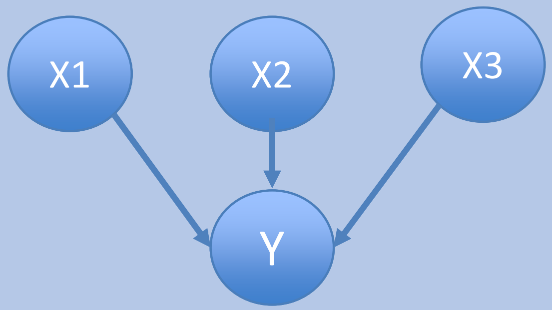


Infer a model (Y) that generates the data (X)

Example: Infer the neural network properties that generate observed MRI data (X)

Advantage: enables causal and mechanistic inferences

Disadvantage: need to assess model fit



Use the data (X) to discover a model based on the ability to predict the indices of Y

Example: Use MRI data to infer salient network features for prediction

Advantage: identify most important indicator for prediction

Disadvantage: causal and mechanistic inference difficult