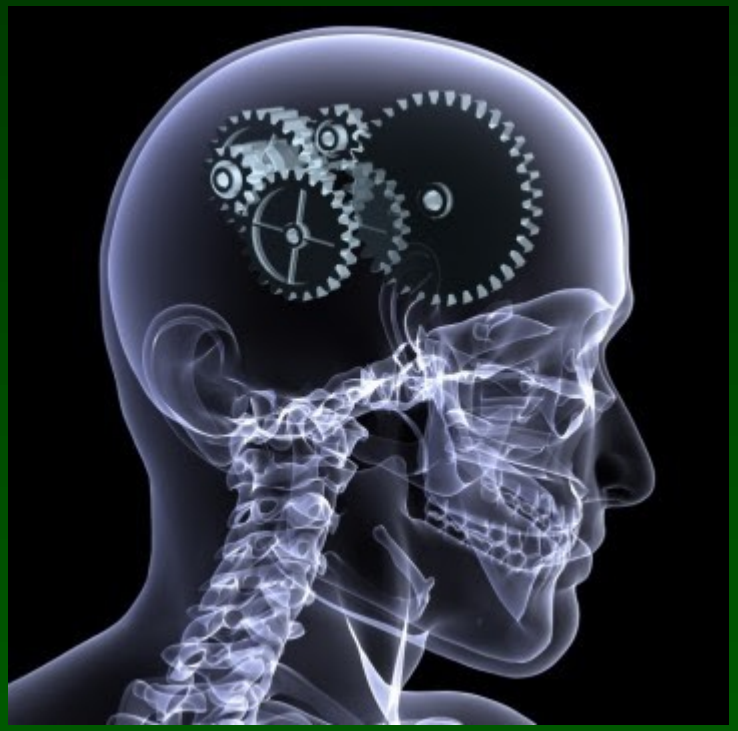
Selected topics in cognitive science and biomodeling

L5. Phenomics and brain networks.



Włodzisław Duch

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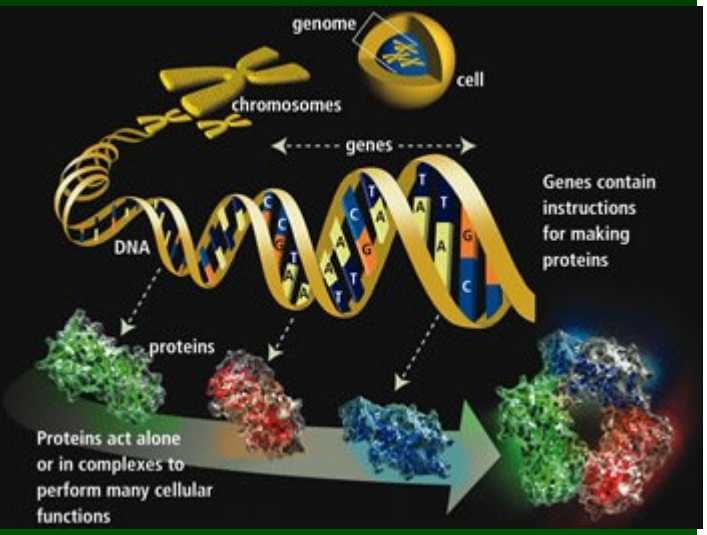
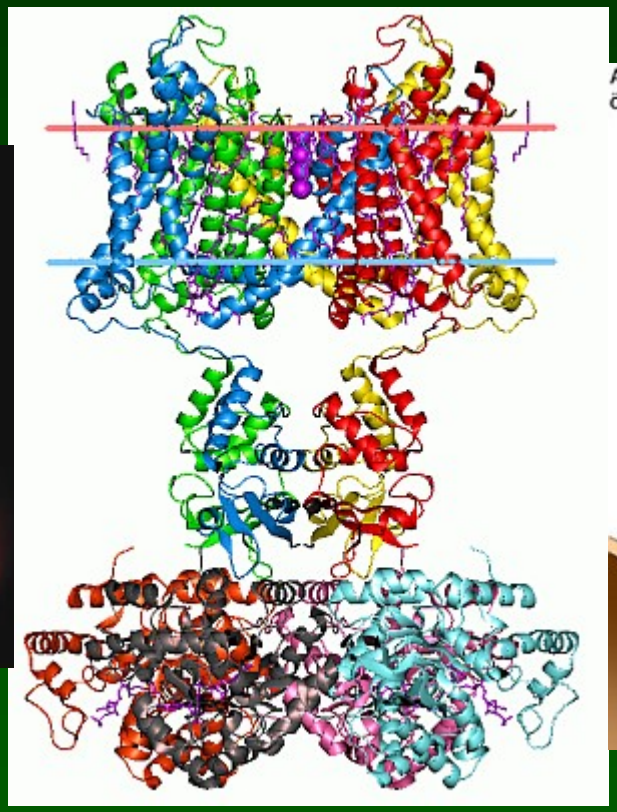
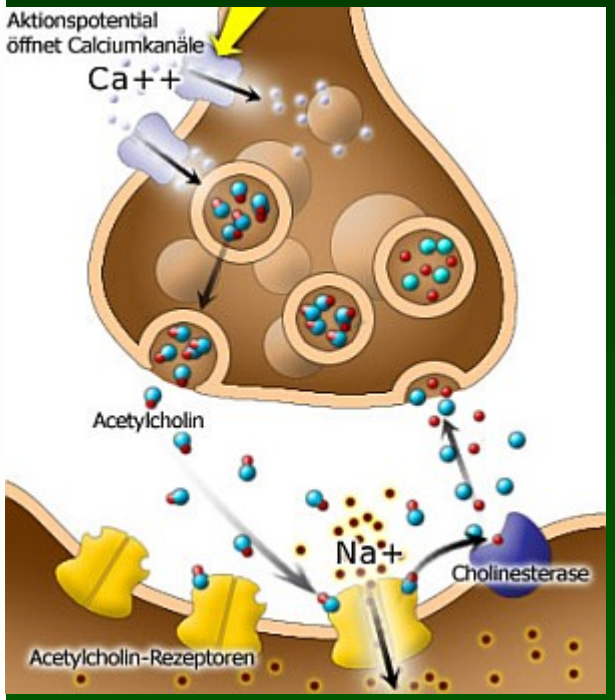
Google: Wlodek Duch

From Genes to Neurons

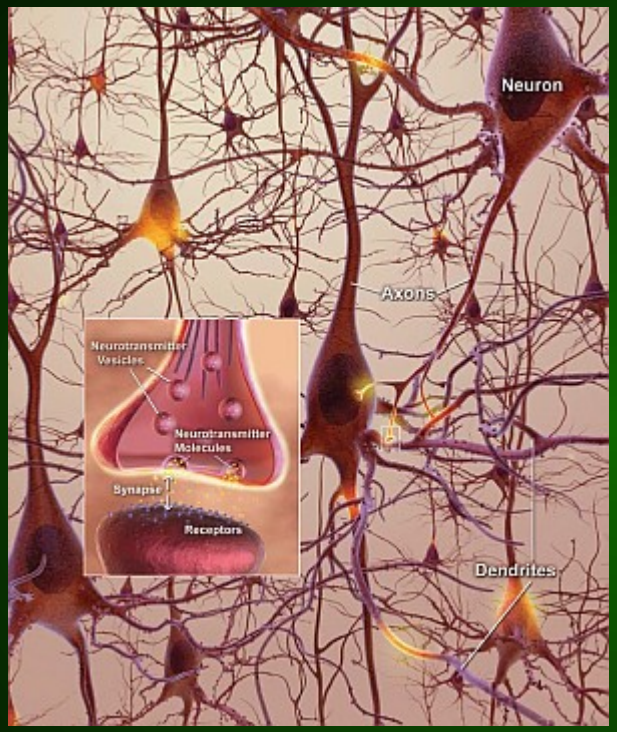


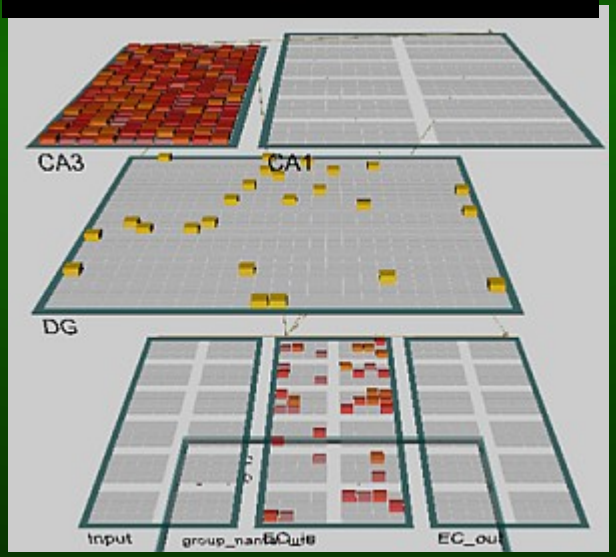




DNA (1953), genes (1972) => proteins => receptors, ion channels, synapses, soma => neuron properties

From neurons to behavior





$\Rightarrow$ network structure **=> neurodynamics** => neuron properties

$\Rightarrow$ behavior (abnormal), cognitive phenotypes,

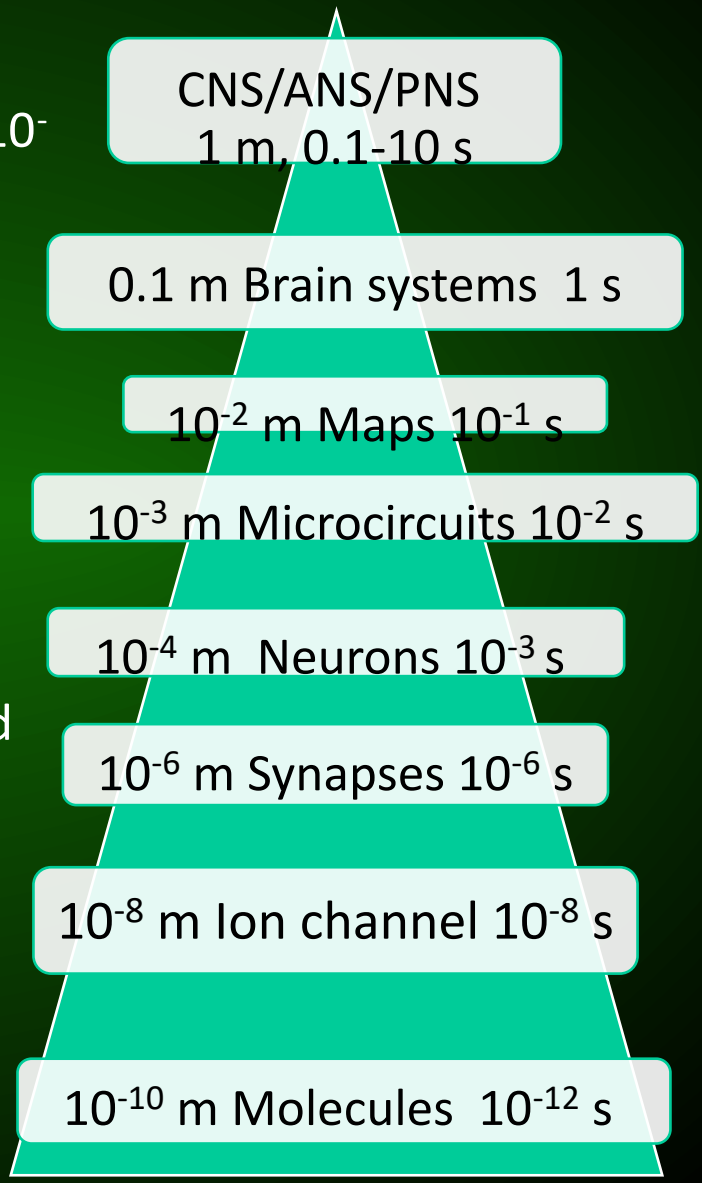
Space/time scales

Spatiotemporal resolution:

- spatial scale: 10 orders of magnitude, from 10^{-10} m to 1 m.
- temporal scale: 10 or more orders of magnitude, from 10^{-10} s to 1 s.

Architecture:

- hierarchical and modular
- ordered in large scale, chaotic in small;
- specific projections: interacting regions wired to each other;
- diffused: regions interact through hormones and neurotransmitters;
- functional: subnetworks dedicated to specific tasks.



Genes ⇔ Behavior

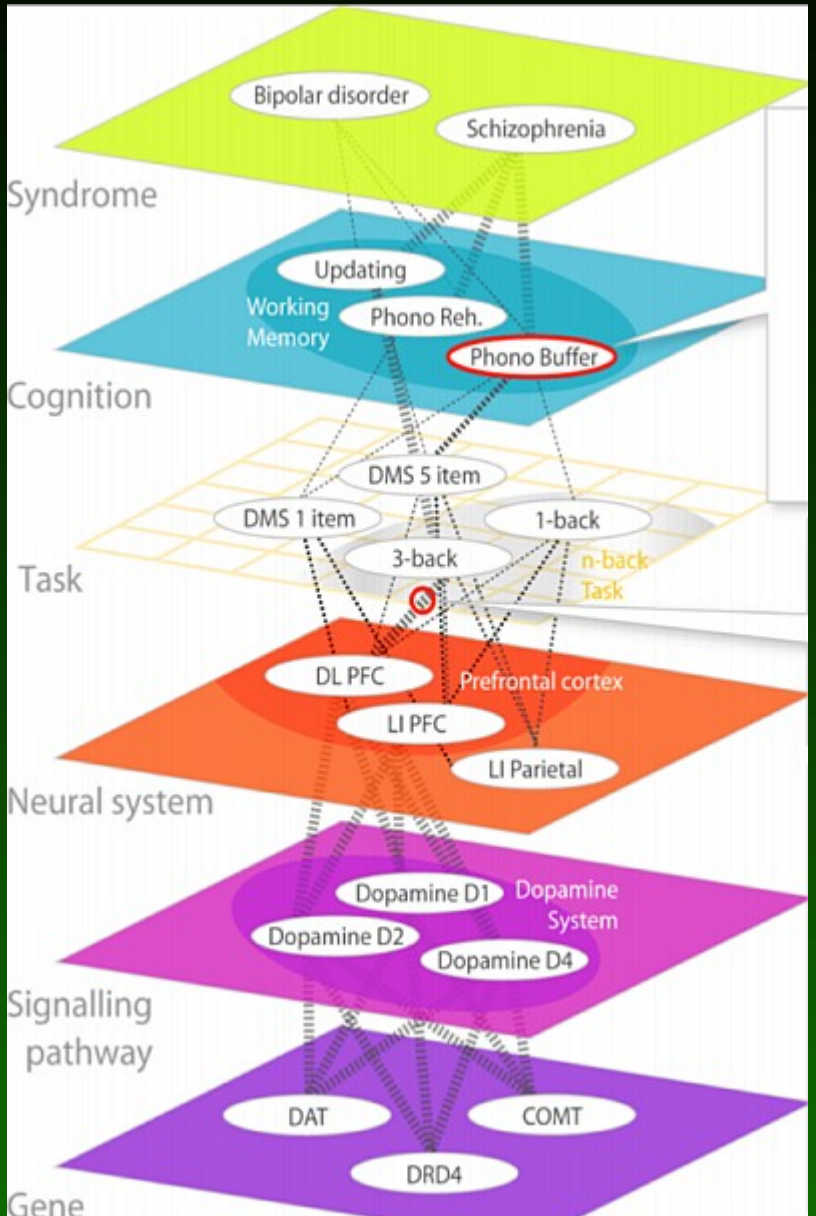
Heritability: % of the total phenotypic variation due to genetic differences.

Phenotypic Variance: V_p

- Components of phenotypic variance
  $V_p = V_G + V_E + V_{GE}$
  - genetic variance: V_G
  - environmental variance: V_E
  - genetic-environmental Interaction V_{GE}

- Components of genetic variance:
  $V_G = V_A + V_D + V_I$
  - additive genetic variance: V_A
  - dominance genetic variance: V_D
  - genic interaction variance: V_I

Total: $V_p = V_A + V_D + V_I + V_E + V_{GE}$



Phenomics => behavior

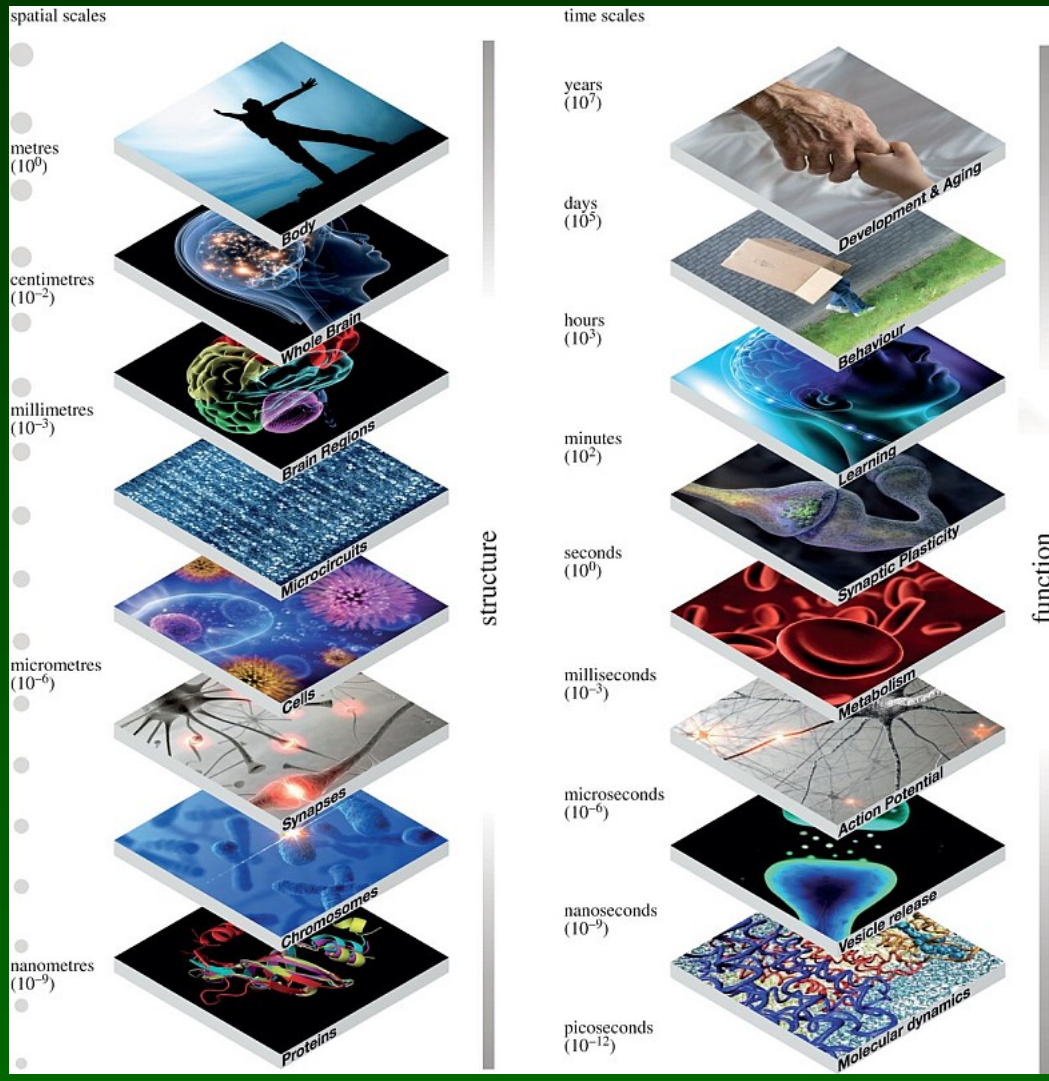
2008: The Consortium for Neuropsychiatric Phenomics

"… categories, based upon presenting signs and symptoms, may not capture fundamental underlying mechanisms of dysfunction" (Insel et al., 2010).

New approach: RDOC NIMH.

Description of organisms at different levels will help to answer different types of questions.

Network level is in the middle and can be connected to the mental level via computational models.



RDoC
Research Domain Criteria Initiative

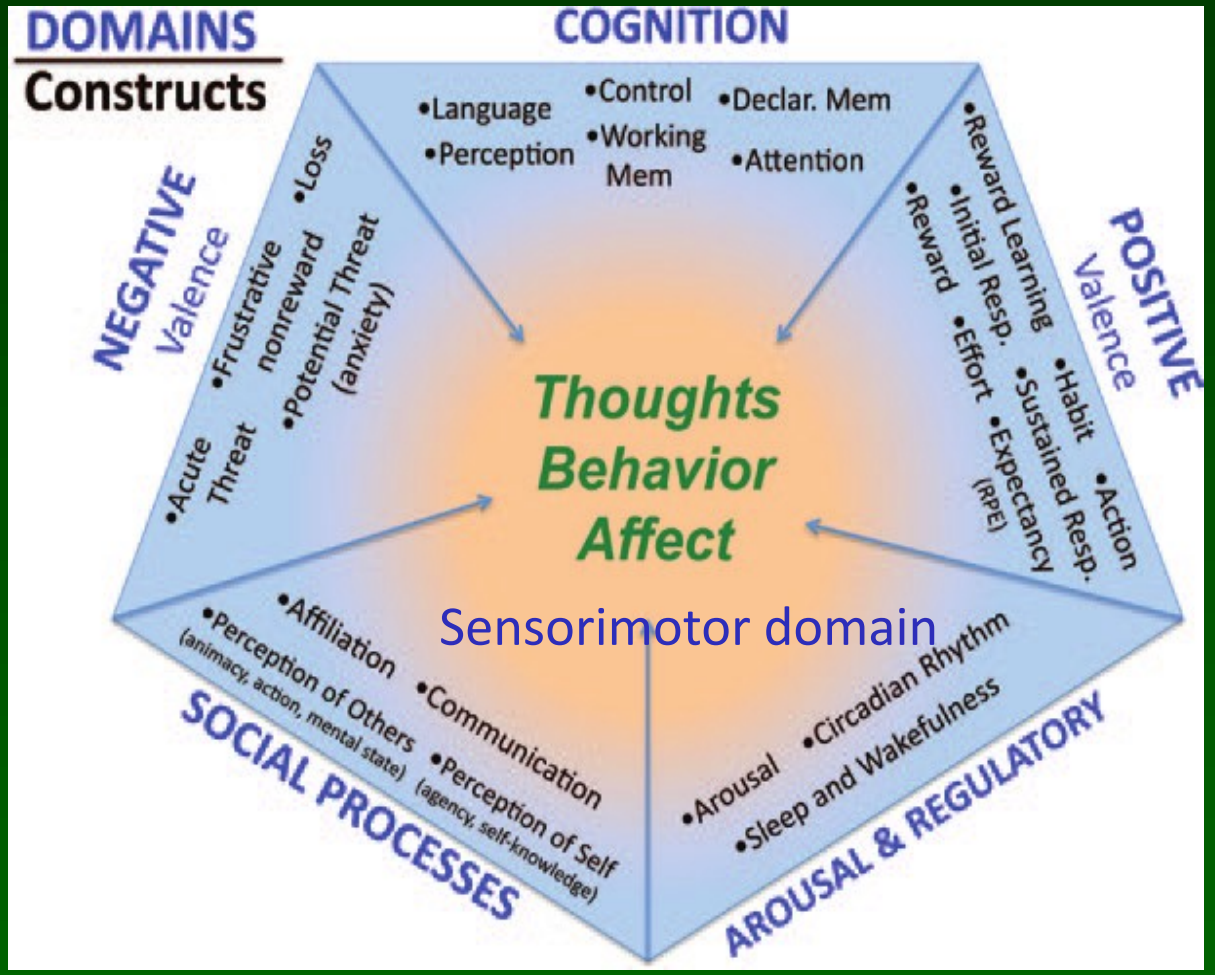
NIMH RDoC Matrix for analysis of (de)regulation of 6 large brain systems.

Psychological constructs are necessary to talk about mental states.

Regulation of these 6 large networks forms the basis of all human behavior.

Sensorimotor systems added in Jan. 2019 as the sixth brain system.

How are these functions implemented in the brain and **what contributes** to their activity?



RDoC Matrix for „cognitive domain”

Construct/Subconstruct		Genes	Molecules	Cells	Circuits	Physiology	Behavior	Self-Report	Paradigms
Attention		Elements	Elements	Elements	Elements	Elements	Elements		Elements
Perception	Visual Perception	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Auditory Perception	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Olfactory/Somatosensory/Multimodal/Perception								Elements
Declarative Memory		Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
Language		Elements			Elements	Elements	Elements	Elements	Elements
Cognitive Control	Goal Selection; Updating, Representation, and Maintenance ⇒ Focus 1 of 2 ⇒ Goal Selection				Elements			Elements	Elements
	Goal Selection; Updating, Representation, and Maintenance ⇒ Focus 2 of 2 ⇒ Updating, Representation, and Maintenance	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Response Selection; Inhibition/Suppression ⇒ Focus 1 of 2 ⇒ Response Selection	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Response Selection; Inhibition/Suppression ⇒ Focus 2 of 2 ⇒ Inhibition/Suppression	Elements	Elements	Elements	Elements	Elements	Elements	Elements	Elements
	Performance Monitoring	Elements	Elements		Elements	Elements	Elements	Elements	Elements
Working Memory	Active Maintenance	Elements	Elements	Elements	Elements	Elements			Elements
	Flexible Updating	Elements	Elements	Elements	Elements	Elements			Elements
	Limited Capacity	Elements	Elements		Elements	Elements			Elements
	Interference Control	Elements	Elements	Elements	Elements	Elements			Elements

Concepts and reality

Psychological constructs,
such as memory or attention, try to group continuous brain processes into common patterns, adding more specific constructs.

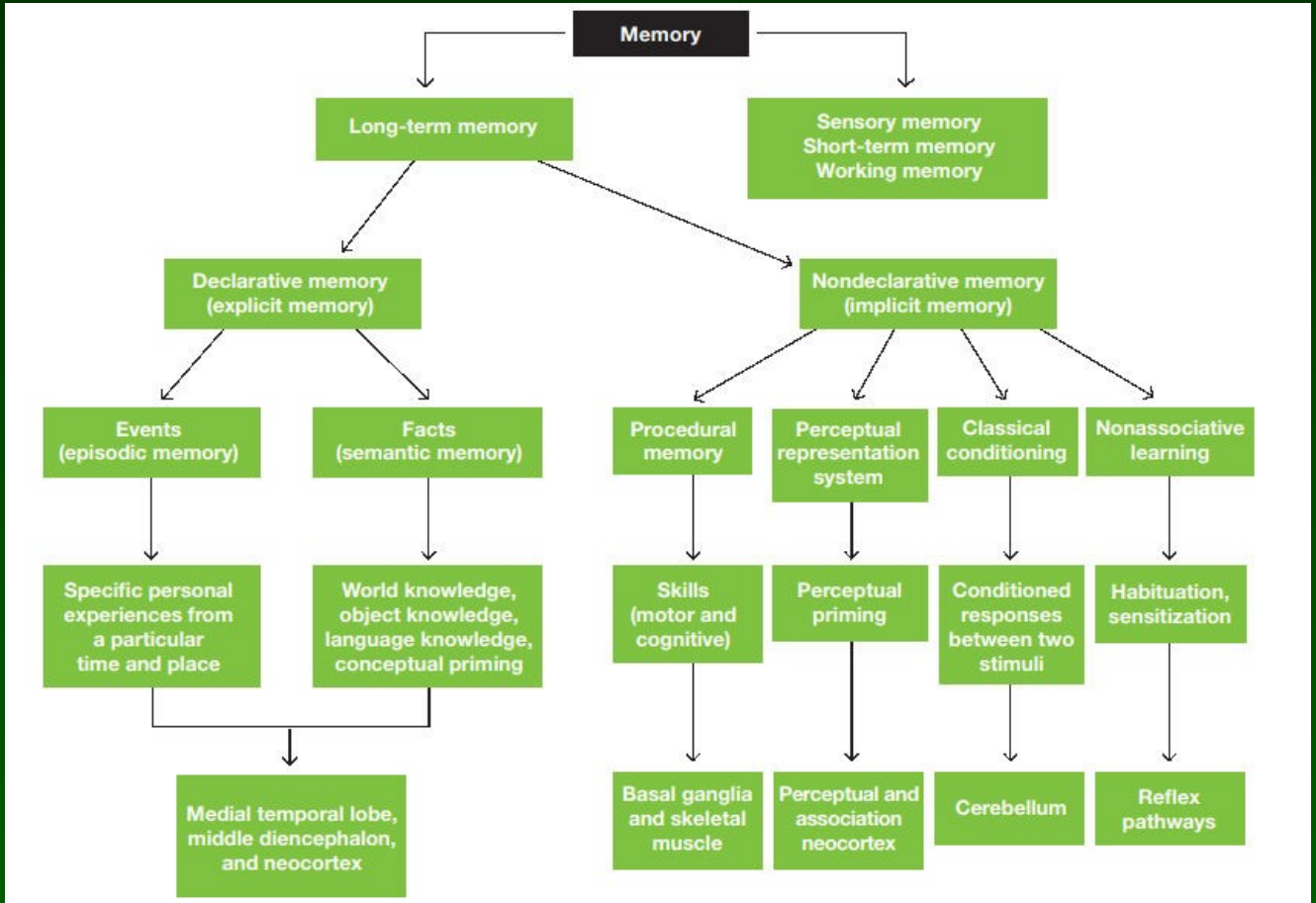


FIGURE 9.2 The hypothesized structure of human memory.
The brain regions that are thought to contribute to different types of memory are indicated.

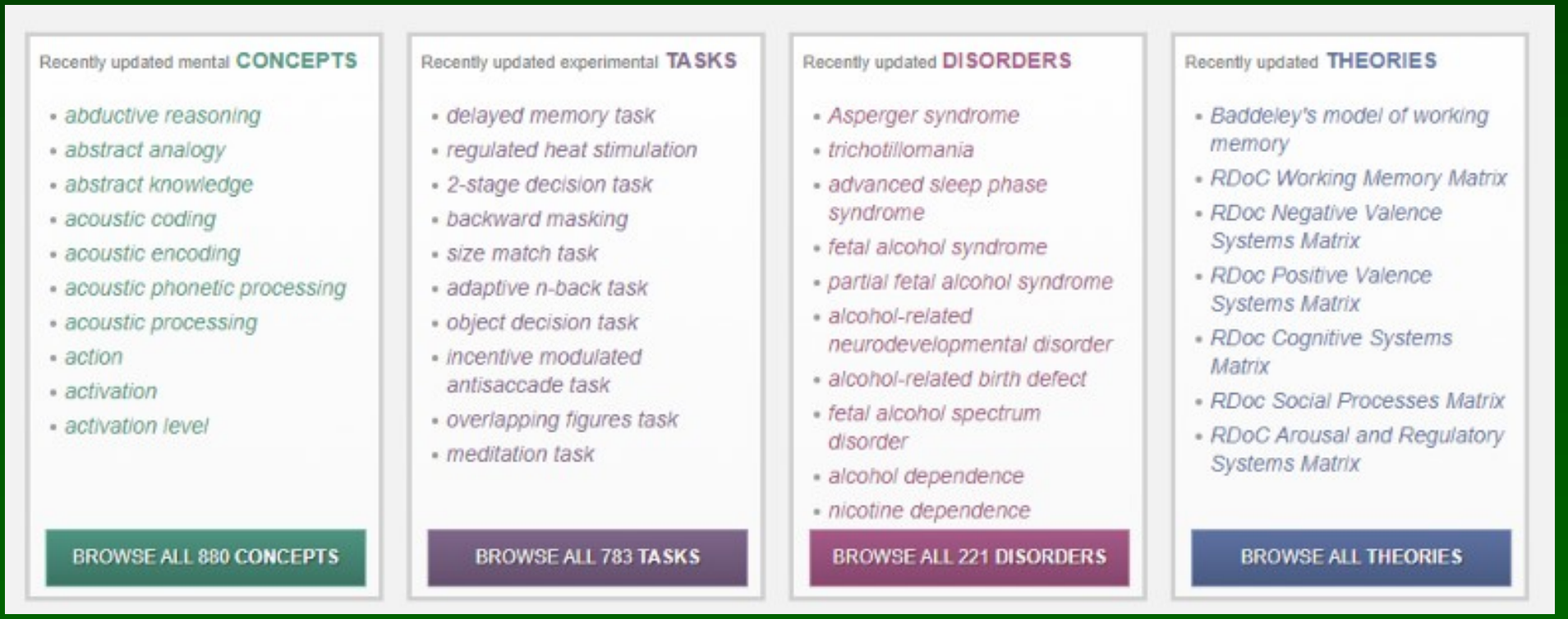
Fig. from: Cognitive Neuroscience. The Biology of the Mind 5th ed, M Gazzaniga, 2019
Duch W. (2018), Kurt Lewin, psychological constructs and sources of brain cognitive activity.

Cognitive Atlas

Collaborative knowledge building project to develop ontology of cognitive science (coordinated by Russel Poldrack/NIMH).

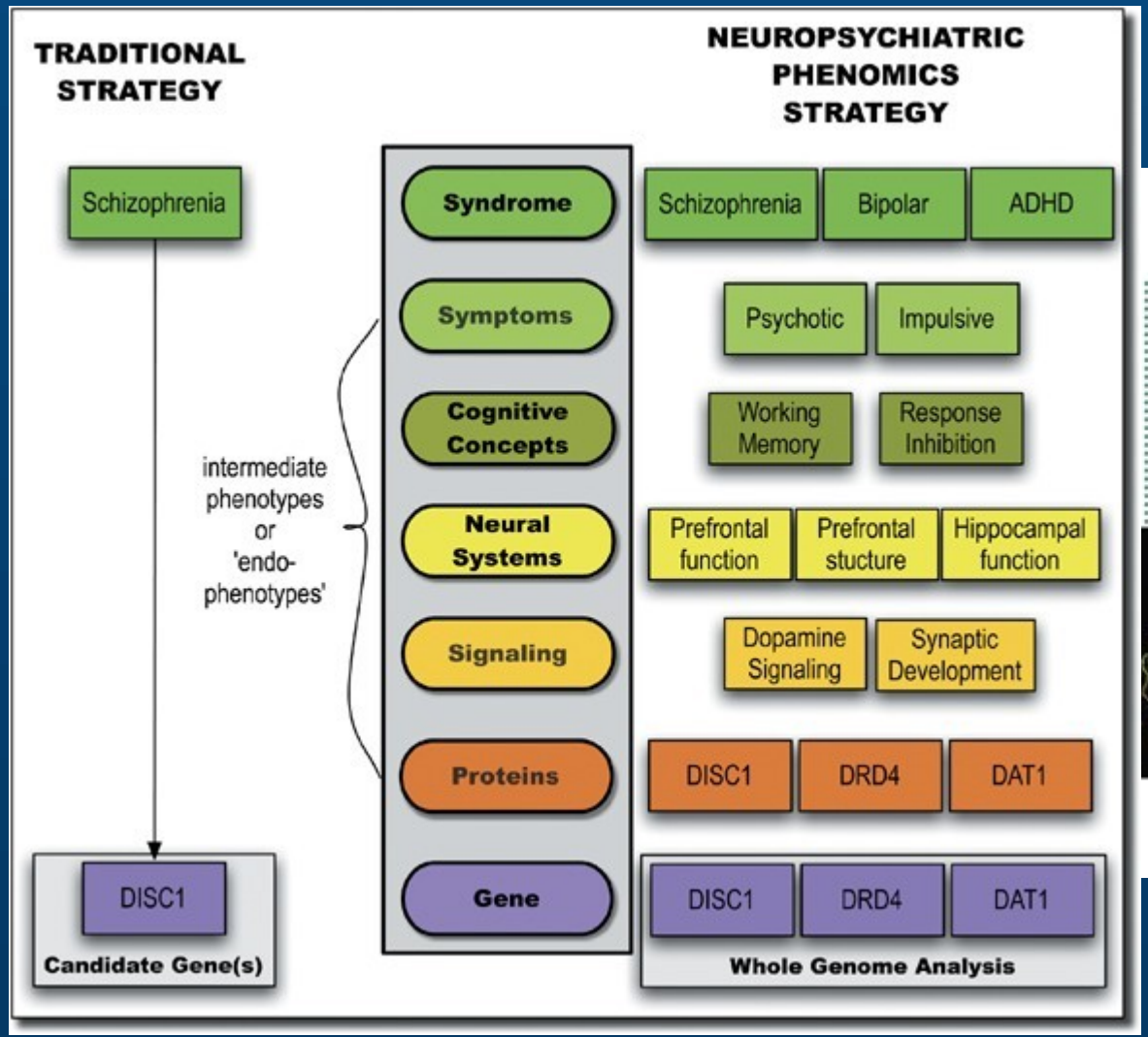
Concepts are related to both physical and mental level.

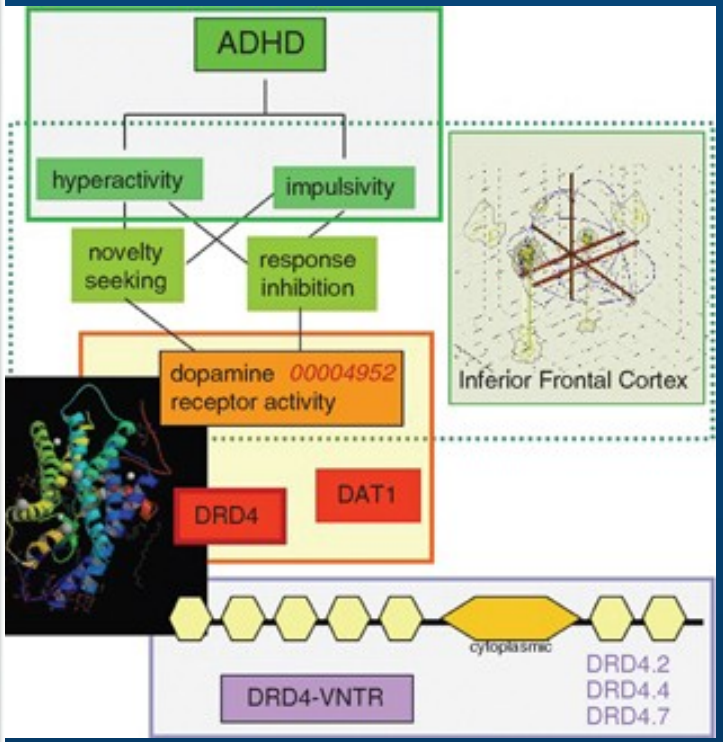
Theories are linked to NIMHRDoC and Neurosynth.



NIMH Strategy

This approach ignores environment, epigenetic influences, developmental processes that determine structure and function of brain networks.





Genes => proteins
=> cells => brains

Genes and brains

Large-scale programs to link genes with behavior.

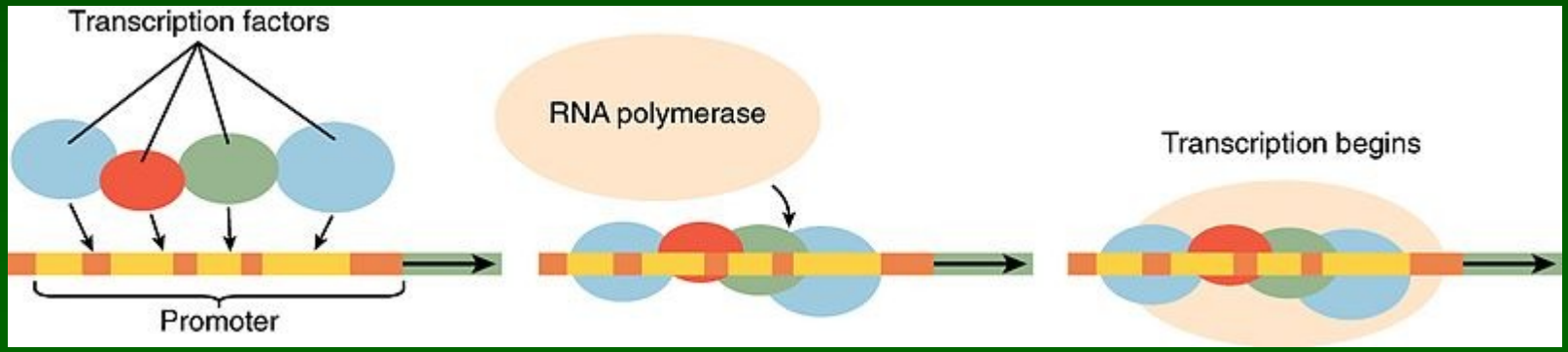
Worm (C. Elegans)

19 000 genes
302 neurons
7 800 synapses

Human

~ 20 000 genes
~ 100 B neurons (10^{11})
~ 10^{14} – 10^{15} synapses

Environment turns genes on/off via transcription factors. Genes do not control our behavior, but provide a substrate for cognition & behavior.



Genes/molecules

Nano/millisecond scale incredible complexity!

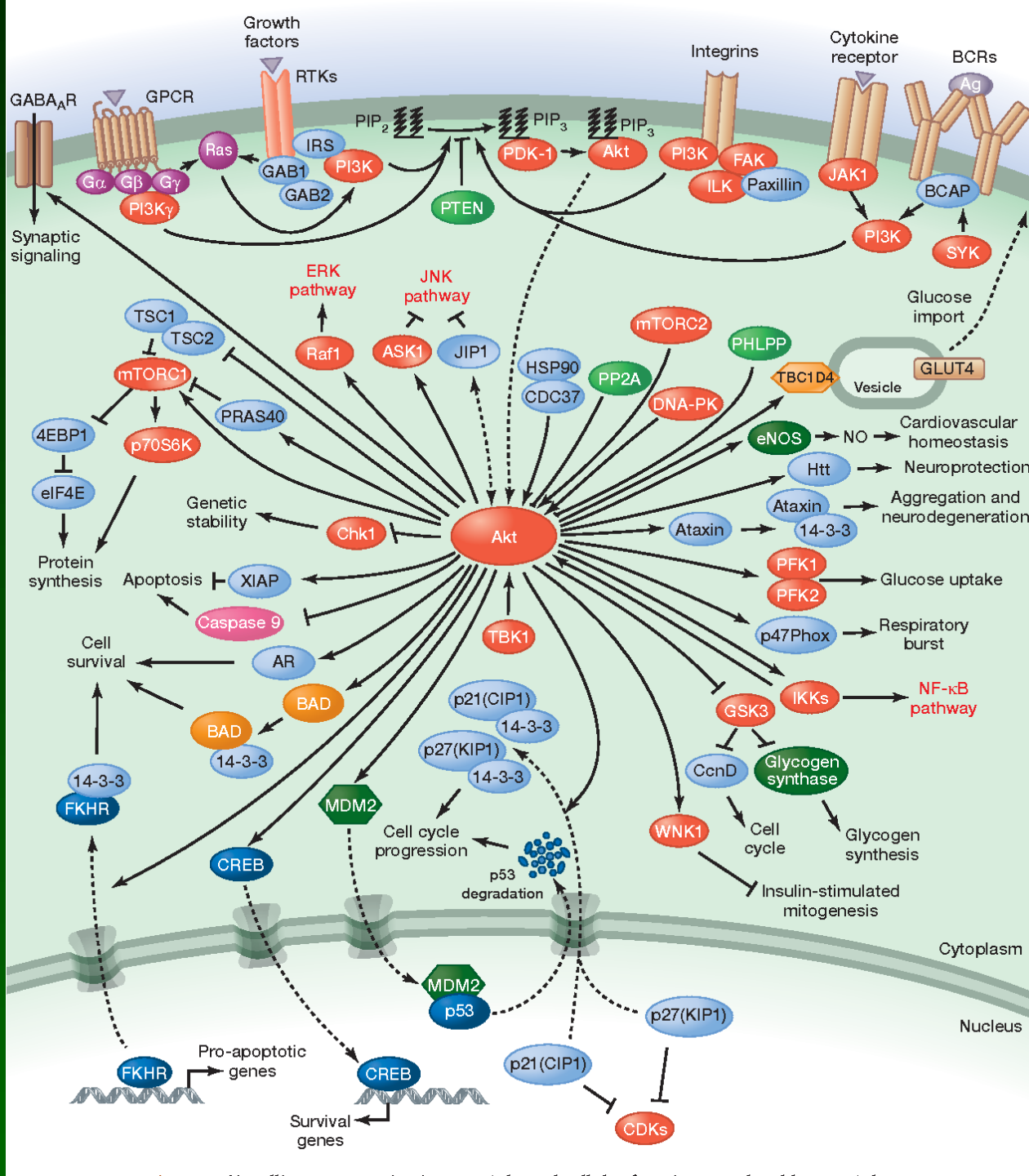
Dscam gene => 38 000 variants of proteins!

Total length of our DNA in 50 trillion body cells is 100 billion km, or about 666 times the distance to the Sun.

100 mln ions/sec in a single ion channel.

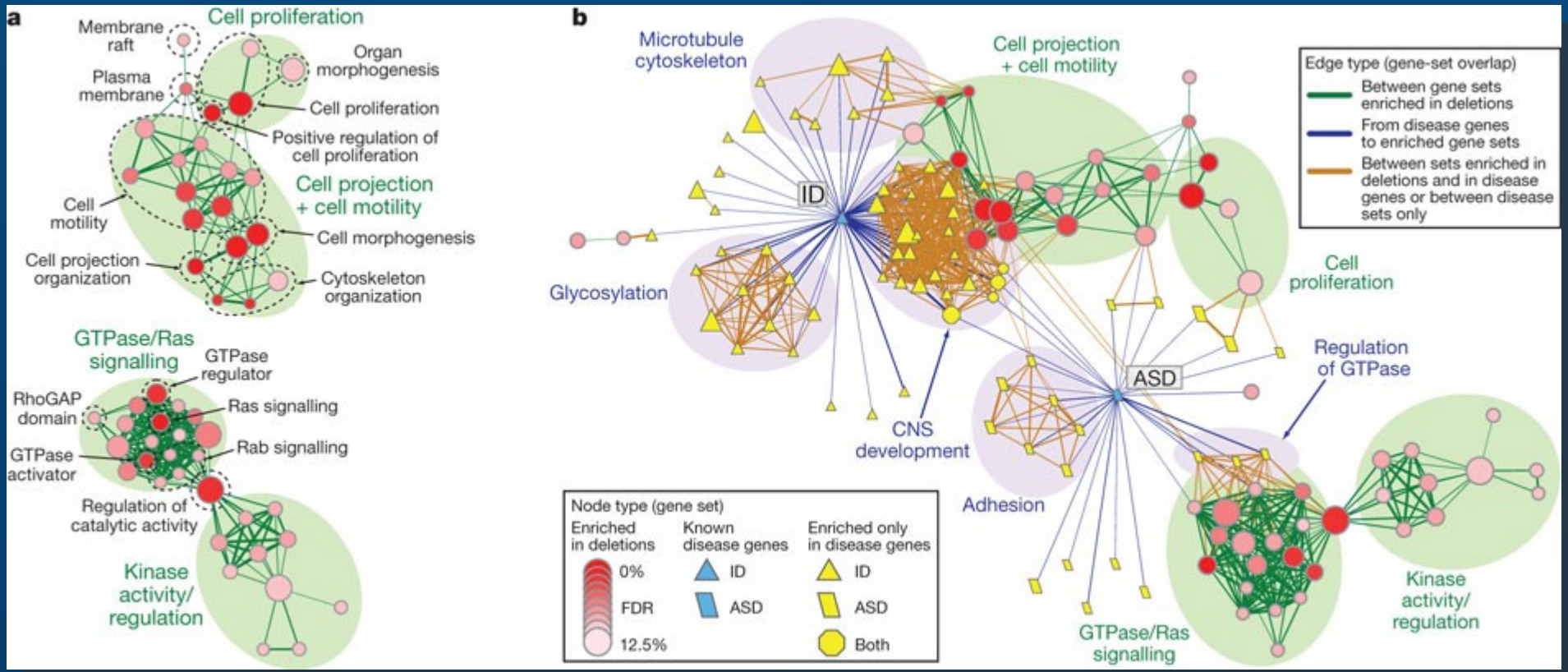
Neuron has 10 000 ion channels, billions of ions flow in each second.

Simple loops => infinite complexity (ex. fractals).



Genes & functions

Pinto, D. + 180 coauthors ... (2010). Functional impact of global rare copy number variation in autism spectrum disorders. *Nature* **466**, 368–372 (2010)



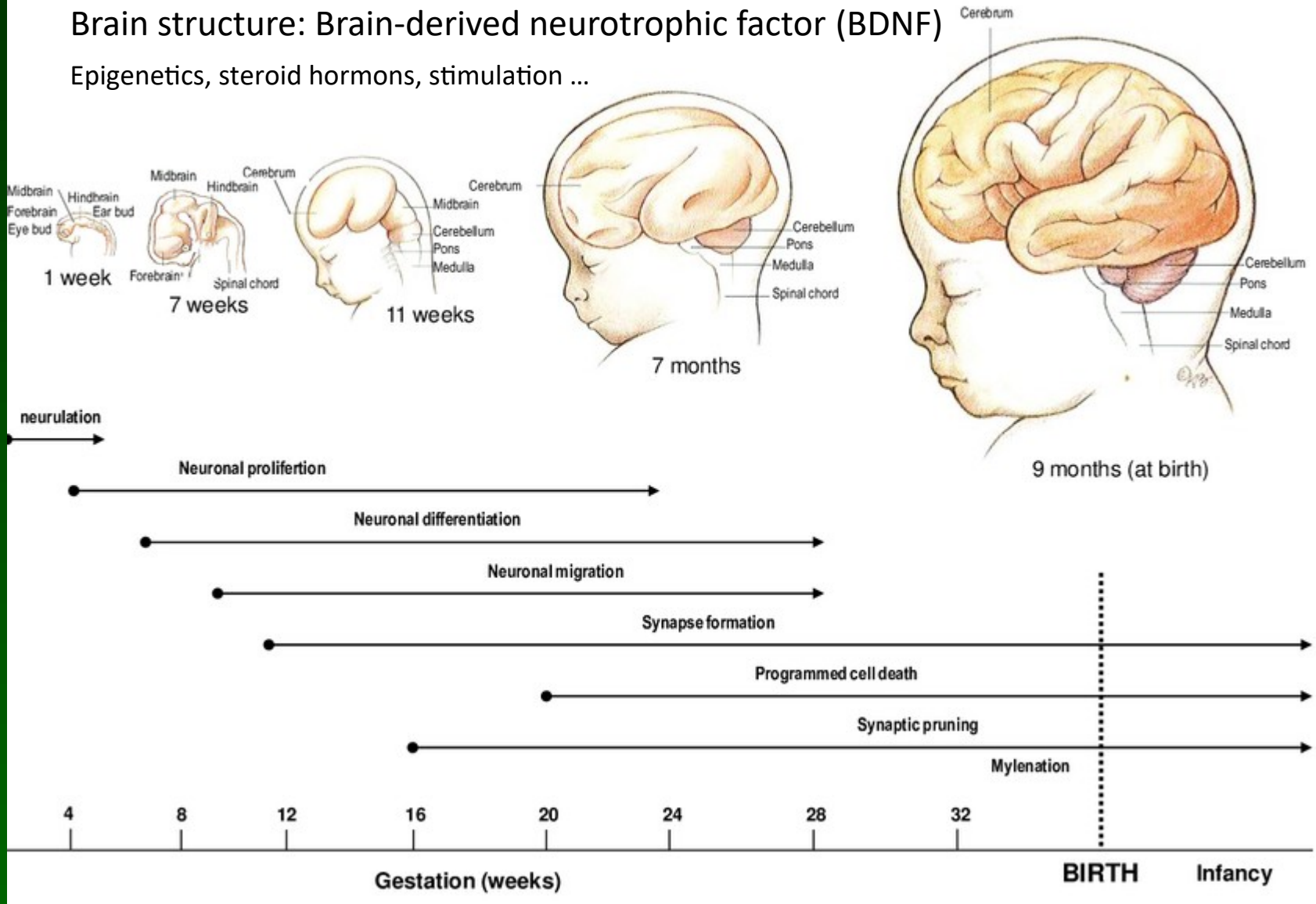
ASD heritability is ~90%, SFARI Human Gene Module database in 9/2021 listed 1028 ASD genes, implicated in 10-20% of cases, single genes in less than 1%.

Genetic variants ⇔ educational attainment: 126,559 subjects, 180 authors, most predictive genetic variant (SNP) accounted for 0.02%, all genes 2%.

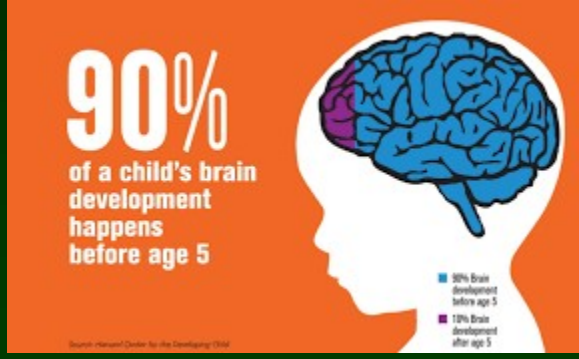
Formation of the brain

Brain structure: Brain-derived neurotrophic factor (BDNF)

Epigenetics, steroid hormons, stimulation …



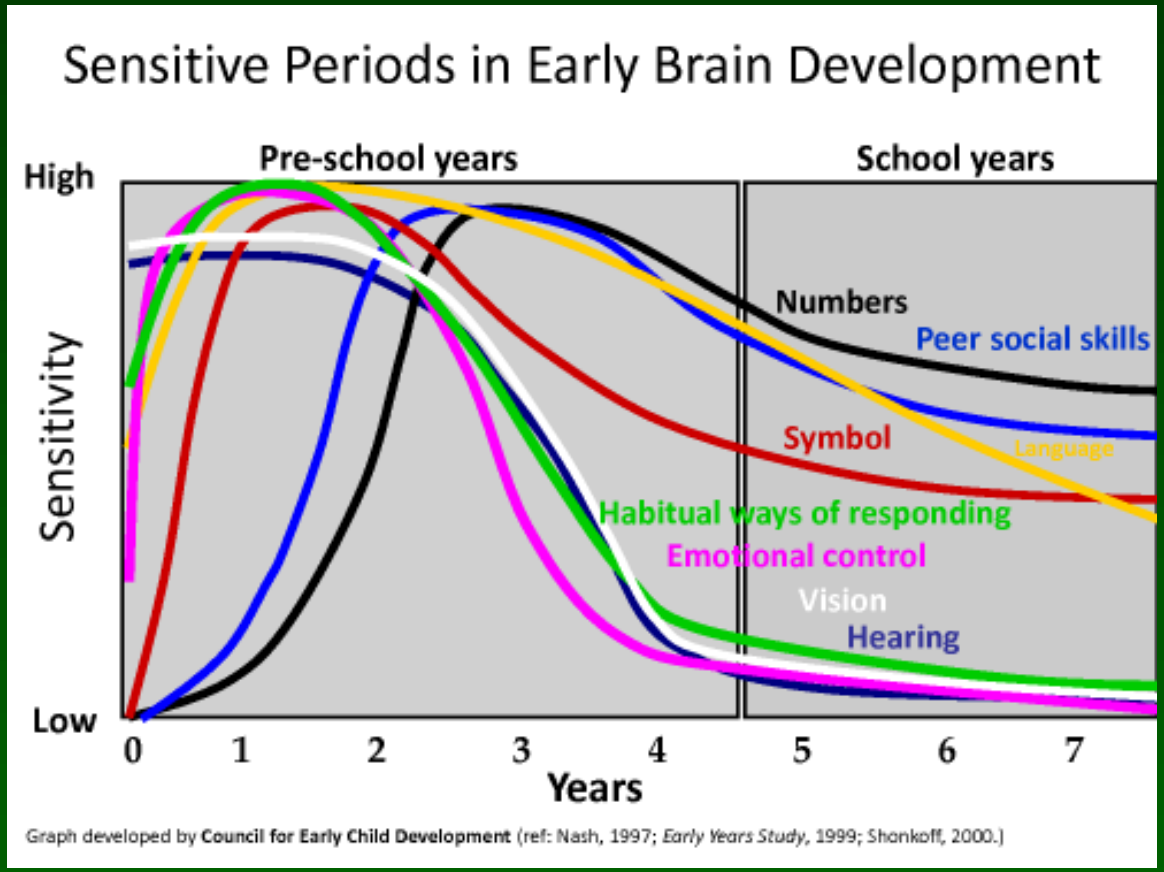
Childhood matters



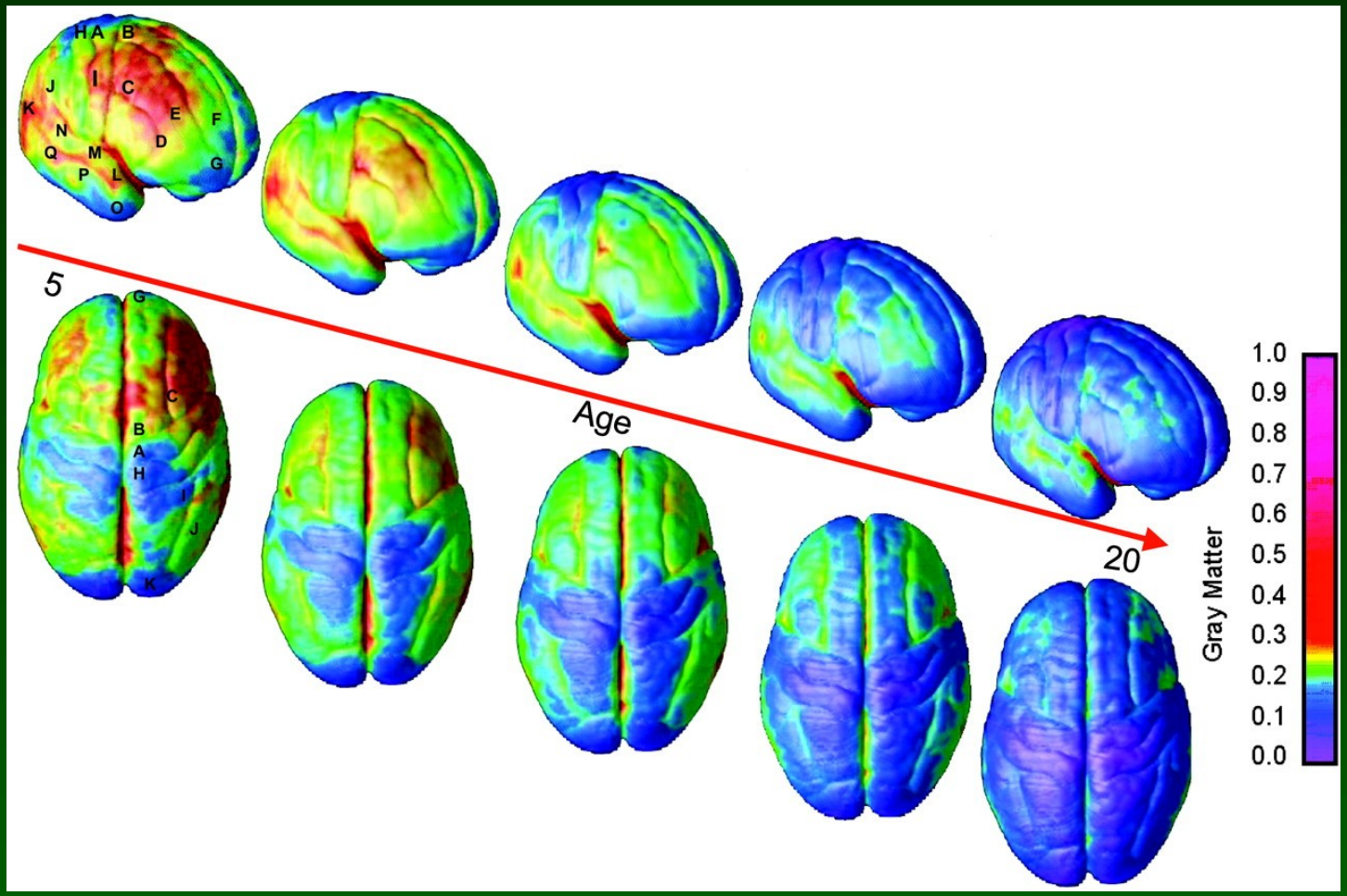
To reach full potential of a child attention must be paid to early environment in relation to sensitive periods of development.

Genes specify the structure of all the proteins, therefore structure of all cells, neurotransmitters, hormones, receptors, etc.

Their effects depend on particular environment, are expressed in a particular network of other genes, creating context-dependent tendencies, predispositions, potentials, and vulnerabilities.



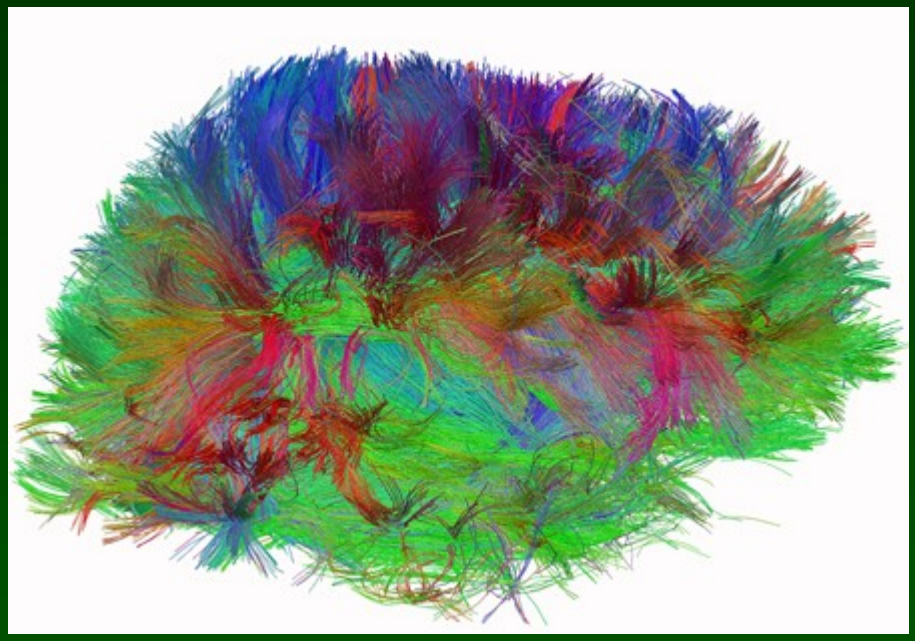
Brain maturation



Decreasing amount of gray matter over the cortical surface. The side bar shows a color representation in units of GM volume. Movies.

N. Gogtay et al, Dynamic mapping of human cortical development during childhood through early adulthood. PNAS 101 (21) 8174-8179, 2004

Neural determinism

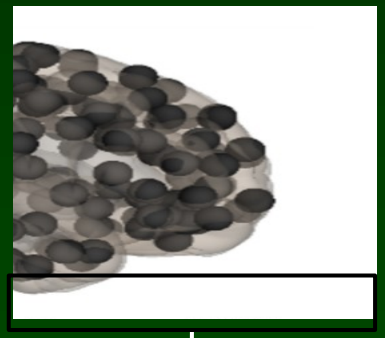


Genetic determinism: general anatomy and functions of the brain.

Neural determinism: connections are formed by interactions with the environment, individual experiences and culture.
We can only think in a way that is determined by neuronal activity!
Neurodynamics = dynamical state on top of brain structure, **the true source of our thoughts**, understanding. We confabulate in search for explanations.
Metaphor: mind is the shadow of neurodynamics.

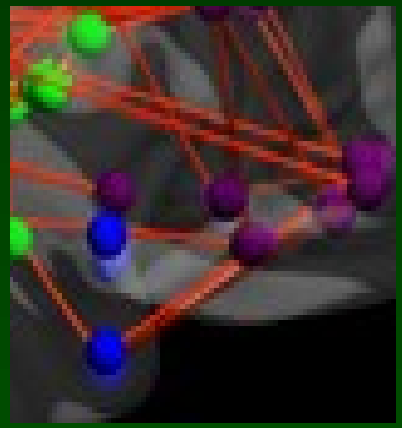
Human connectome and MRI/fMRI

Node definition (parcelation)



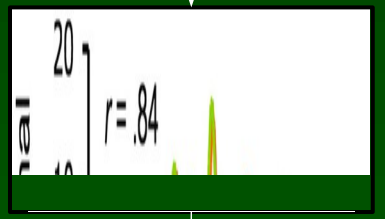
Structural connectivity

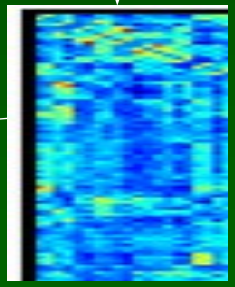
Functional connectivity



Signal extraction

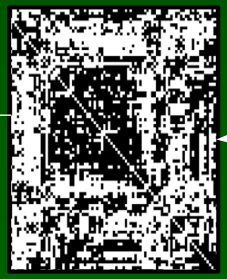
Correlation calculation

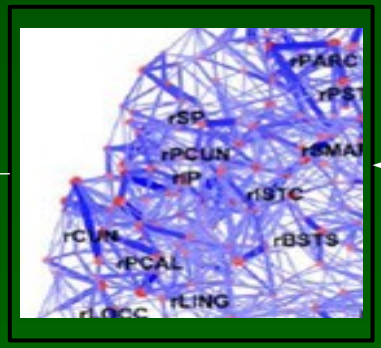




Correlation matrix

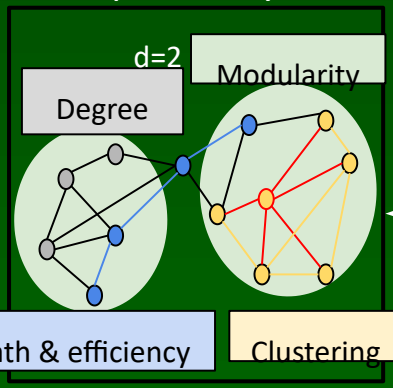
Binary matrix





Whole-brain graph

Graph theory



Many toolboxes available for such analysis.

Bullmore & Sporns (2009)

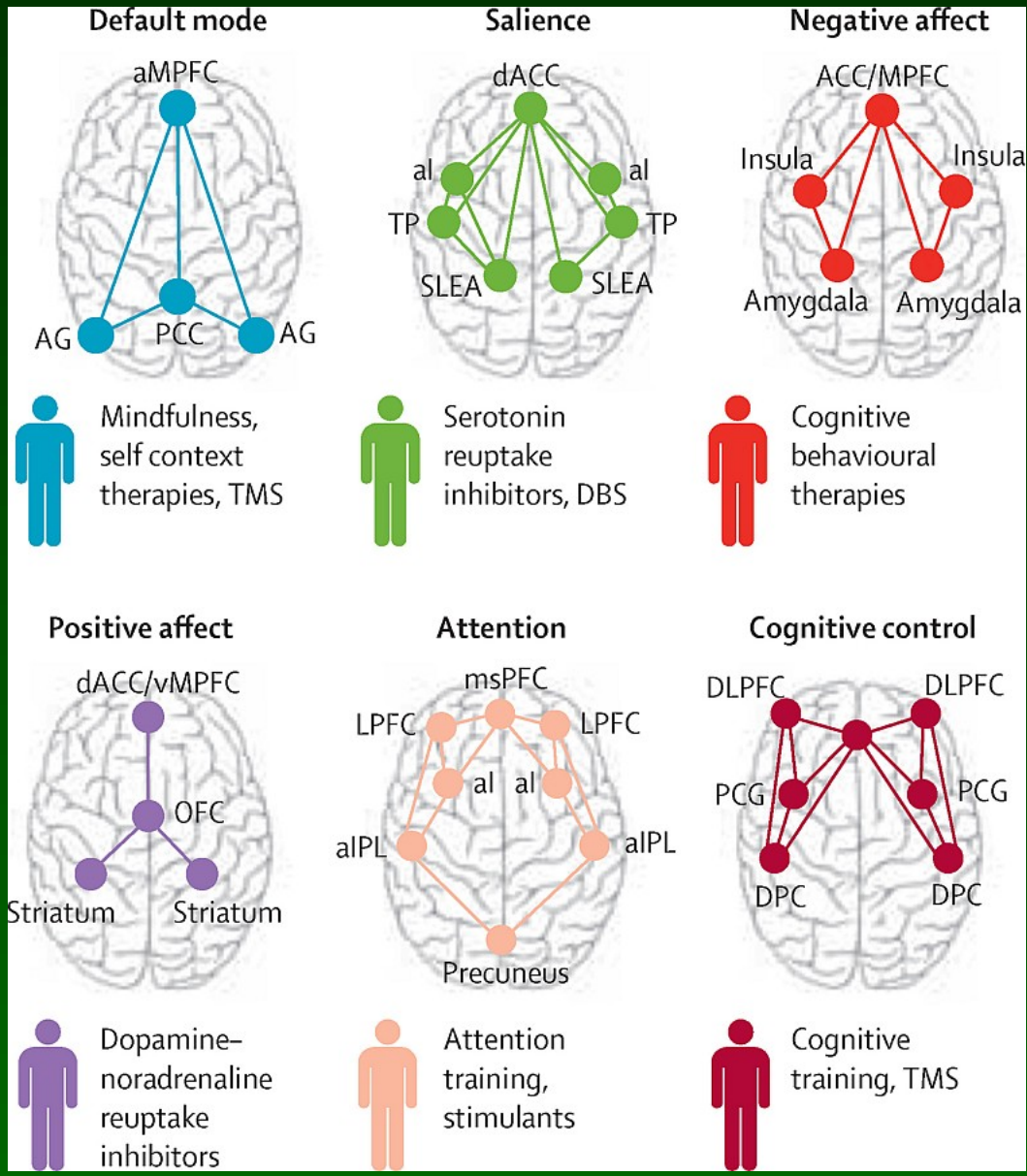
Large-scale networks and phenomics

Functions used in **Research Domain Criteria** (RDoC) matrix are connected with synchronized activation of specific brain regions (ROIs), neurotransmitters and therapeutic targets.

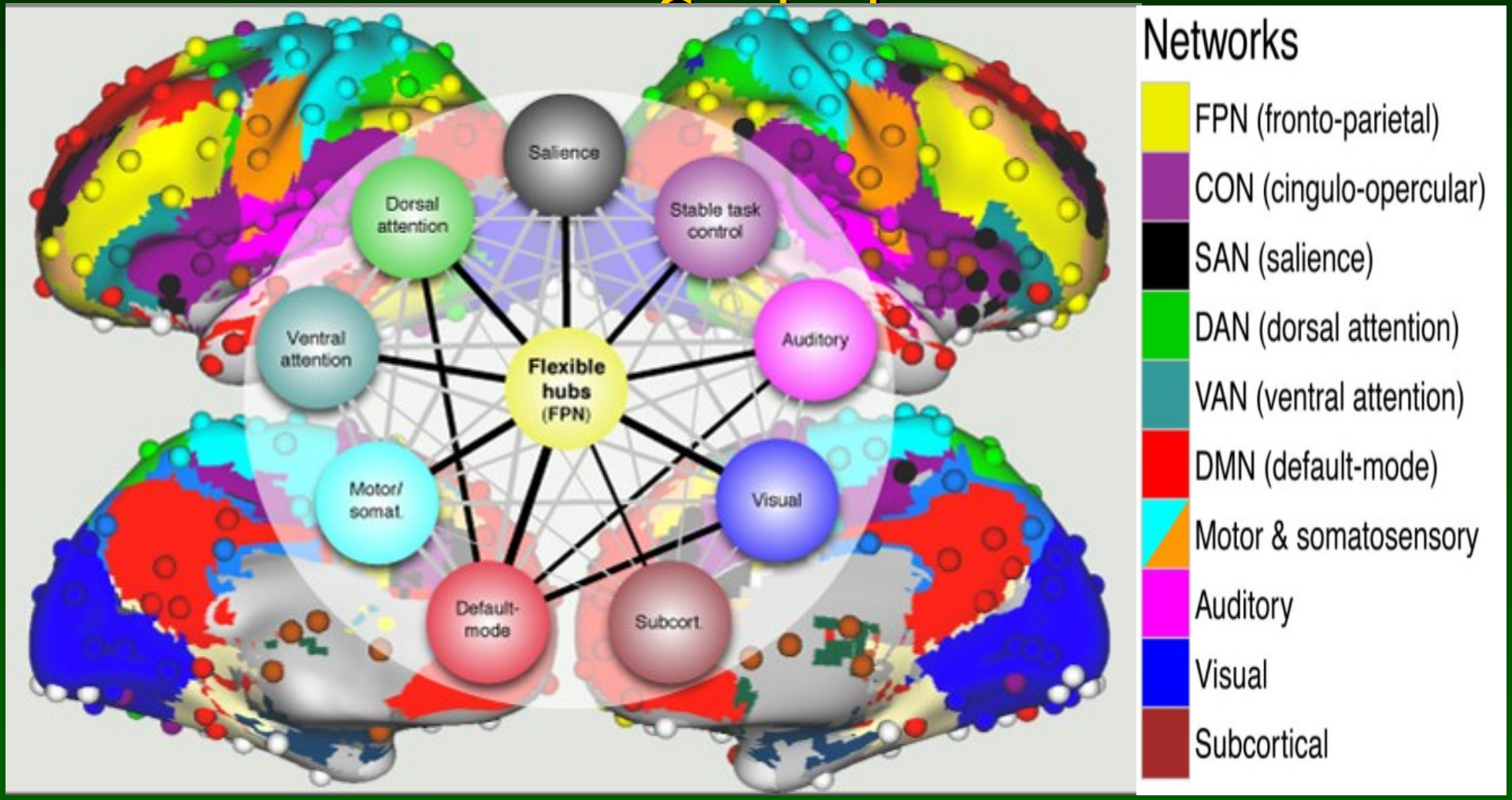
Include genes, molecules, cells, **circuits**, physiology, behavior, self-reports and paradigms.

Sung et al. (2018). A Set of Functional Brain Networks for the Comprehensive Evaluation of Human Characteristics. *Frontiers in Neuroscience*, *12*.

Using 163 brain regions identified functional networks related to 111 psychometric parameters.



Neurocognitive Basis of Cognitive

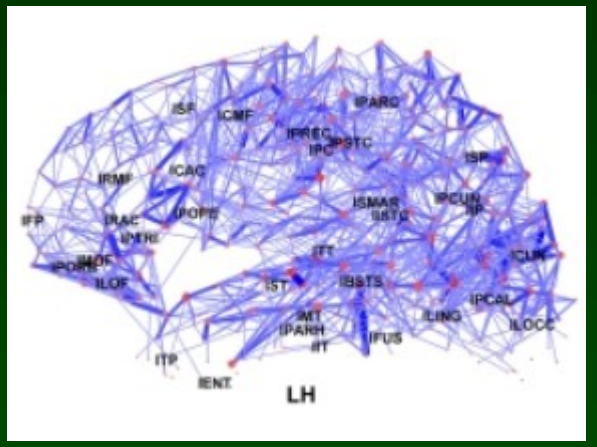


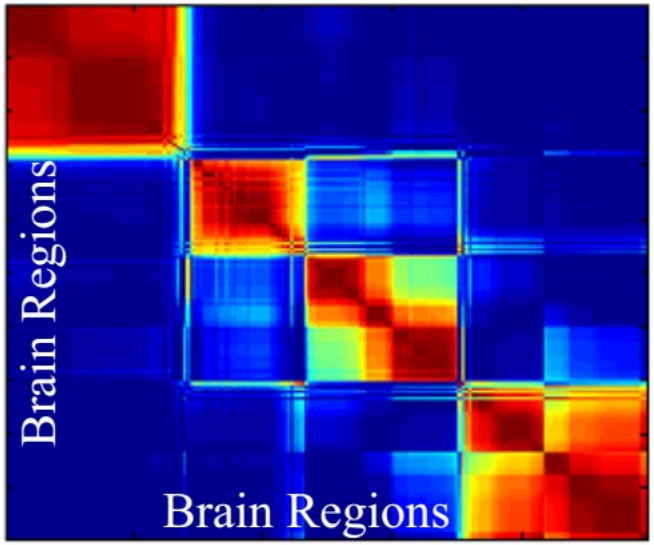
Central role of fronto-parietal (FPN) flexible hubs in cognitive control and adaptive implementation of task demands (black lines=correlations significantly above network average). Cole et al. (2013).

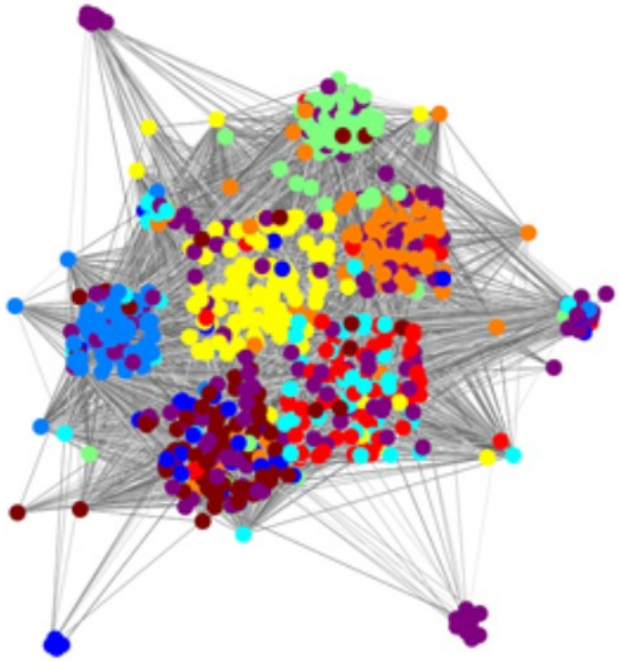
Neuronal subnetworks

Hierarchy and modularity is observed at large scale: several subnetworks are responsible for arousal, attention, positive/negative valence, perception.

At the microcircuit level similar hierarchy and modularity is seen.







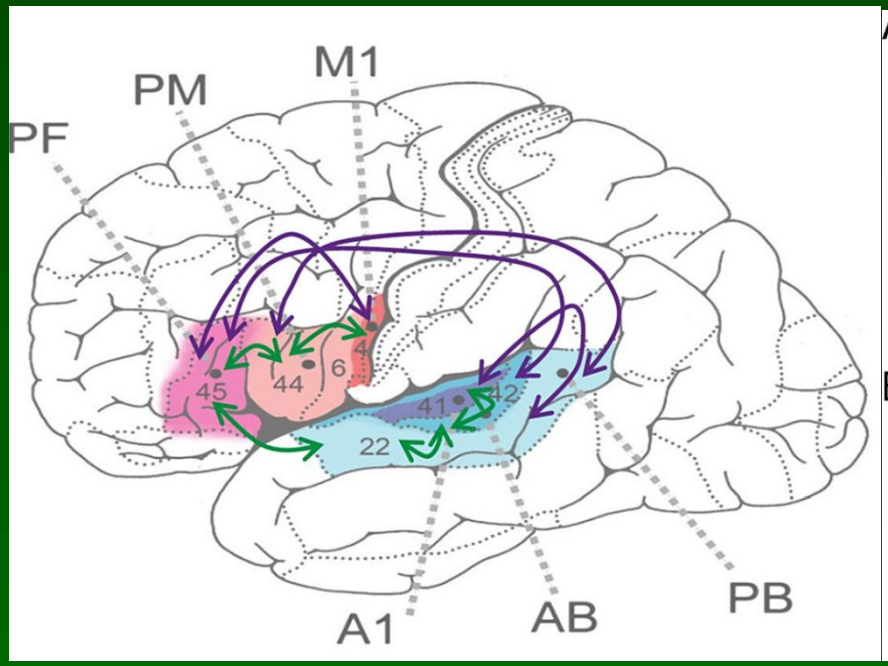
Fluid nature

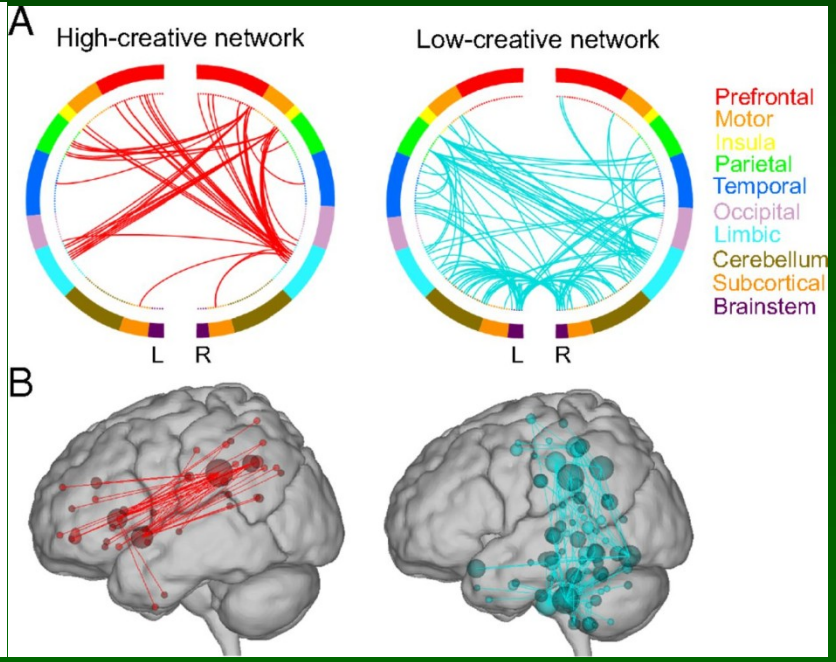
BABY a UNC / UMN collaboration
Connectome Project

Development of brain in infancy: first learning how to move, sensorimotor activity organizes brain network processes.

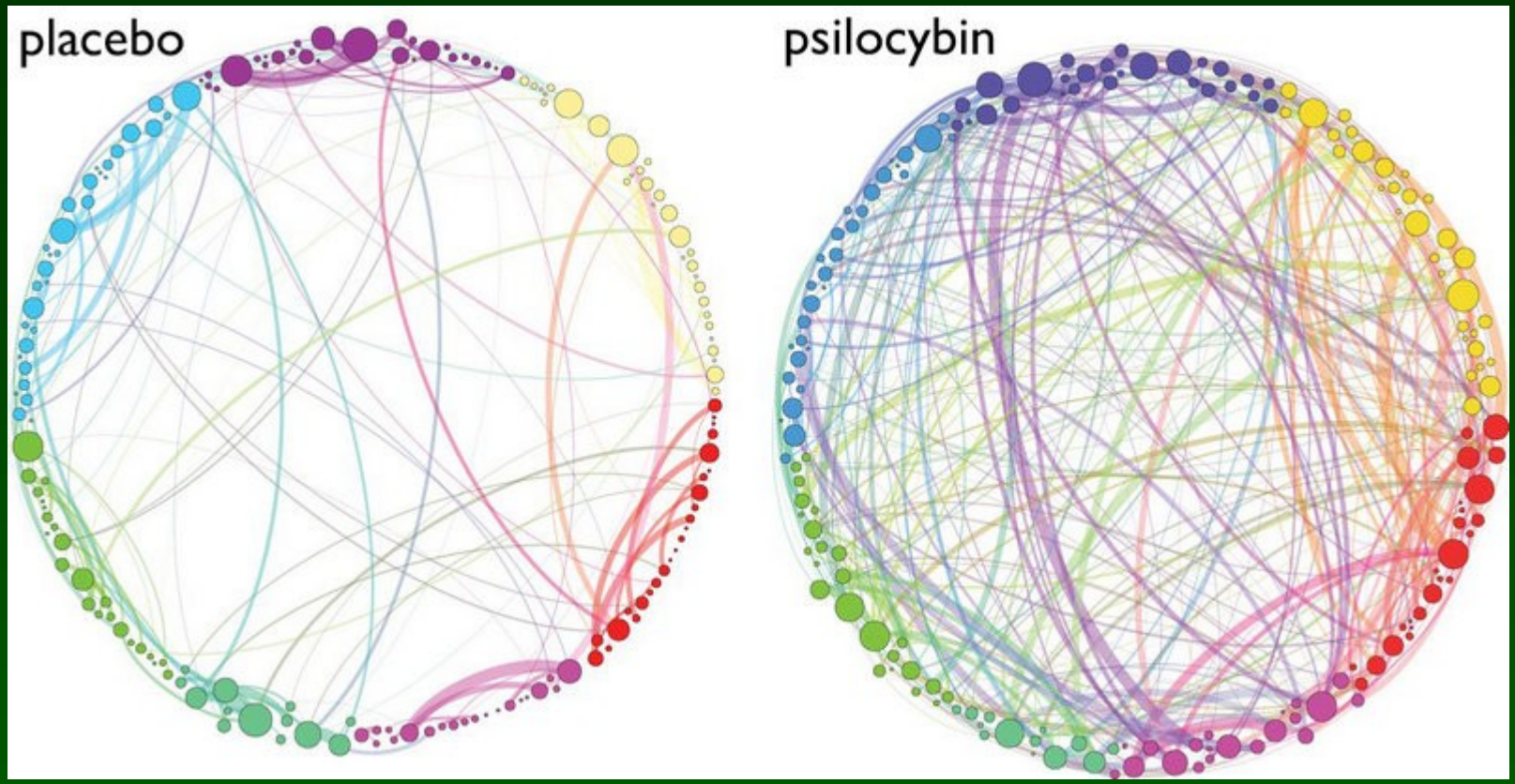
The Developing Human Connectome Project: create a dynamic map of human brain connectivity from 20 to 44 weeks post-conceptional age, which will link together imaging, clinical, behavioral, and genetic information.

Pointing, gestures, pre-linguistic (our BabyLab has a lot of EEG recordings).





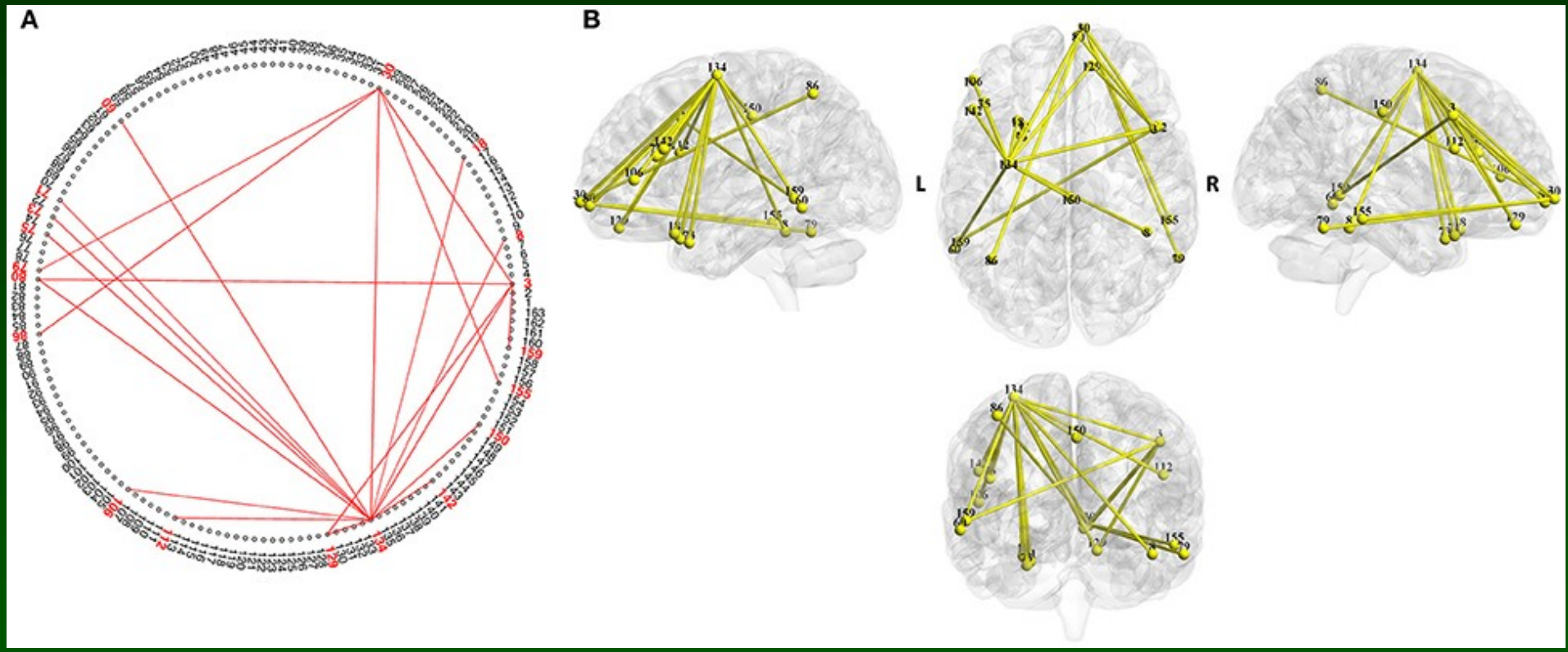
Hallucinations



What happens when 2mg of psilocibin (produced by fungi) is injected (or less than 100 micrograms of LSD or other hallucinagenic substances)?

All brain regions talk to other regions. Magic mushrooms and the brain article, and 2-min therapeutic brain effects of psylocibin and molecular aspects of neuroscience psylocib in activity. Human brain on LSD.

Verbal intelligence quotient



Brain map of the functional network for the psychometric parameter “verbal intelligence quotient (VIQ).” Line width ≈ the strength of the correlation. Approximates some mechanisms behind complex cognitive functions.

Sung et al. (2018). A Set of Functional Brain Networks for the Comprehensive Evaluation of Human Characteristics. *Frontiers in Neuroscience*, *12*.

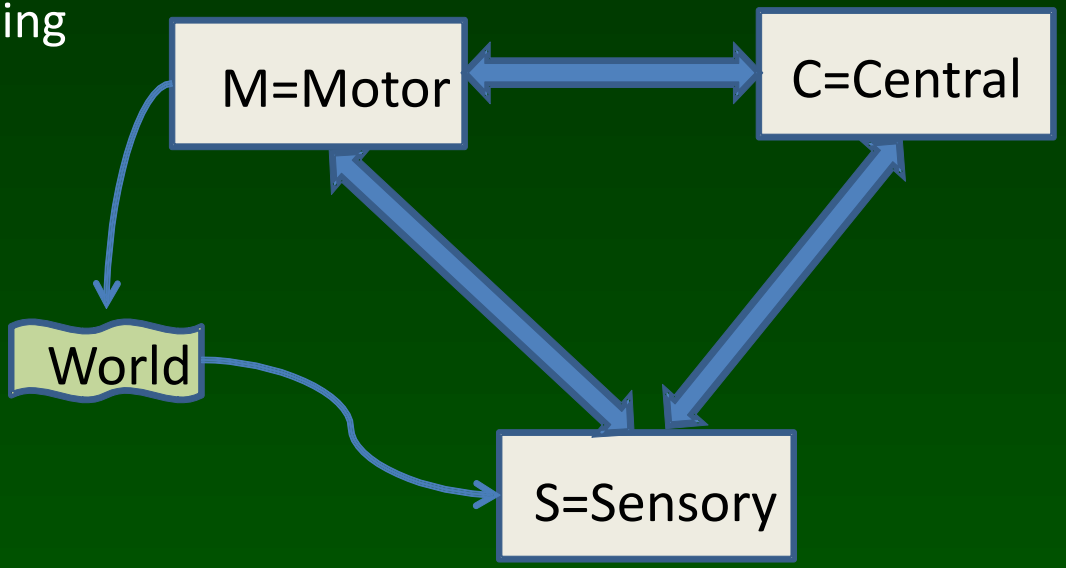
Connectome and learning styles

Simplest connectome models may help to explain and improve learning abilities.

S, Sensory level, occipital, STS, and somatosensory cortex;

C, central associative level, abstract concepts that have no sensory components,

mostly parietal, temporal and prefrontal lobes.



M, motor cortex, motor imagery & physical action.
Frontal cortex, basal ganglia.

Even without emotion and reward system predominance of activity within or between these areas explains many learning phenomena.

Duch. W. (2020) Experiential Learning Styles and Neurocognitive Phenomics. PsyArXiv. August 30, 2020

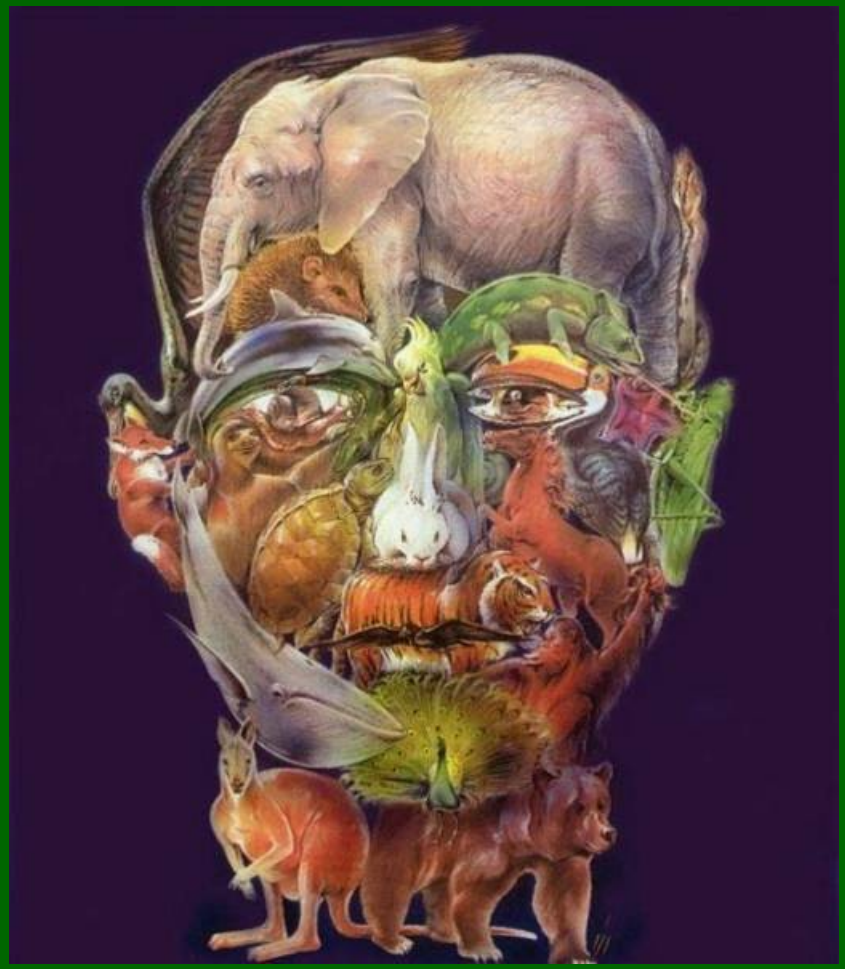
Learning abilities

Connectomes develops before birth and in the first years of life.

Achieving harmonious development is very difficult and depends on low-level (genetic, epigenetic, signaling pathways) processes, but may be influenced by experience and learning.

- Excess of low-level (sensory) processes S ⇔ S. Ex. ASD children.
- Poor C⇔C neural connections and synchronization, frontal⇔parietal necessary for abstract thinking, weak functional connections prefrontal lobe ⇔ other areas.
- Patterns of activation in the brain differ depending on whether the brain is doing social or nonsocial tasks.
- "Default brain network" involves several brain areas (mPFC, cingulate cortex, lateral PC), shows low activity for goal-related actions; strong activity in social and emotional processing, mindwandering, daydreaming.

Thank you for
synchronization
of your neurons



Google: Wlodzislaw Duch
=> talks, papers, lectures, Flipboard ...