PSYCH 260/BBH 203

History & Methods

Rick O. Gilmore

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Prelude (9:01)

Today's topics

- History of neuroscience
- Levels of analysis
- Methods to the madness

Warm-up

Neuroscience is harder than physics because…

- A. The brain has more parts than any other physical entity we know about.
- B. Physicists have largely ignored biology.
- C. Nervous systems are influenced by multiple factors we can’t (yet) measure effectively.
- D. Physicists only study “toy” problems.

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- D. Inputs and outputs
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History of neuroscience

Why study history?

- What can *observation* tell us about brain and behavior?
- Vital role of *tools/methods/techniques* in discovery
- *"If I have seen further, it is by standing on the shoulders of giants."* – Isaac Newton, 1676

What did early humans know about the mind and brain?

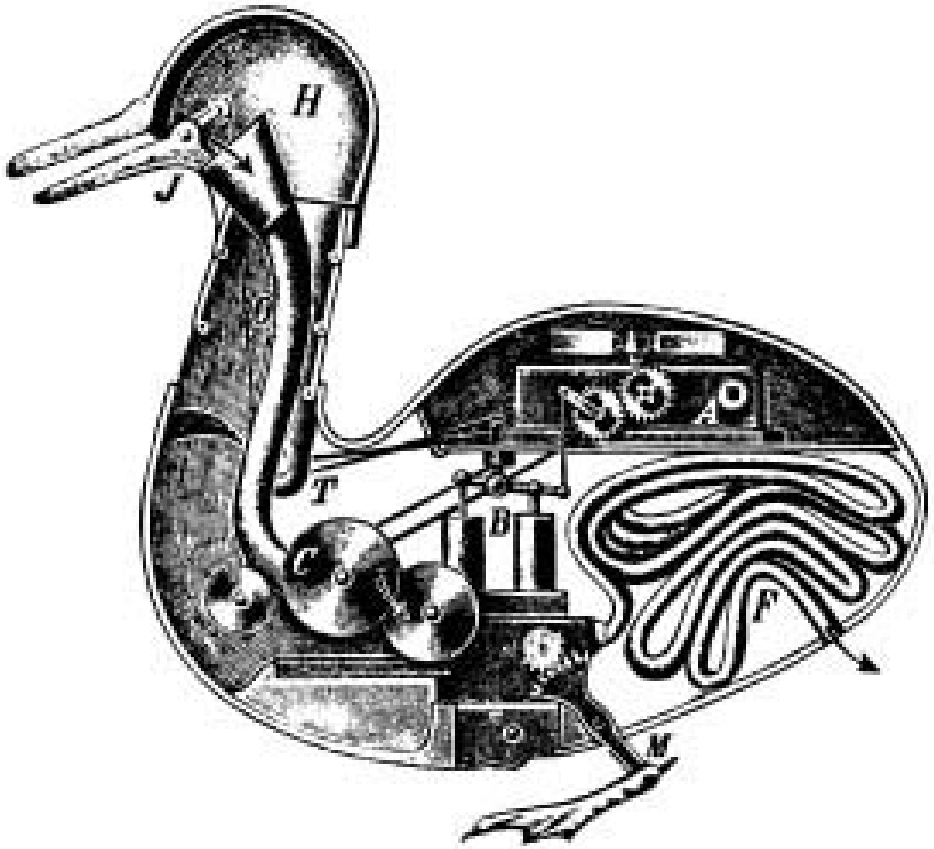
- Mental functions controlled by organs in the head, i.e., the brain
- Mental functions can be influenced by substances we consume
- Head injury can impair behavior and thinking
- Something flows from brain to body via nerves

Why didn’t they know more?

Why didn’t they know more?

- A. Limited technology.
- B. Limited cultural support for systematic observation & description. = SCIENCE
- C. Lack of ability to use knowledge even if it were acquired.

The body as machine (René Descartes – mid 1600's)



Descartes' 'reflexes'

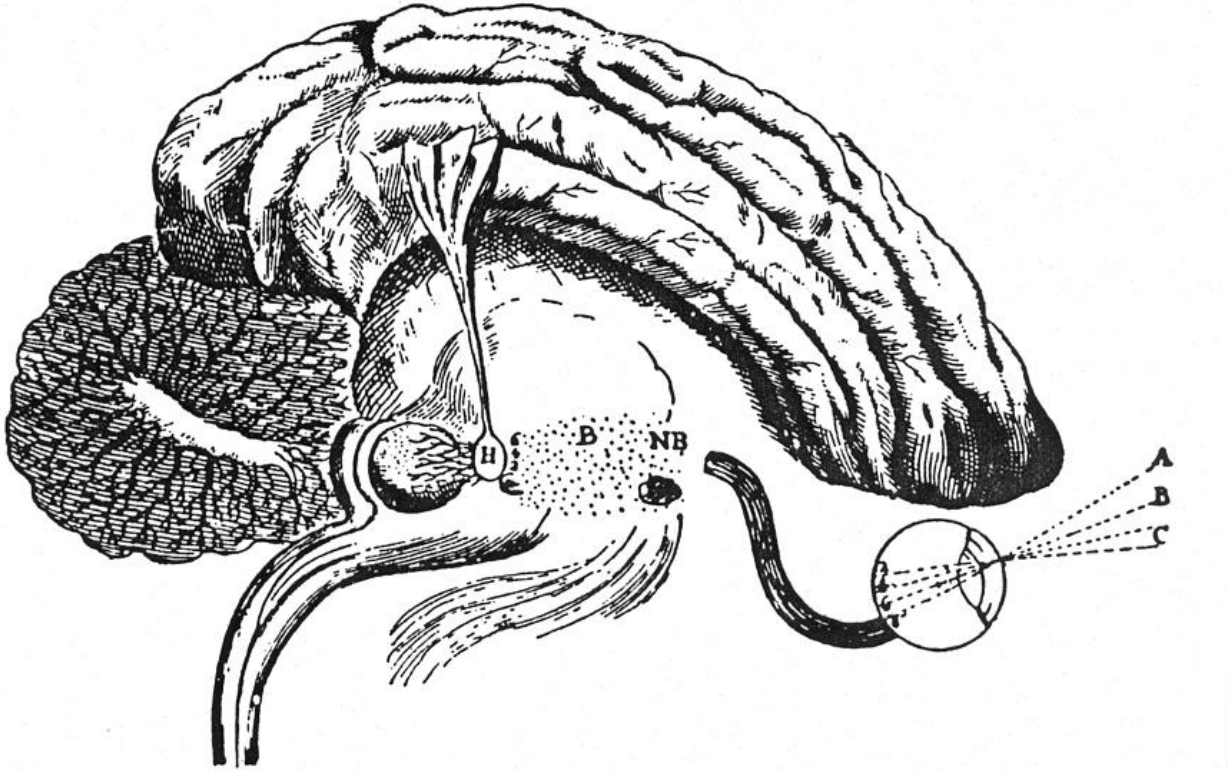
- Reflexes "reflect" events in the world
- Not the same as voluntary functions

Descartes' reflexes

Descartes' 'dualism'

- Reflexes and animal "minds" are physical, machine-like
- Human mind is not
  - "Dual" influences on behavior
  - Physical + spiritual
- Soul controls body via *pineal gland*
  - Causes muscles to "inflate"

Pineal gland



Do you agree with Descartes?

- A. **Yes**, human minds are fundamentally different from animal minds. The human mind is influenced by both physical and extraphysical processes.
- B. **No**, human minds are similar to animal minds. The human mind arises solely from physical processes.

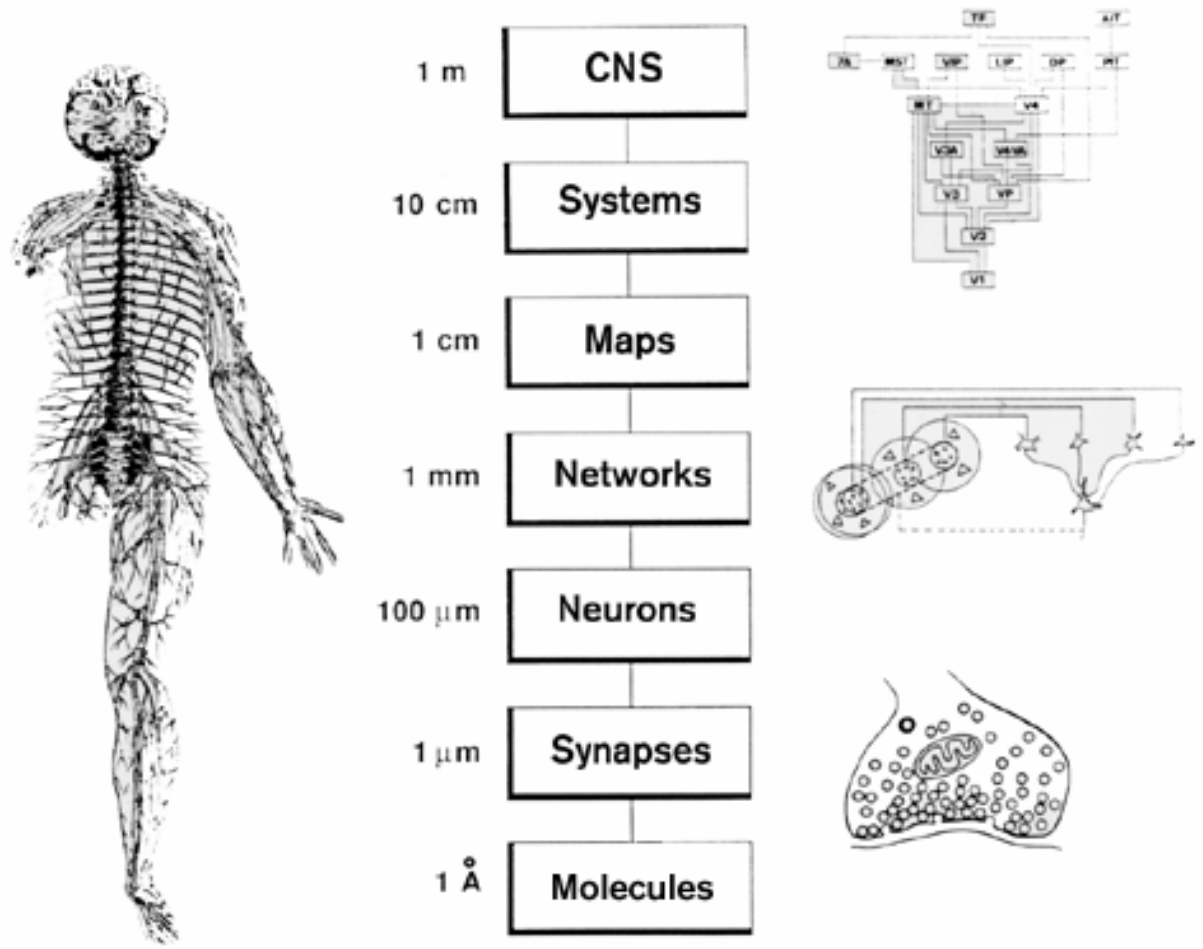
How would you test Descartes idea about the role of the pineal gland?

The lessons from history

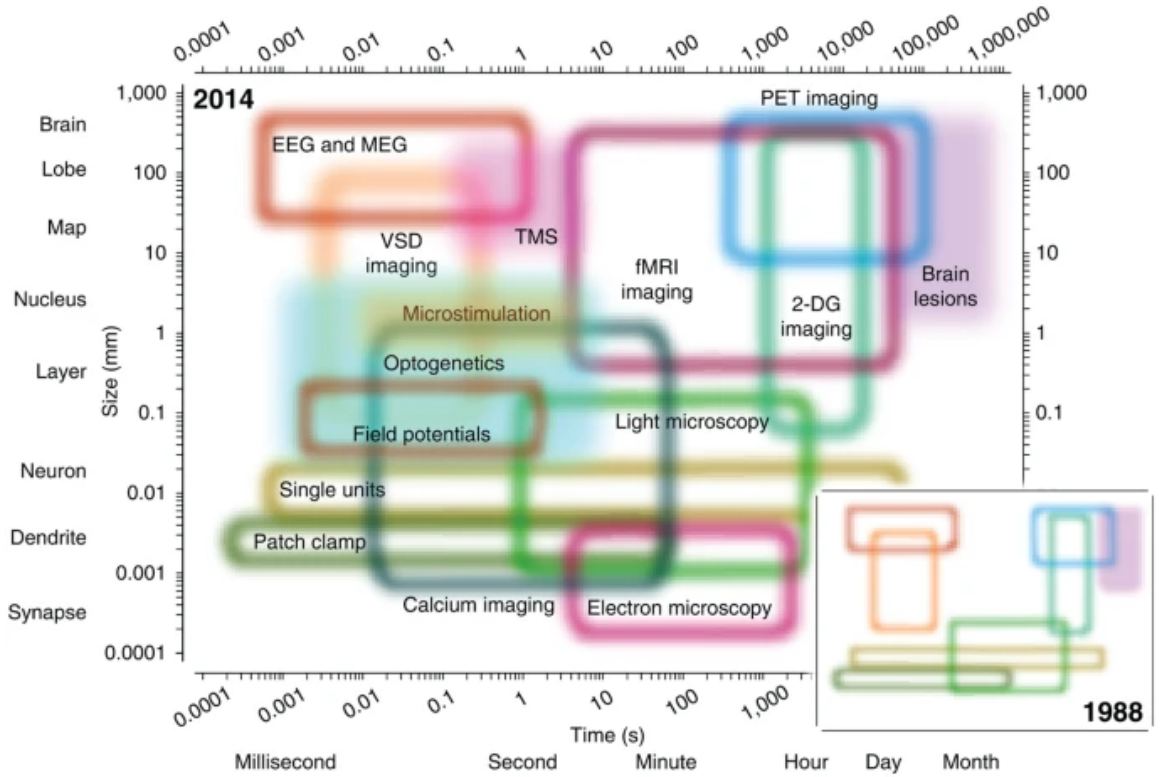
- Neuroscience shaped by new methods, tools
- Neuroscience shaped by great debates
  - Mind == brain debate
  - Are functions local or distributed?
  - Do neurons connect like pipes or pass info like relay runners?
- Forms at multiple levels of analysis contribute to function

Levels of analysis

Spatial resolution



Spatial and Temporal Resolution



(Sejnowski, Churchland, & Movshon, 2014)

Your turn

- What's a micro (spatially small) influence on/aspect of behavior?
- What's a macro (spatially large)…
- What's a micro (temporally short)…
- What's a macro (temporally long)…

Why does this matter?

- Different methods, different levels of analysis
- Challenge of linking phenomena across levels
    - How does the micro affect macro or vice versa?
- Challenge of interpretation

Neuroscience methods

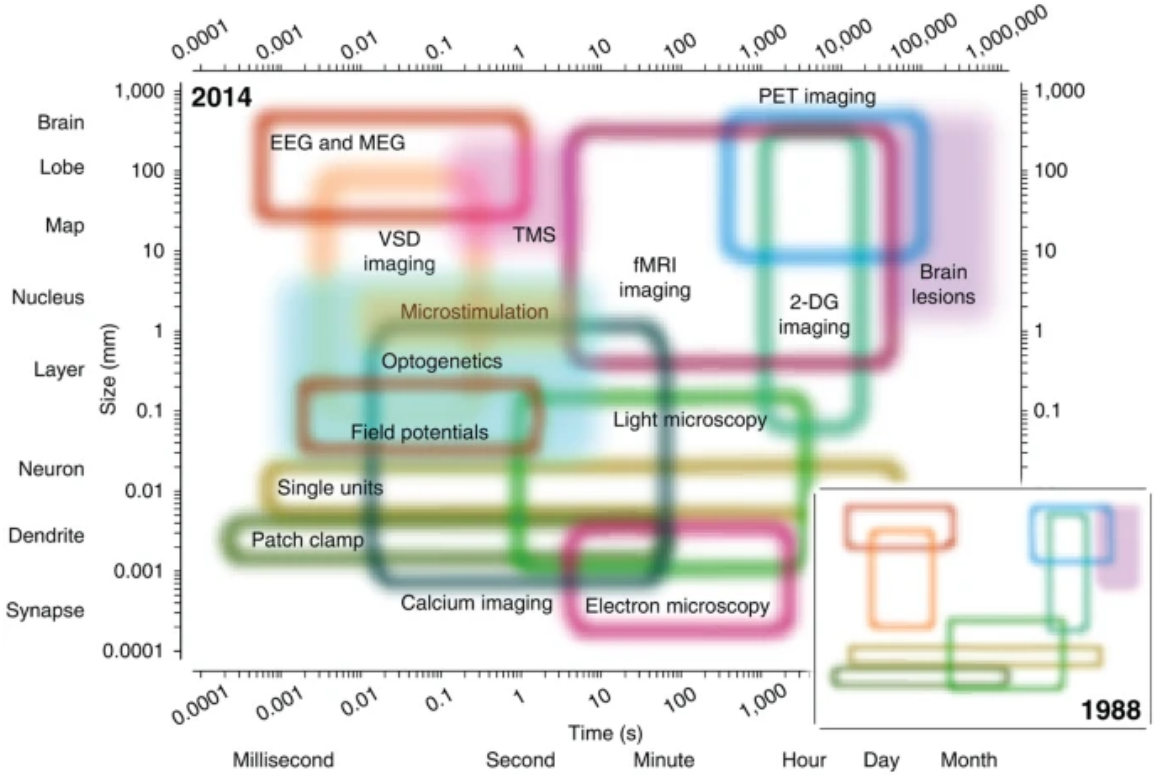
Methods to the madness

- Tools in the neuroscientist's toolkit
- What they tell us, and what they don't

Evaluating methods

- What question does method X answer?
- What are we measuring?
  - Structure
  - Activity
- Strengths & Weaknesses
  - Cost (time/$)
  - Invasiveness
  - Spatial/temporal resolution

Spatial and Temporal Resolution



Sejnowski et al. 2014

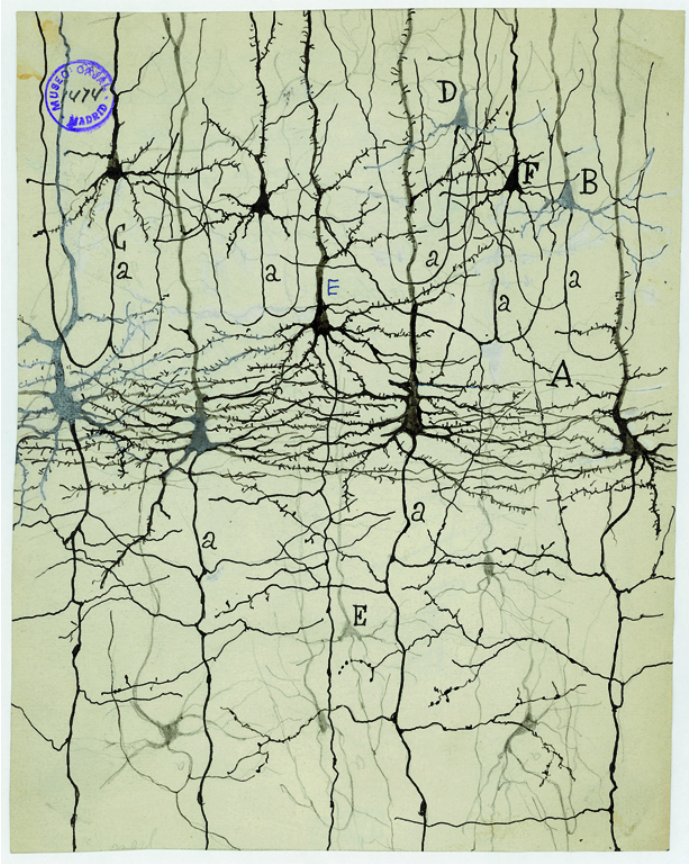
Types of methods

- Structural
  - What are the parts?
  - How do they connect?
- Functional (next time)
  - What do the parts do?

Mapping structures

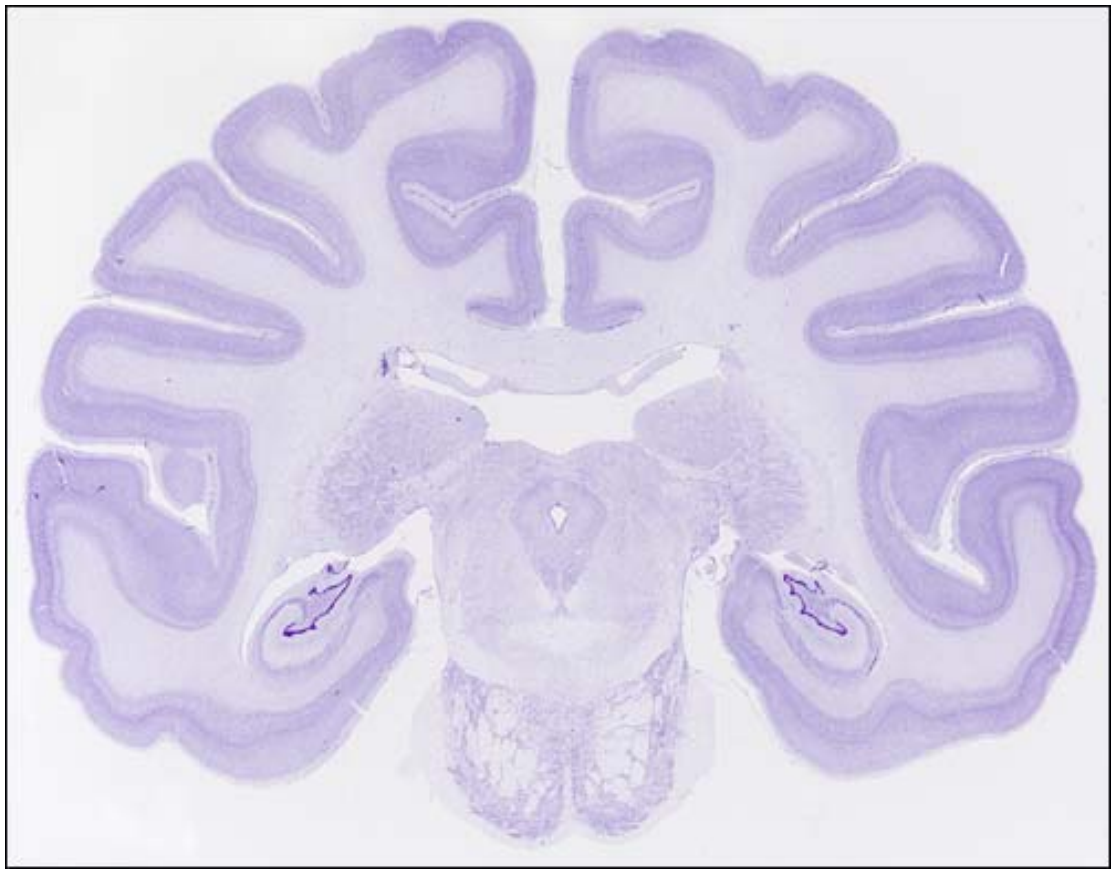
- Cell/axon stains
  - *Golgi stain* – whole cells
    - Camillo Golgi
  - *Nissl stain* – cell bodies only
    - Franz Nissl
  - Cellular distribution, concentration, microanatomy

Golgi stain



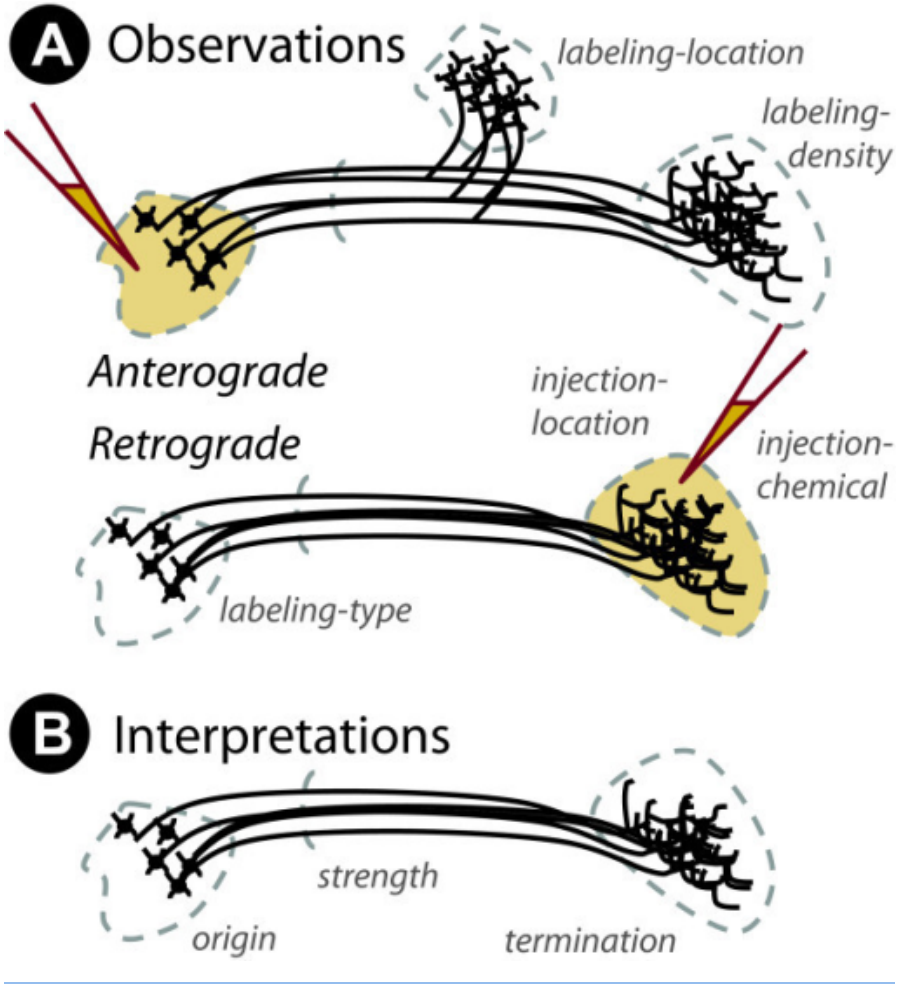
- Soak tissue in Potassium Dichromate ($K_2Cr_2O_7$) then apply Silver Nitrate ($AgNO_3$)
- Complete nerve cells, but only 1-5% of total
- Santiago Ramon y Cajal argued for *neuron doctrine*, shared 1906 Nobel Prize with Golgi

Nissl stain



- Only cell bodies
- Density of staining ~ cell density/number

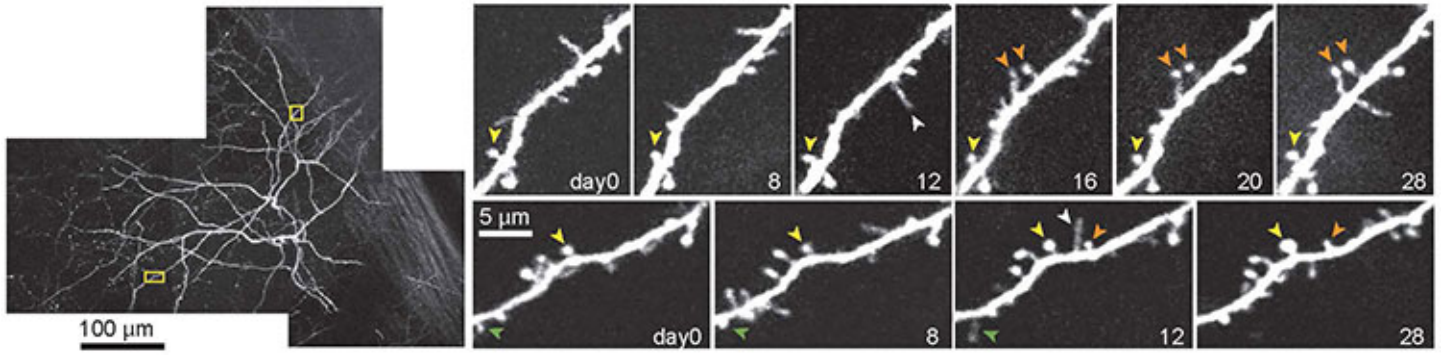
Histochemical tracers



Retrograde vs. anterograde tracers

- Neuron information flow *polarized*–flows in one direction
    - ≠ electronic wires, but like pipes
- *Retrograde* (from *axon terminal* to *cell body*)
- *Anterograde* (from cell body to axon terminal)

Two-photon microscopy



https://www.brainfacts.org/in-the-lab/tools-and-techniques/2021/meet-the-inventors-of-two-photon-microscopy-120721

“If understanding everything we need to know about the brain is a mile, how far have we walked?” – J. Lichtman

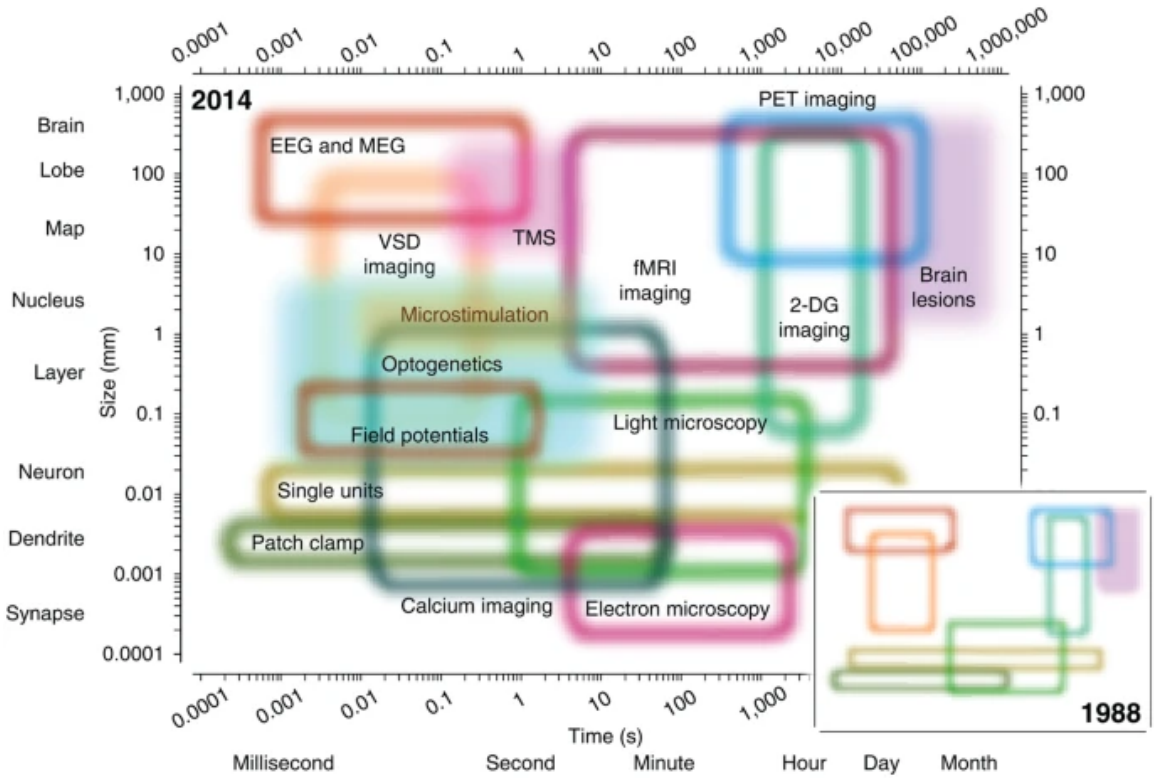
(National Geographic, 2014)

Clarity

[Video2013-bj]

Evaluating cellular techniques

- Pros:
  - High spatial resolution
- Cons:
  - Poor temporal resolution
  - Invasive

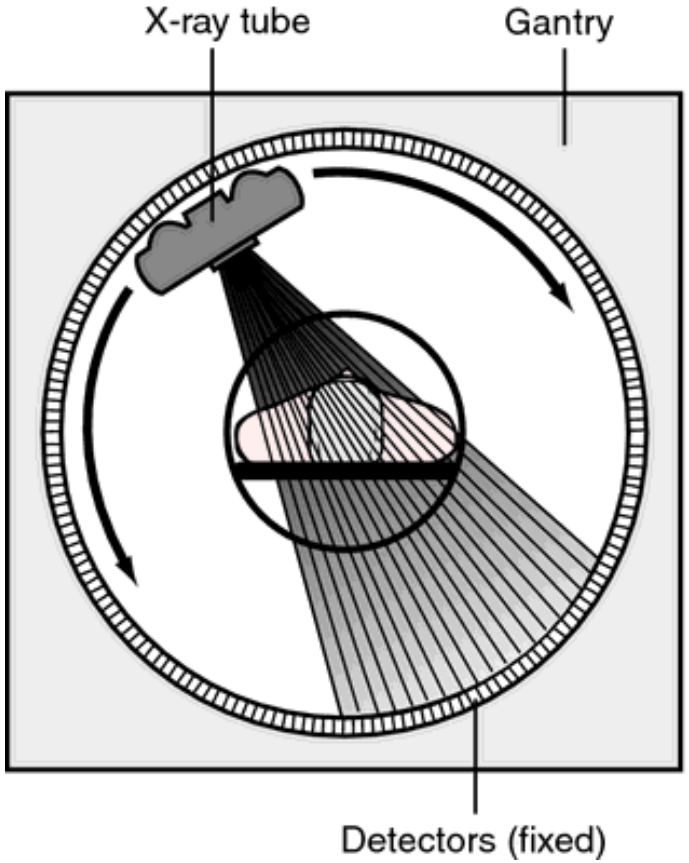


Sejnowski 2014

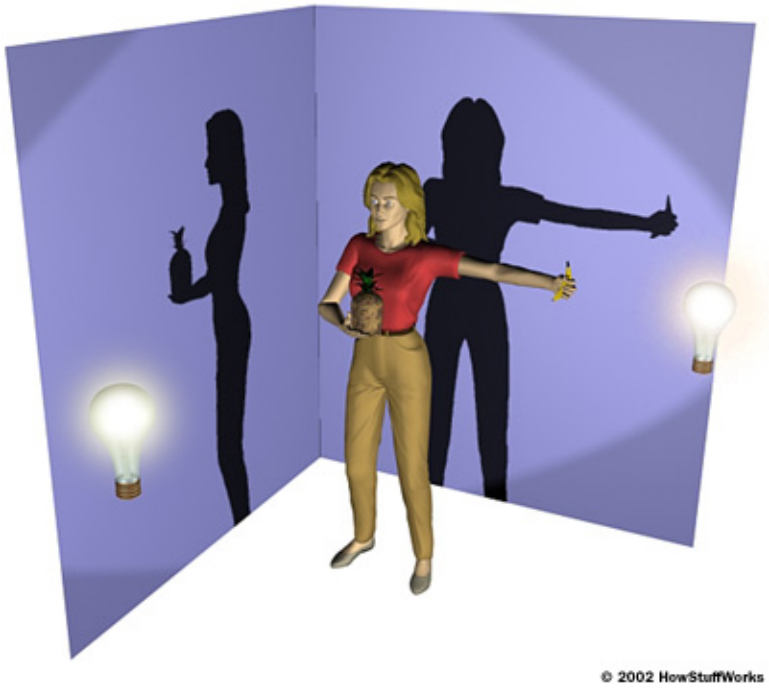
Computed axial tomography (CAT)

- Computed tomography CT
- X-ray based

Tomography

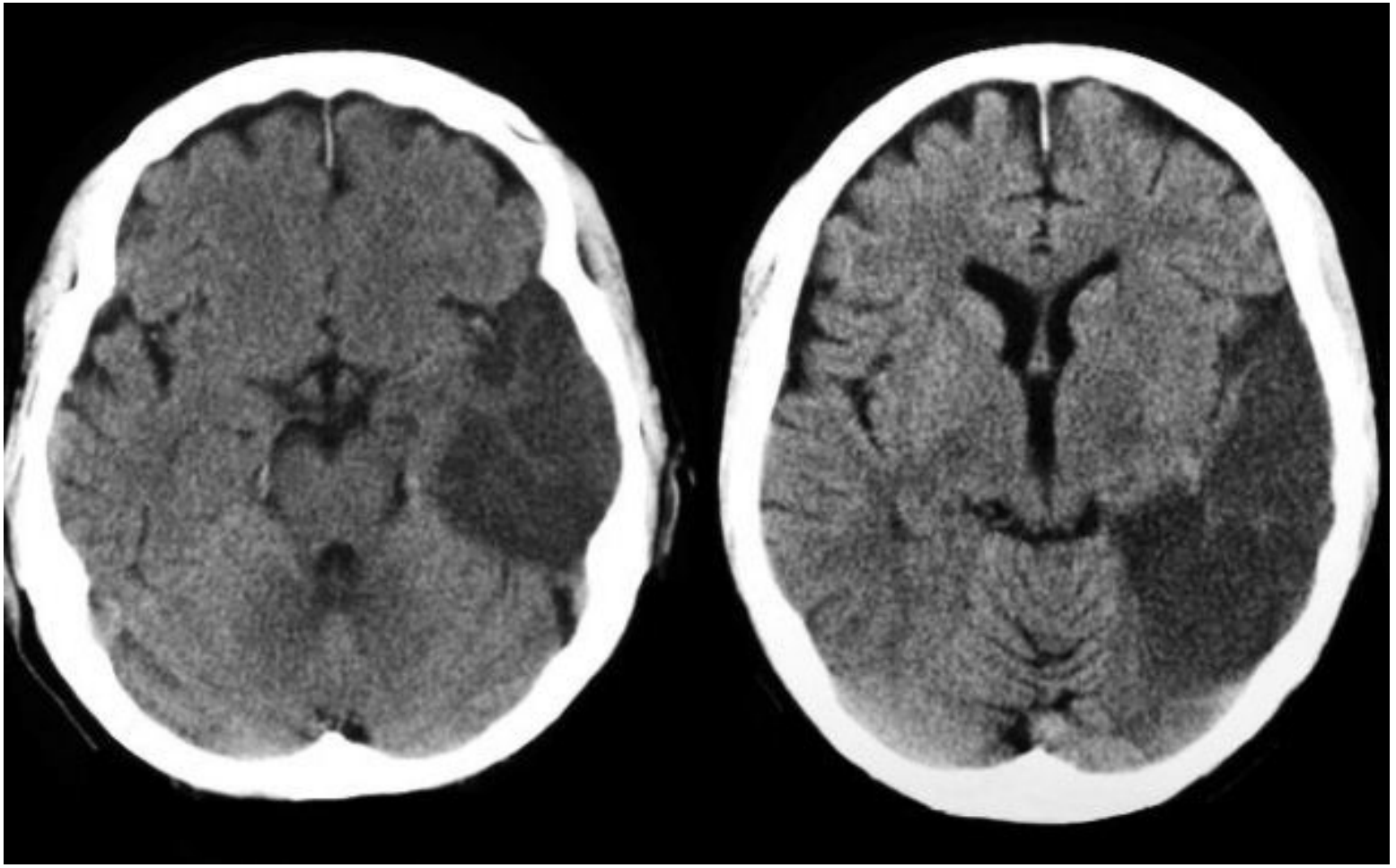


Tomography



https://cdn.hswstatic.com/gif/cat-scan-pineapple.jpg

CT scan of stroke



Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI)

- Magnetic resonance
- Some common isotopes (e.g., H) & complex molecules have a magnetic dipole
- Axes align with strong magnetic field
- When alignment perturbed by radio frequency (RF) pulse, speed of realignment varies by tissue
- Realignment emits RF signals
- How MRI works

Types of MRI

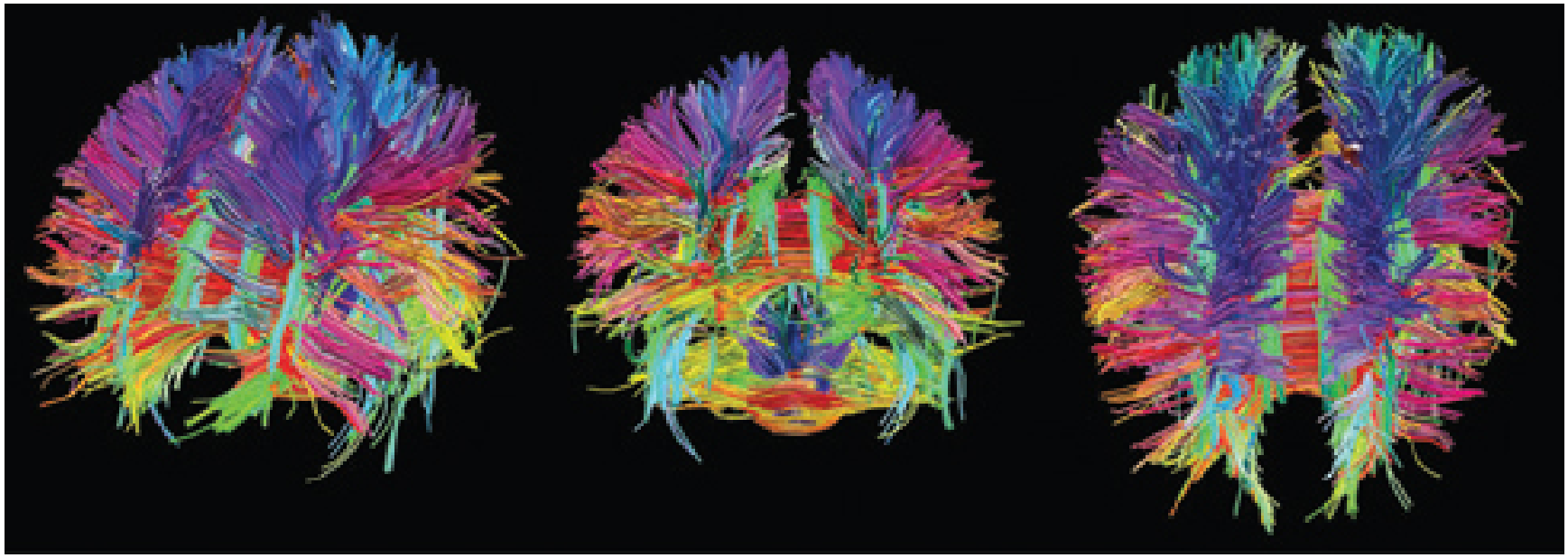
- Structural
- Functional

Structural MRI of the brain

Structural MRI

- Reveals tissue density/type differences
- Gray matter (neurons & dendrites & axons & glia) vs. white matter (mostly axons)

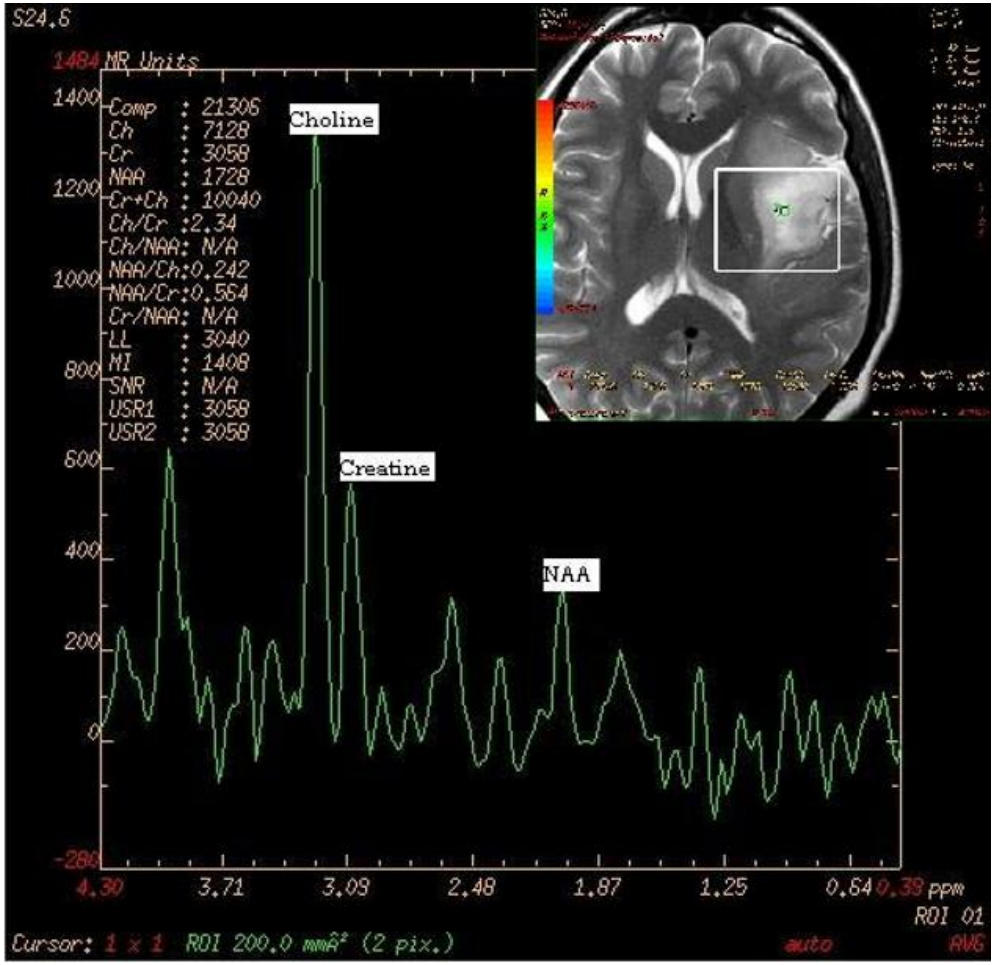
Diffusion tensor imaging (DTI)



Diffusion tensor imaging (DTI)

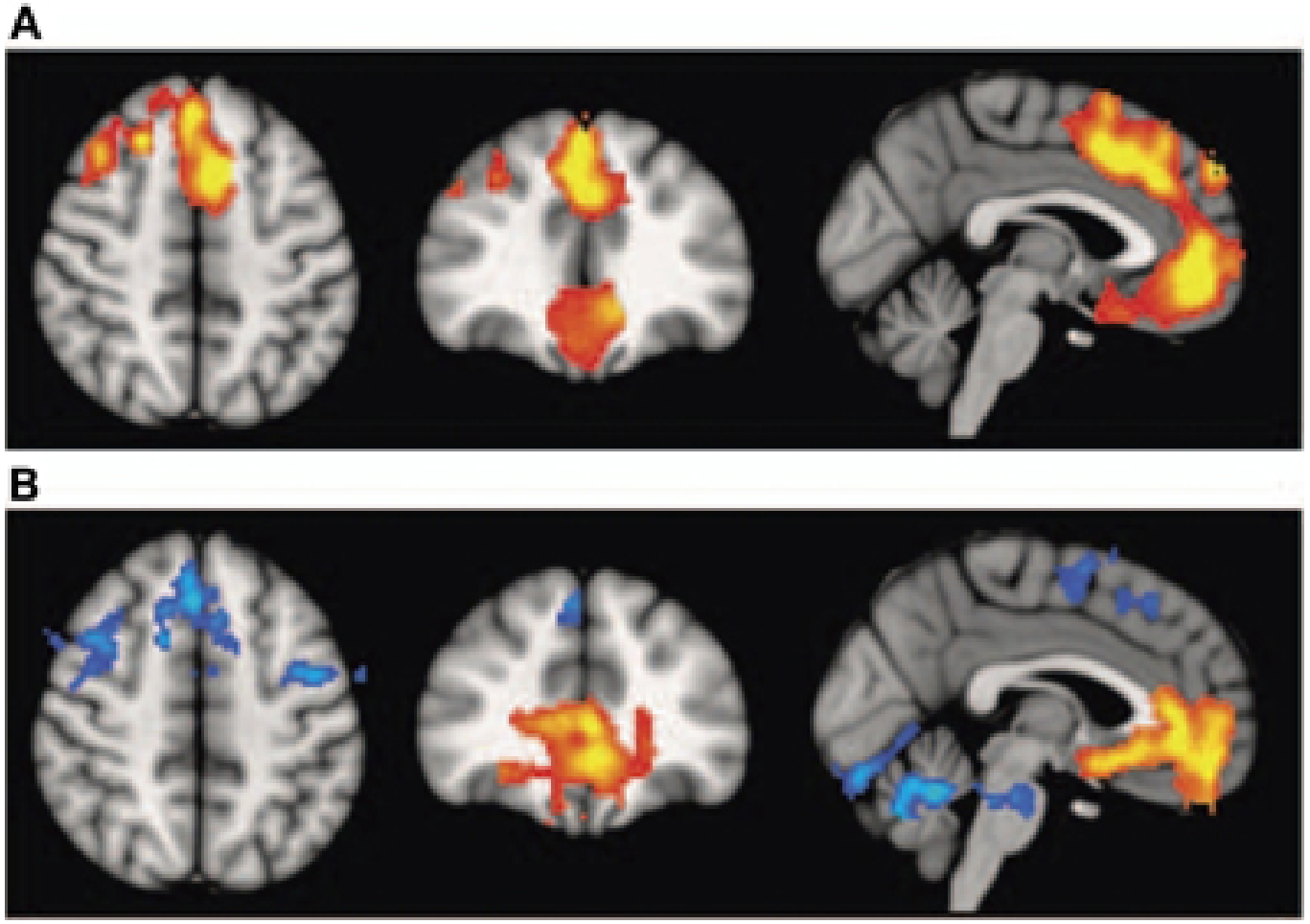
- Type of structural MRI
- Measures patterns of movement/diffusion of H_2O
- Reveals integrity/density of axon fibers
- Measure of connectivity

MR Spectroscopy



https://radiopaedia.org/cases/glioma-mr-spectroscopy

Voxel-based morphometry (VBM)



(Williamson & Allman, 2012)

Voxel-based morphometry (VBM)

- Voxels (volume-based elements)
  - like pixels in an image, but volumes of tissue
- Morphometry, measure (“metry”) form/morphology
- How does brain size or thickness vary by age, disease status, etc.?

Main points

- Spatial vs. temporal resolution
- Structural methods (parts, sizes, connectivity)

Next time…

- *Functional* neuroscience methods

References

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