Growing older: exploring directional connectivity through fMRI

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THE AGING PROCESS

EACH YEAR

- 3-5% of individuals will develop *Mild Cognitive Impairment* (MCI)
- 10-15% of individuals with MCI are likely to develop *Alzheimer's Disease*

UNDERSTAND AGE-RELATED CHANGES, WHY?

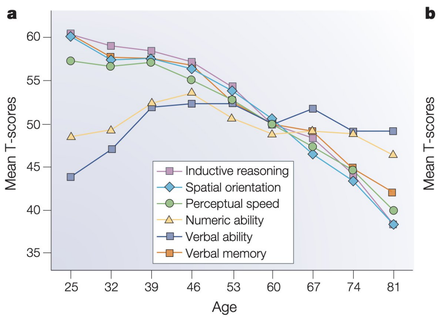
Age cannot be experimentally manipulated. Each conclusion that regards aging must be correlational.	It is difficult to separate healthy aging from pathological processes that compromise cognition.	Variability across subjects increase with age. High difference between high/low performing adults.	Experimental setups (e.g. recruitment methods) can influence the sample	Most of the studies are based on cross-sectional comparisons

FACTORS THAT CAN AFFECT AGING

BIOLOGY	PHYSIOLOGY	ENVIRONMENT	ANTROPOLOGY
genetics, metabolism, endocrine and cardiovascular systems, etc.	mood, motivation, habits, resilience, personality, etc.	nutrition, exercise, social status, sleep, relationships, etc.	traditions, education, culture,etc.

BACKGROUND

COGNITIVE DECLINES



LIFE-LONG
processing speed, working memory

RELATIVELY STABLE
automatic processes, emotional/implicit memory

LATE-LIFE
preserved knowledge, experience for strategies

Figure 1. a. Cross-sectional data. **b.** Seven-year longitudinal data from the same study.[1]

STRUCTURAL CHANGES

White matter abnormalities seem to be associated with processing speed, executive function, immediate and delayed memory but *not* with intelligence.

Differences in sex have been reported, but they are not indicative of clinical and cognitive outcomes.

Structures of the Prefrontal Cortex decline 5% in volume per decade after 20y.

The hippocampus and parahippocampal gyrus volume decline 2-3% per decade, and increase of 1% after 70y.

Structural changes are *not homogeneous* across the brain, both in velocity and volume.

Volume decrease is observed in individuals without dementia or hypertension. For MCI and AD the loss in volume is higher.

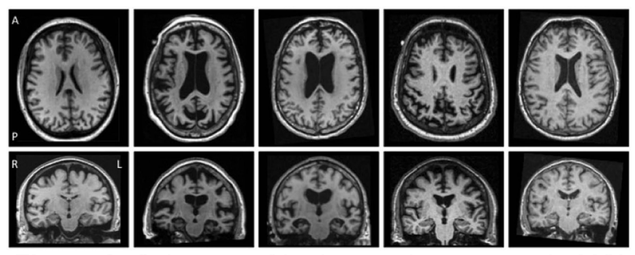


Figure 2: Subtypes of brain atrophy patterns in MCI from visual rating scales. In sequence: healthy control, AD, limbic predominant, hippocampal predominant and minimal atrophy.[2]

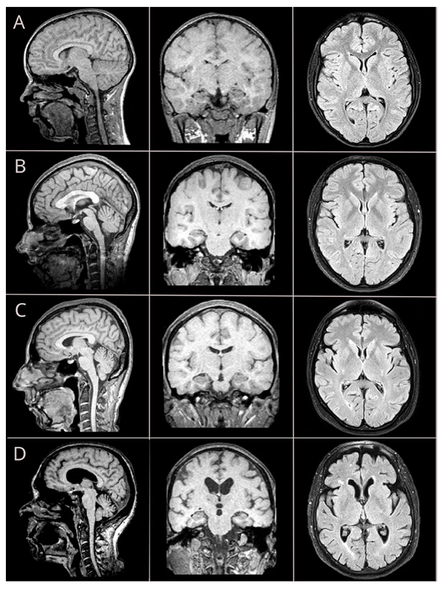


Figure 3: Brain MRI changes across adolescence (A), young adulthood (B), midlife age (C), and older adulthood (D).[3]

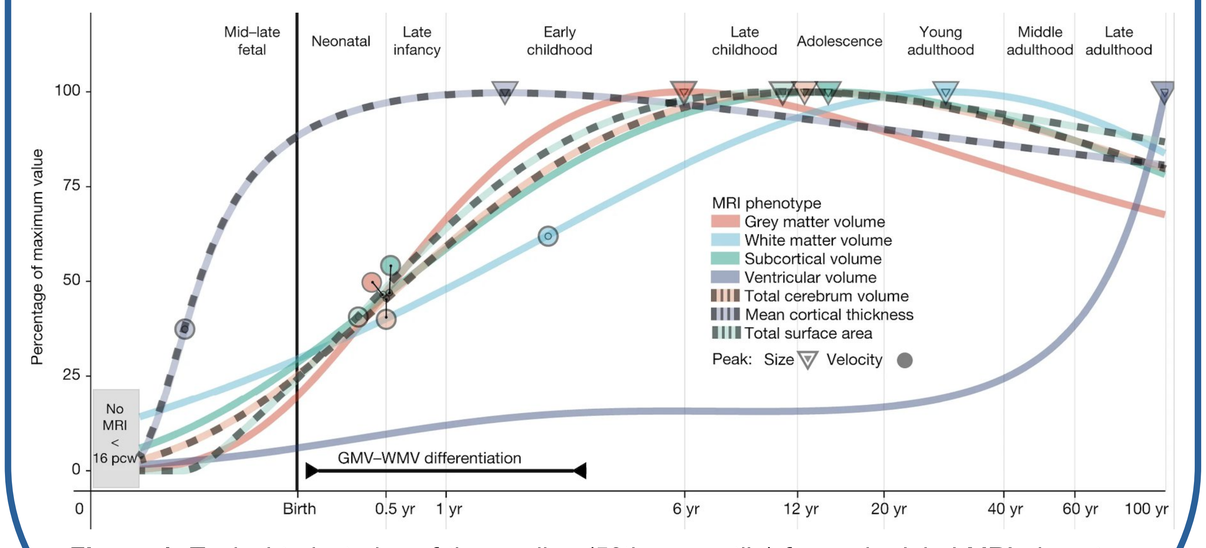


Figure 4: Typical trajectories of the median (50th percentile) for each global MRI phenotype, and key developmental milestones, as a function of age (log-scale).[4]

METHODOLOGY

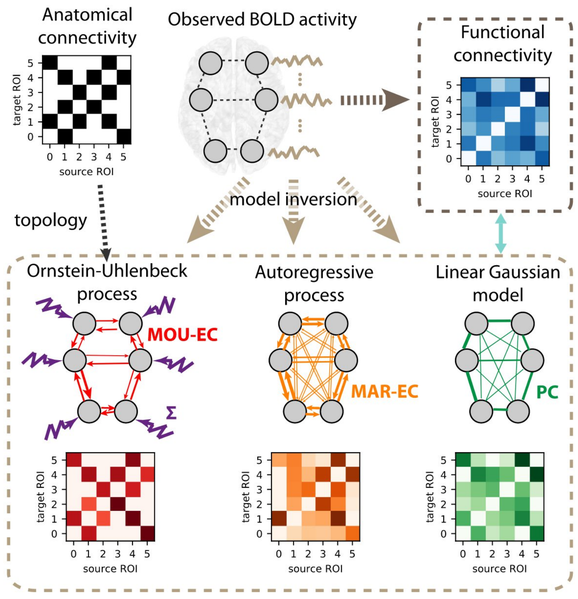


Figure 5. Schematic diagram of six brain regions of interest (ROIs) and how the fMRI* activity can be generated and measured.[5]

GC* gives a measure of asymmetric connectivity, e.g. the effect of node *i* on node *j*.

In the context of fMRI data analysis and first-order autoregressive models, GC and EC* are linked by an approximately quadratic relation.

Positive and negative values of EC are associated with identical values of GC.

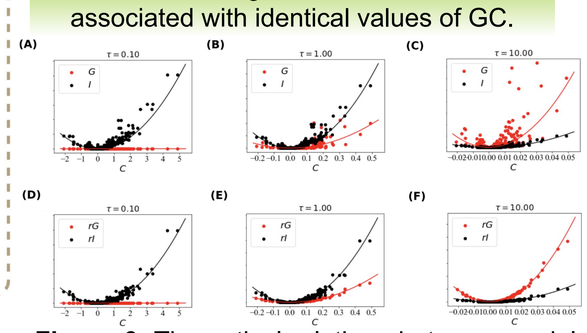
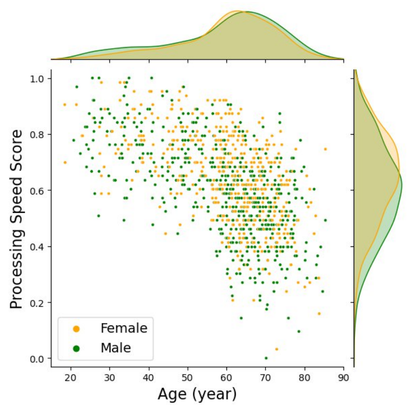


Figure 6. Theoretical relations between model EC and conditional GC and IC.[6]

*fMRI = functional Magnetic Resonance Imaging

*EC = Effective Connectivity, GC = Granger Causality, IC = Instantaneous Causality

DATA - 1000BRAINS[7]



N = 1079 individuals (52% females)

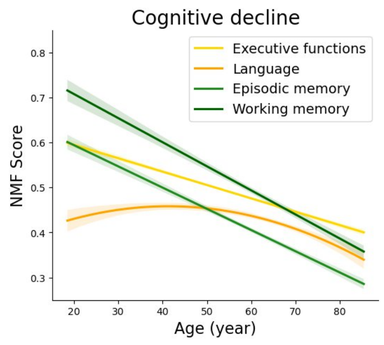
86,5% of the individuals are over 50 years old. Only 24,5% are under.

The variability across subjects is high, and increases with age.

For some of the cognitive scores, there is a significant difference for the females and males distributions.

There is no significant difference on the population distribution based on sex.

Figure 7. Processing speed score across the 1000brains dataset. On top is shown the population distribution. On the right is shown the processing speed score distribution.



Executive functions are slightly decreasing with age.

Language is following an inverted U-shape.

Episodic and working memory are decreasing with age.

Figure 8. First NMF (Non-negative Matrix Factorization) component of the cognitive scores divided in four domains: executive functions, language, episodic and working memory.

Seven Resting-State Networks (RSNs) for each hemisphere: VN, SMN, DAN, VAN, LN, FPN and DMN.

The within-network connectivity (FC) is significantly decreasing with age ($p<0.001$).

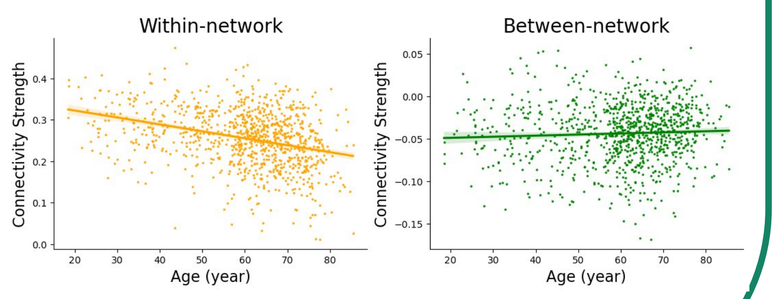


Figure 9. Median of the within-network (left) and between-network (right) connectivity. The within-network connectivity is significantly decreasing with age ($p<0.001$).

DISCUSSION

Considering directional connectivity will we improve our understanding?	Some older adults can perform as well as the young adults, how?	Can sex difference be seen in directional connectivity? If yes, why?

Acknowledgment

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