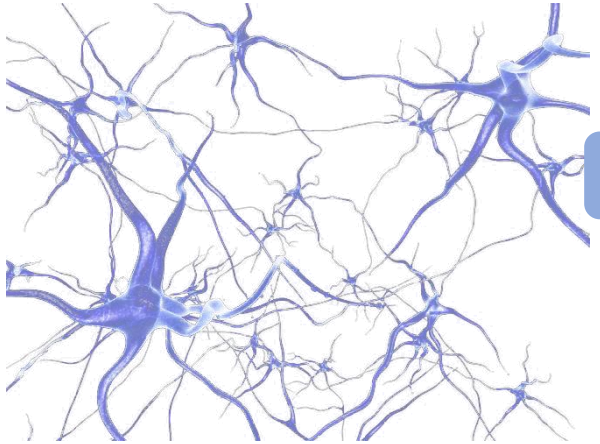
Healthy Aging is Marked by Entropy Reduction in Cortical Spotaneous Activity

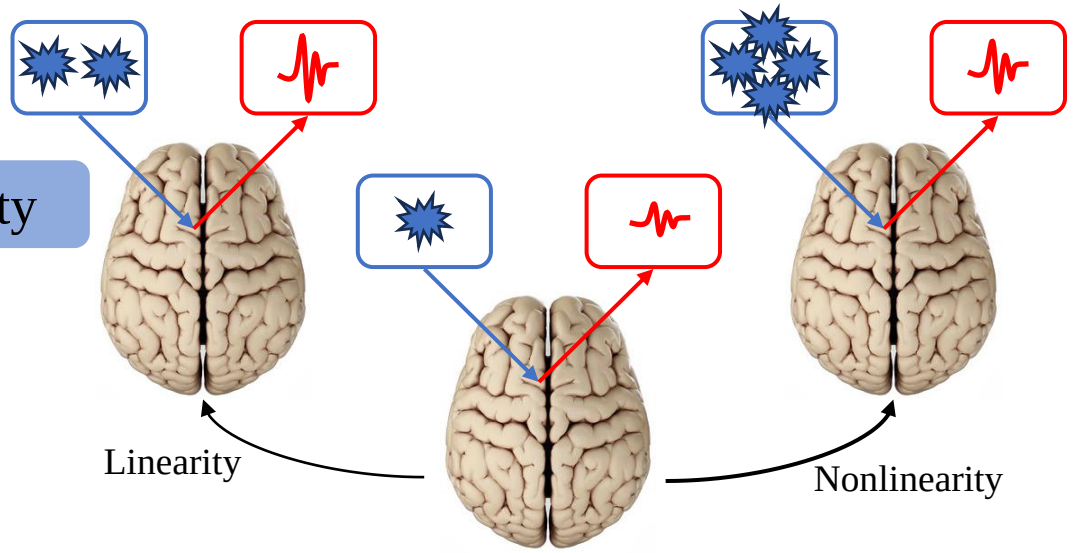
Da Chang 2024/04/19

• Brain – Complex System

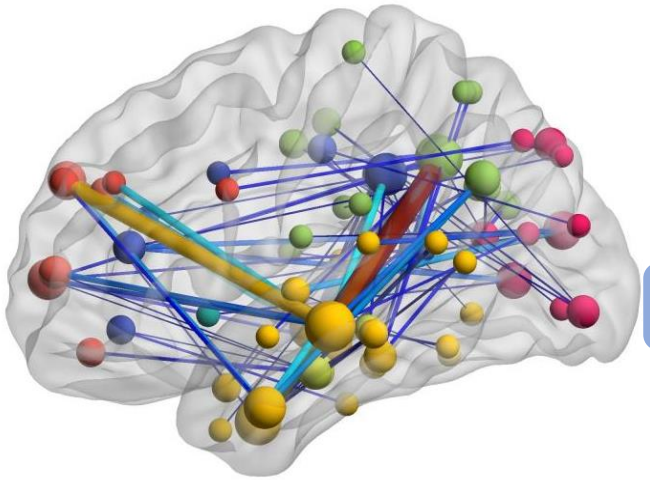


Multiplicity

Nonlinearity

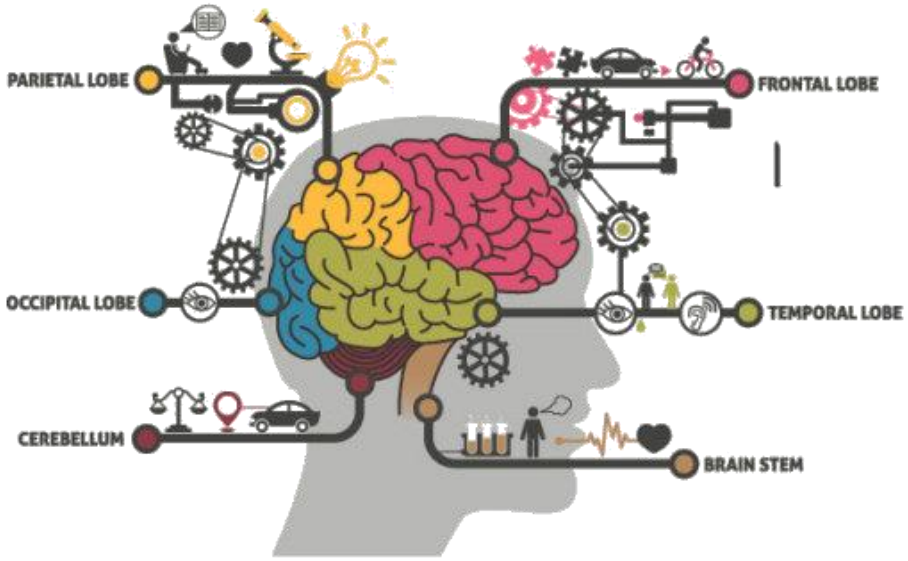


Properties



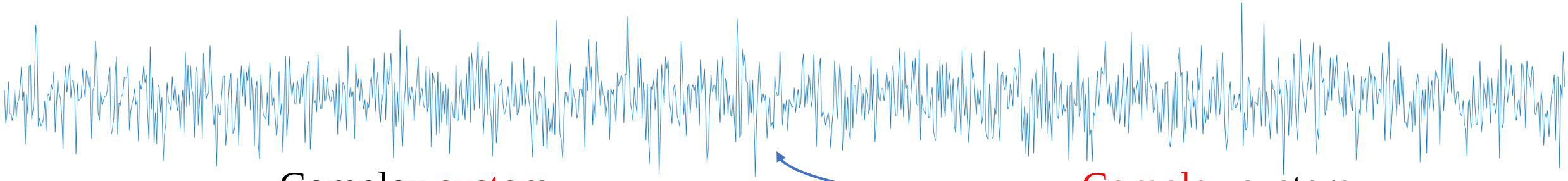
Self-organization

Emergence

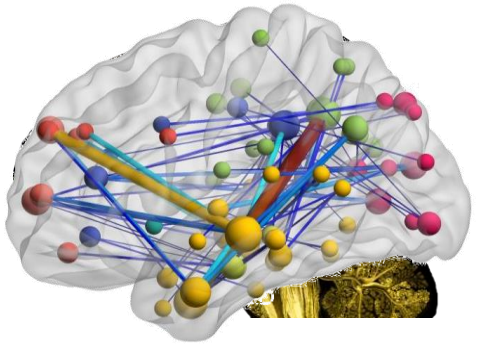


• Brain Entropy (BEN)

resting-state functional magnetic resonance imaging, rs-fMRI

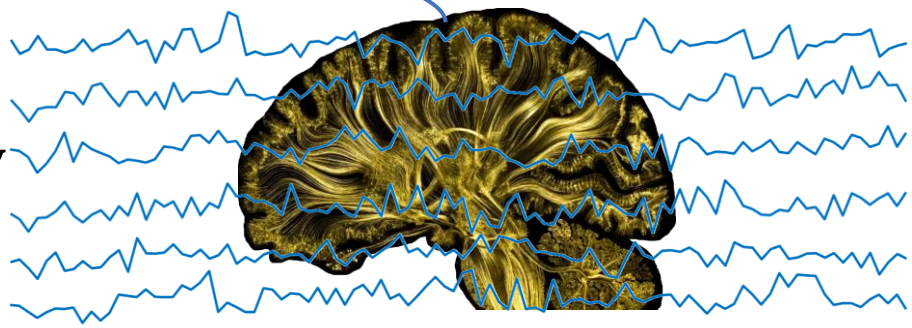


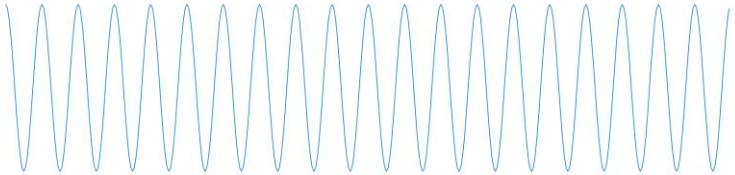
Complex system



Entropy

Complex system





Low entropy

High entropy

• Sample Entropy

m=3

$$B^m(r) = \frac{1}{(N-m)(N-m-1)} \sum_{i=1}^{N-m} B_i^m(r)$$

m+1

$$A^m(r) = \frac{1}{(N-m)(N-m-1)} \sum_{i=1}^{N-m} B_i^{m+1}(r)$$

Cardiovascular data

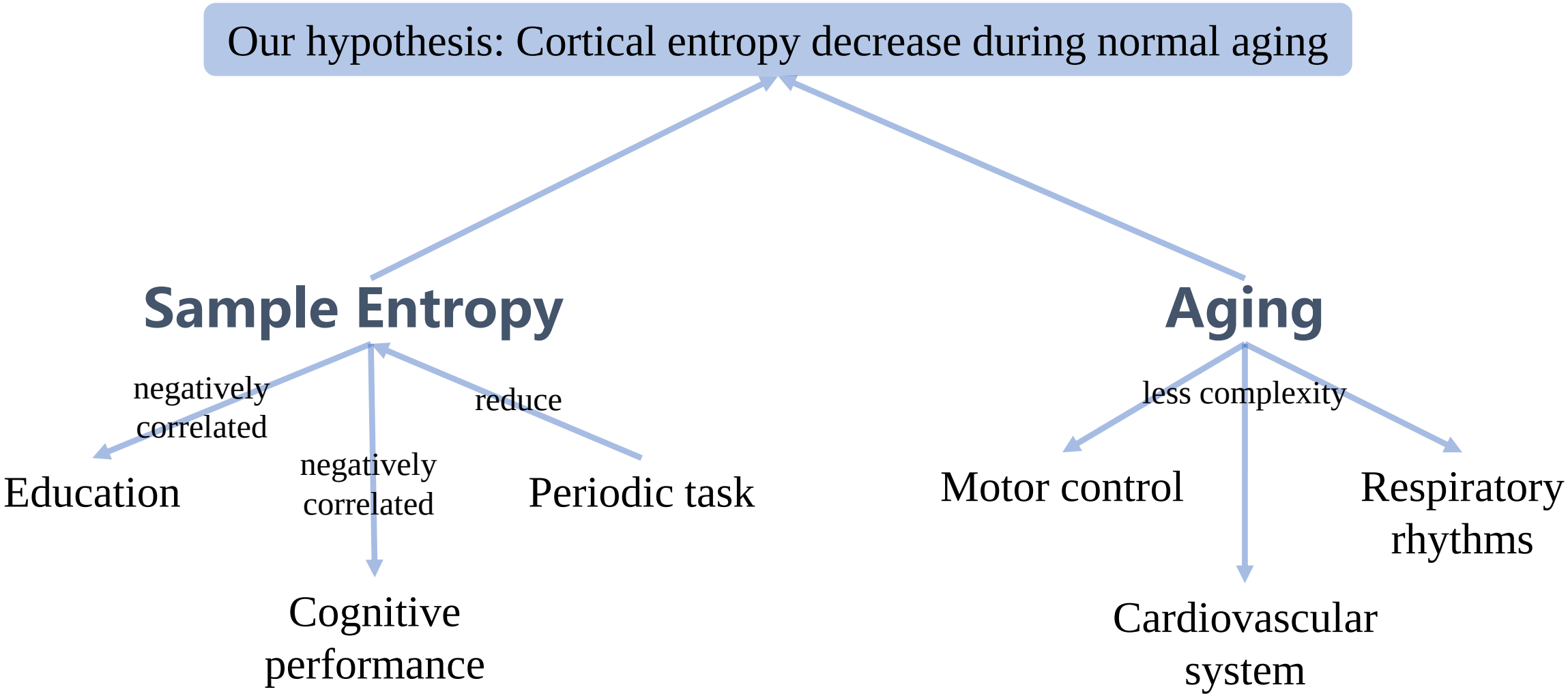
Reliable Measurement

Neuroimaging data

$$\mathrm{SampEn}(m, r, N, x) = -\ln\left[\frac{A^m(r)}{B^m(r)}\right]$$

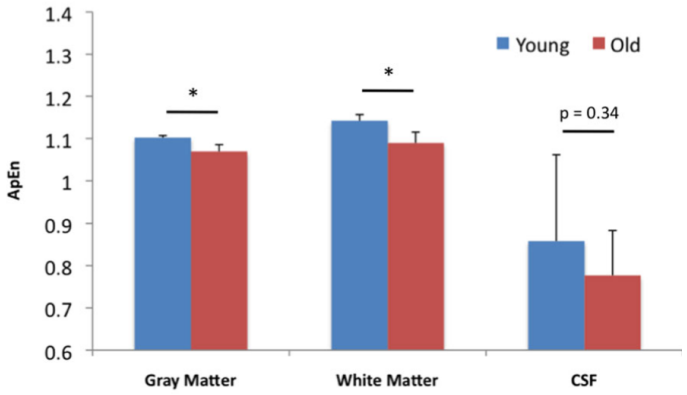
https://cfn.upenn.edu/zewang/BENtbx.php

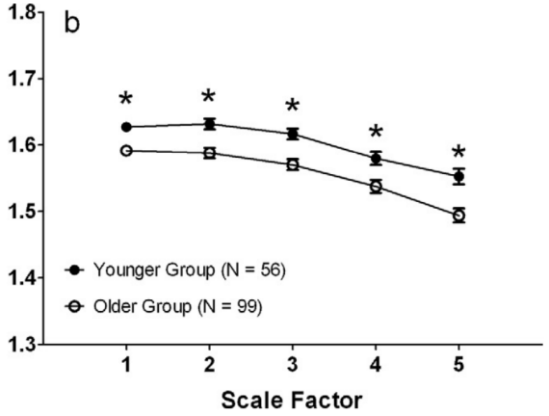
• Aging Pattern

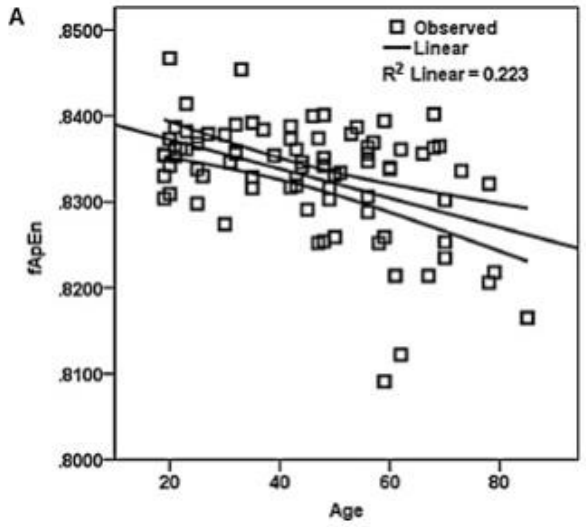


Previous neuroimaging studies

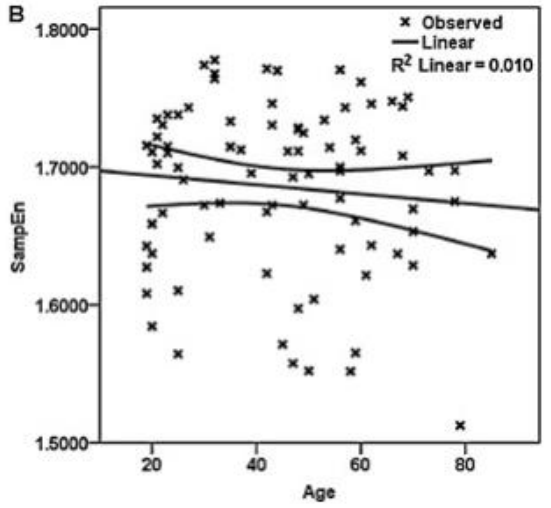
Decrease with age



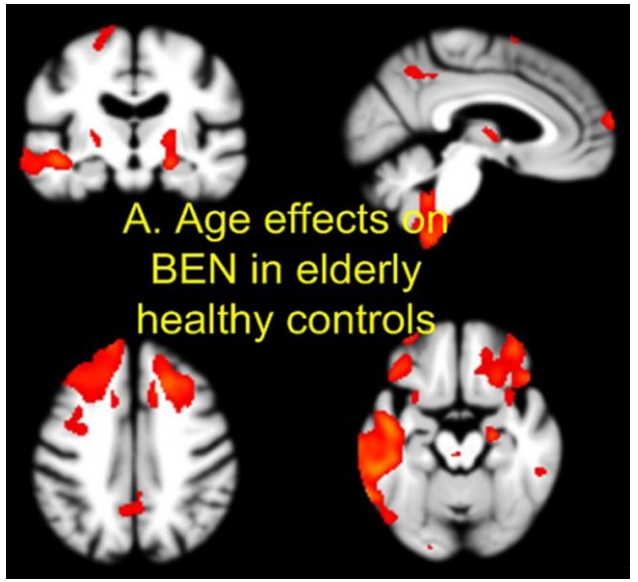




Non-change



Increase with age



All cross-sectional design

Sokunbi et al., 2015; liu et al., 2013; Yang et al., 2013; Wang, 2020; Wang, 2021; Wang et al., 2014

• Data

Douglas CENTRE DE RECHERCHE RESEARCH CENTRE

The Douglas Research Centre

Affiliated with McGill University and the Montreal West Island IUHSSC

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Prevent Alzheimer Program

The PREVENT-Alzheimer Program

The PREVENT-Alzheimer program wants to recruit **500 participants**. Their contributions will be the key to finding strategies that can slow or reverse brain changes that may occur in older people who do not suffer from dementia. Recruitment is currently closed.

Alzheimer's Disease Research links

- STOP-AD Centre
- Prevent Alzheimer program
- STOP-AD Team

Baseline + 4 years follow up

apart 1 year

24 Canadian

120 visits（24 x 5）

Baseline age: 58~77

https://registeredpreventad.loris.ca

• Data

Frequency of APOE-ε4

12.5% (15% for typical Caucasian)

Cognitive evaluation

Repeatable Battery for Assessment of Neuropsychological Status
(Immediate memory, Delayed memory, Language, Visuospatial capacities, Attention)

MRI data

Structural MRI
rs-fMRI

preprocessed by
Connectome Computation System

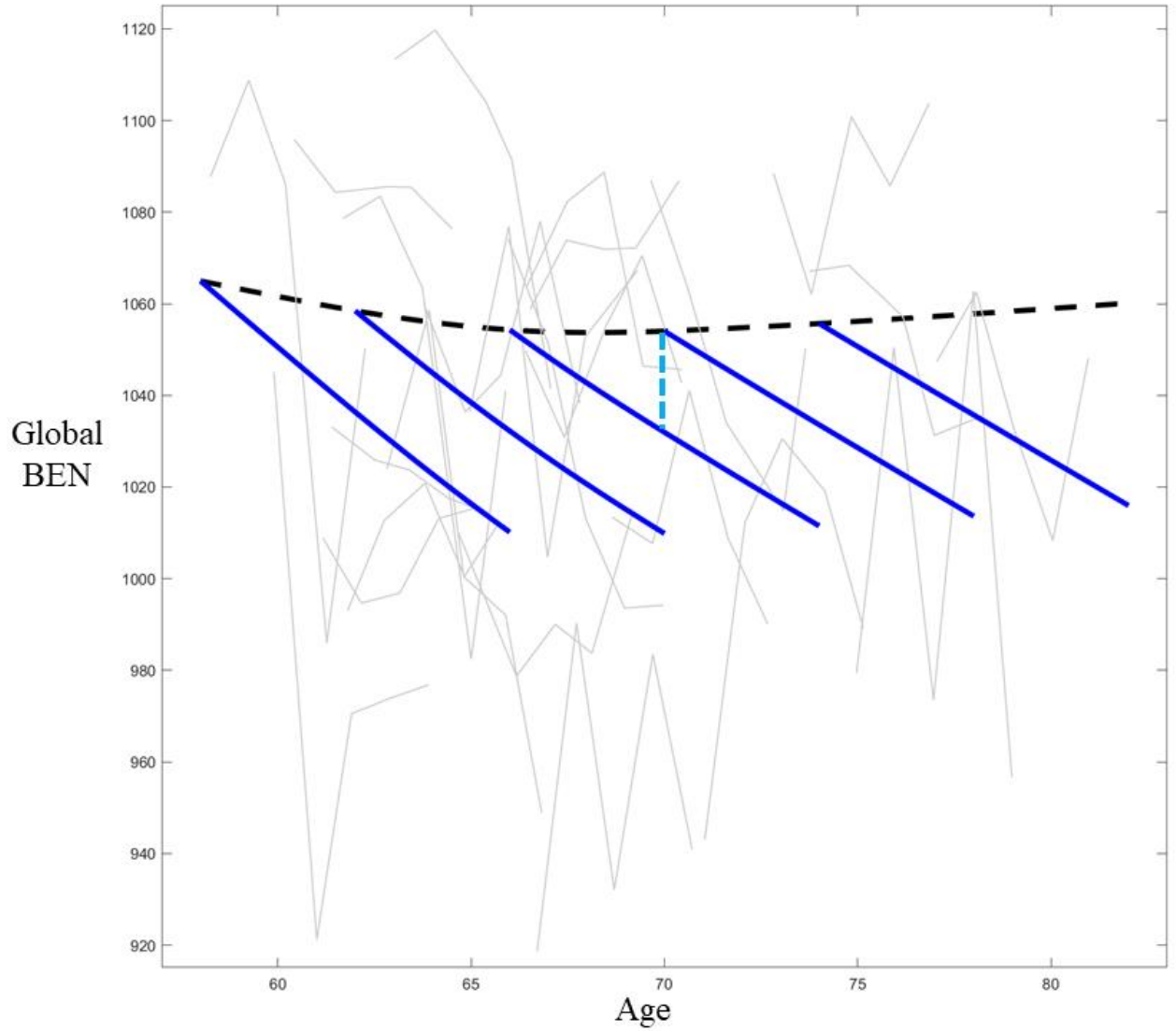
Entropy

https://github.com/zuoxinian/CCS

https://cfn.upenn.edu/zewang/BENtbx.php

● Results 1. Global entropy reduction

BEN ~ Intercept + Age + Cohort + Sex + Education + Gene + Cene x Age + Random + Residual



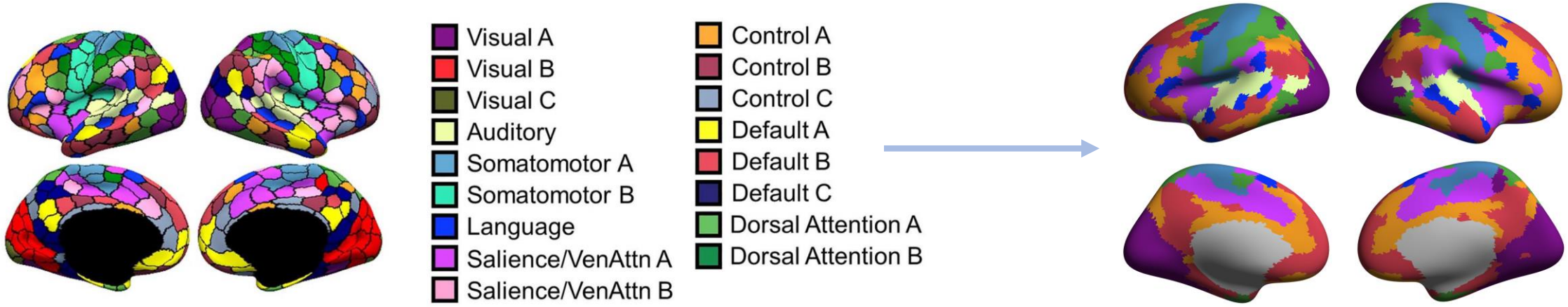
Age (F)	Age (p)	Cohort (t)	Cohort (p)	R-sq. (adj)
8.521	0.0073 **	-2.251	0.0263 *	0.169

* < 0.05, ** < 0.01, *** < 0.001

Generative Additive Mixed Model (GAMM)

https://CRAN.R-project.org/package=gamm4

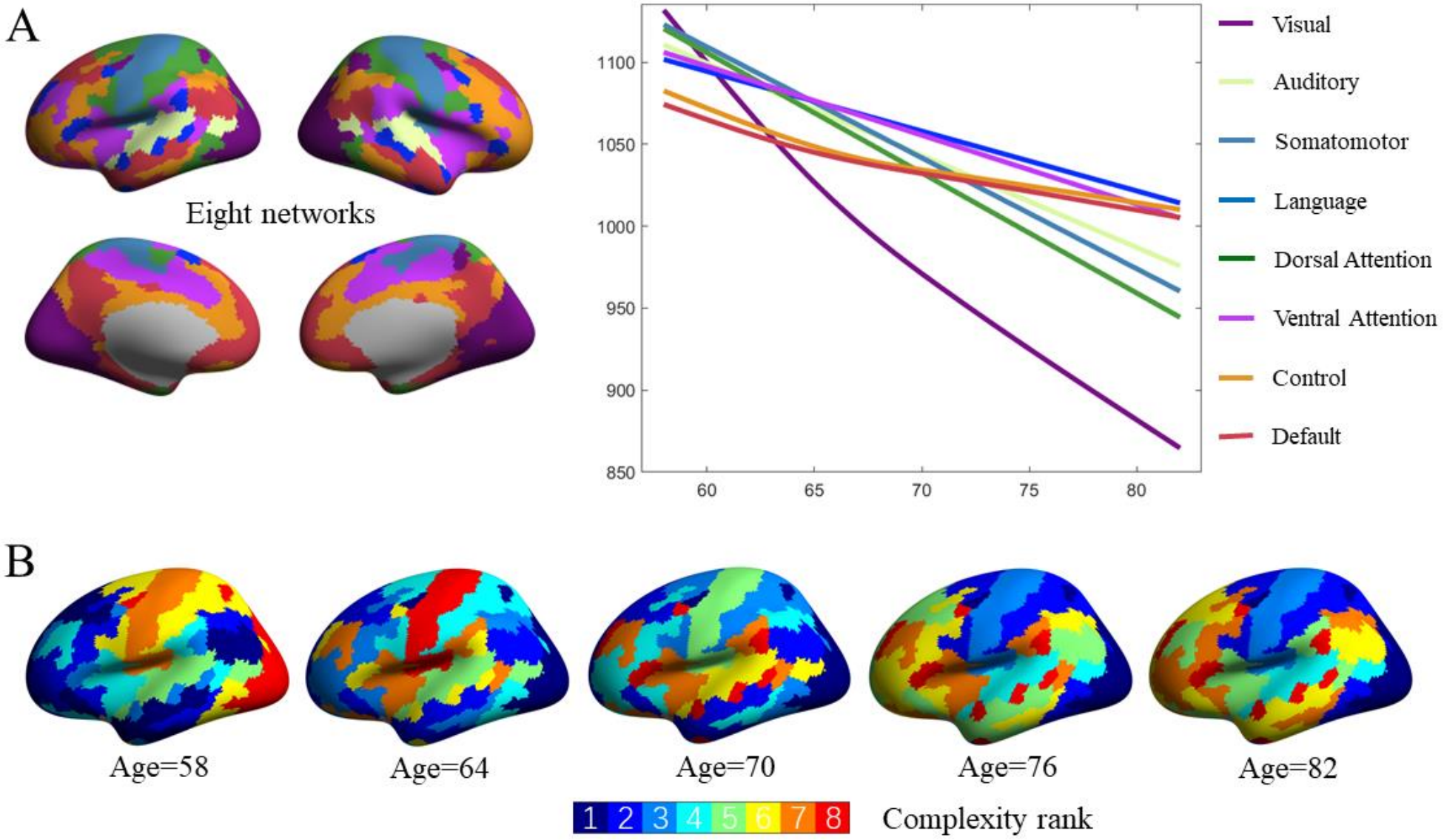
• Results 2. Network entropy reduction



	Age (F)	Age (p)	Cohort (t)	Cohort (p)	R-sq. (adj)
Global	8.521	0.0073 **	-2.251	0.0263 *	0.169
Visual	7.490	0.0105 *	-1.964	0.0541	0.101
Auditory	6.404	0.0128 *	-1.922	0.0571	0.116
Somatomotor	9.104	0.0032 **	-1.917	0.0578	0.149
Language	4.934	0.0283 *	-2.064	0.0413 *	0.167
Dorsal Attention	13.02	0.0005 ***	-2.672	0.0087 **	0.158
Ventral Attention	6.243	0.0139 *	-2.148	0.0338 *	0.194
Control	3.189	0.0973	-1.580	0.1170	0.218
Default	2.484	0.180	-1.664	0.0988	0.193

* < 0.05, ** < 0.01, *** < 0.001

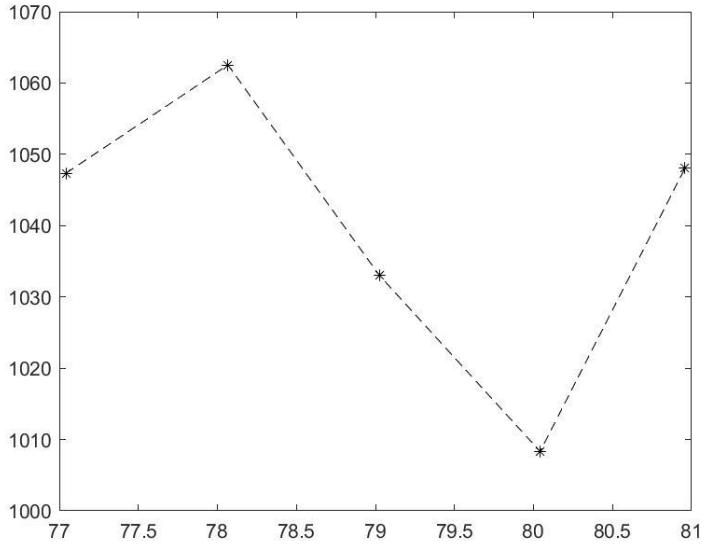
• Results 2. Network entropy reduction



● Results 3. Cognitive evaluation

RBANS ~ Intercept + Age + Cohort + Sex + Education + Gene + Cene x Age + Random + Residual

	Age (F)	Age (p)	Education (t)	Education (p)	R-sq. (adj)
Total	1.040	0.482	2.134	0.035 *	0.283
Visuospatial/Constructional	1.446	0.358	0.792	0.430	0.057
Immediate Memory	0.447	0.474	2.608	0.010 *	0.198
Delayed Memory	0.927	0.484	1.748	0.083	0.131
Language	2.279	0.174	2.499	0.014 *	0.088
Attention	0.720	0.398	1.124	0.263	0.156



One subject was excluded

• Results 3. Cognitive changes with entropy reduction

Total ~ Intercept + BEN + Baseline age + Random + Residual

	BEN (F)	BEN (p)	Age_bl (t)	Age_bl (p)	R-sq. (adj)
Visual	4.319	0.0400 *	-1.708	0.0904	0.100
Aud	2.178	0.1860	-1.635	0.1050	0.078
SomMot	5.640	0.0193 *	-1.770	0.0794	0.110
Language	3.844	0.0628	-1.599	0.1130	0.097
DorsAtt	4.402	0.0381 *	-1.708	0.0904	0.103
SalVenAtt	1.462	0.2790	-1.602	0.1120	0.088
Cont	0.551	0.6670	-1.610	0.1100	0.084
Default	0.632	0.4280	-1.586	0.1160	0.086

Delay memory ~ Intercept + BEN + Baseline age + Random + Residual

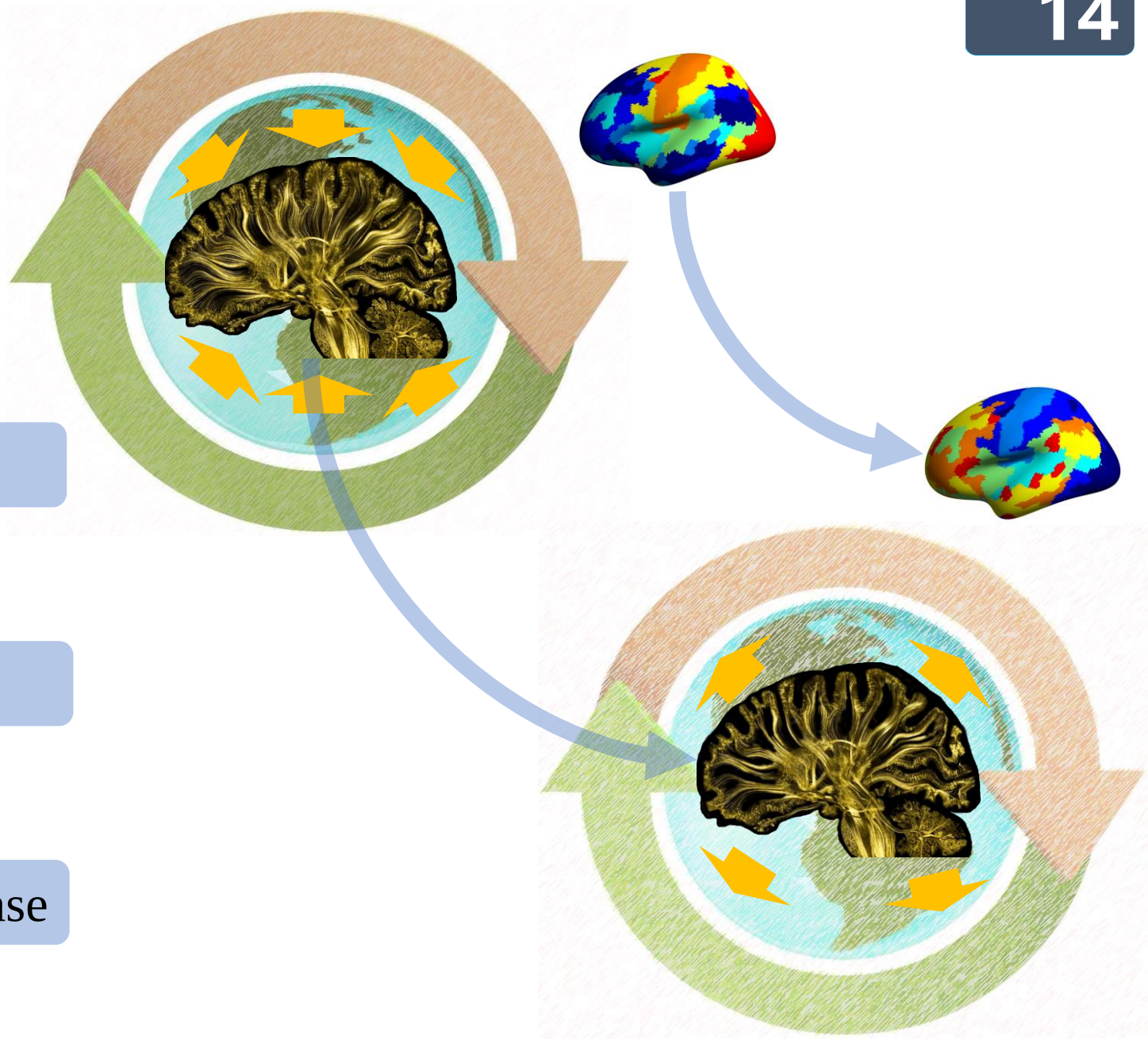
	BEN (F)	BEN (p)	Age_bl (t)	Age_bl (p)	R-sq. (adj)
Visual	2.732	0.1500	-2.086	0.0393 *	0.100
Aud	3.549	0.0622	-2.037	0.0441 *	0.110
SomMot	8.963	0.0034 **	-2.492	0.0142 *	0.159
Language	2.388	0.1490	-1.961	0.0523	0.117
DorsAtt	4.811	0.0303 *	-2.231	0.0277 *	0.123
SalVenAtt	4.825	0.0301 *	-1.971	0.0512	0.129
Cont	3.137	0.0793	-1.967	0.0517	0.112
Default	4.096	0.0454 *	-1.864	0.0649	0.121

• Summary

BEN decrease

Cohort effect

Hierarchical shift & Diversity increase



Thanks!