# Surprising stories about the human brain


## Brian A. Wandell

Wu Tsai Neurosciences Institute
Stanford Center for Cognitive and Neurobiological Imaging



# Wu Tsai Neurosciences Institute building (March 19, 2019)

25 research labs (10 new hires)
Theory center (6 PIs)
Campus hub for 200 neuroscience labs
Building to be occupied fall 2019

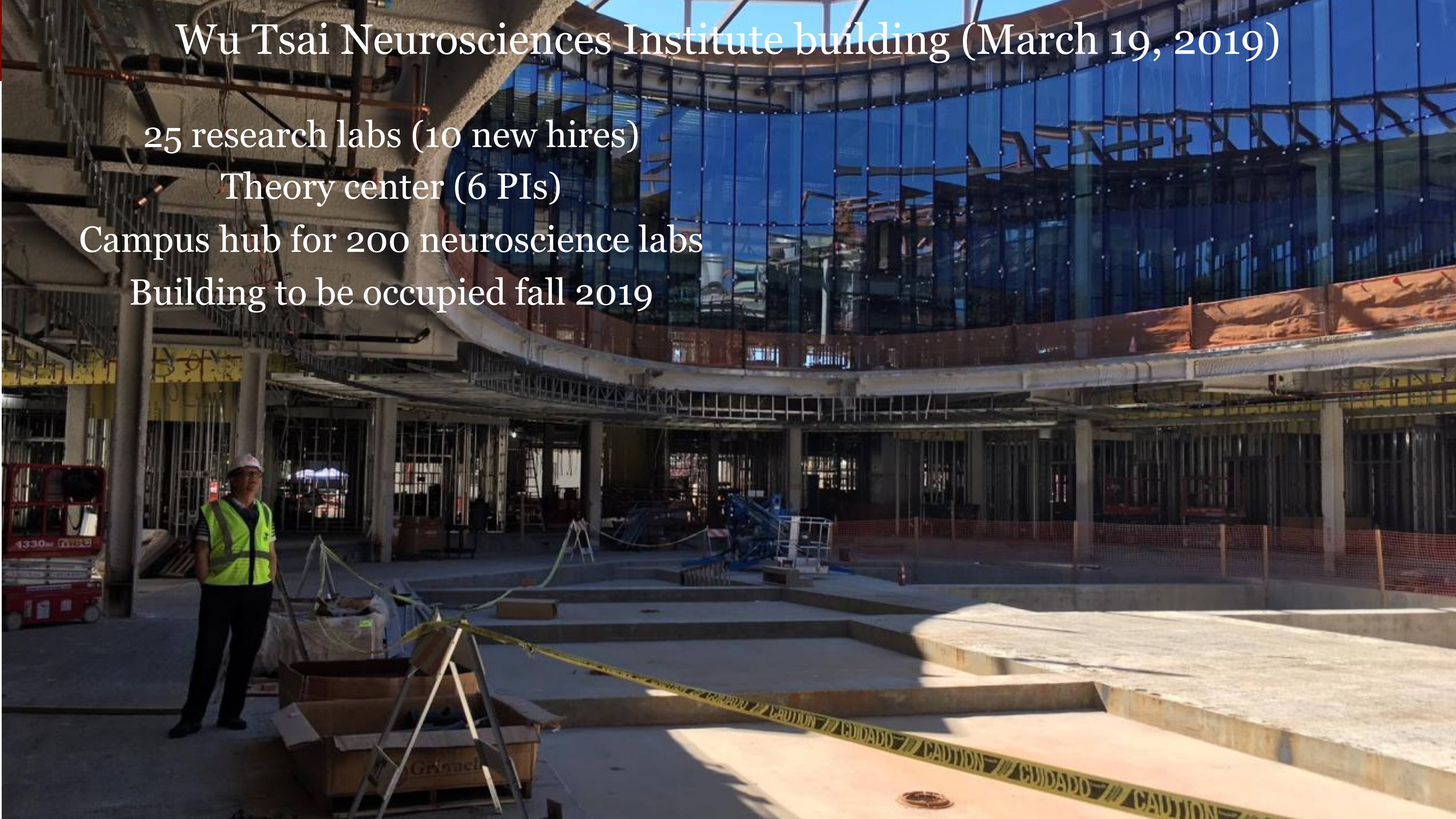
# Wu Tsai Neurosciences Institute building (March 19, 2019)

25 research labs (10 new hires)

Theory center (6 PIs)

Campus hub for 200 neuroscience labs

Building to be occupied fall 2019



# WU TSAI NEUROSCIENCES INSTITUTE - 2014-2019

## *Neuro-Discovery*

Our scientists develop cutting-edge techniques to make fundamental discoveries in brain science — discoveries that could unlock new medical treatments, transform education, inform public policy

## *Neuro-Engineering*

Our engineers are developing ways to manipulate neural circuits with electricity, light, ultrasound and magnetic fields. They are inventing algorithms and theories to guide understanding

## *Neuro-Health*

Our clinicians collaborate with scientists and engineers to pioneer novel treatments for psychiatric and neurological disease, easing the devastating consequences of diseases such as stroke, epilepsy, and depression.

# Stanford's Center for Cognitive and Neurobiological Imaging (CNI)

- Support neuroscience discovery for enhancing society
- Develop and disseminate imaging methods
- Create a structured, safe, and innovative teaching environment for human neuroscience research

# Installing the MRI scanner at the CNI (2008)



# CNI: The most heavily used MRI research scanner on Stanford campus

## CNI Investigators

Users from Med School, Basic Sciences, Engineering, Ed School and Business School

More than 40 research groups and 200 grants

More than 1050 students and postdocs trained

## CNI Data

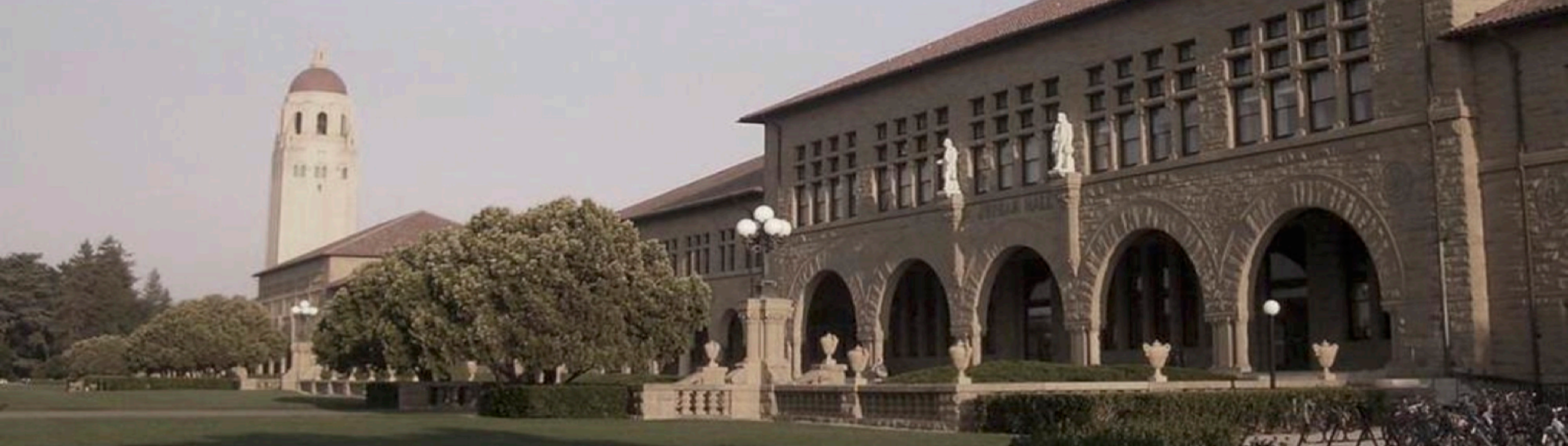
6,000 subjects

100 T of MRI data just at this one center

Scanner uptime estimated at 99%

# Main points

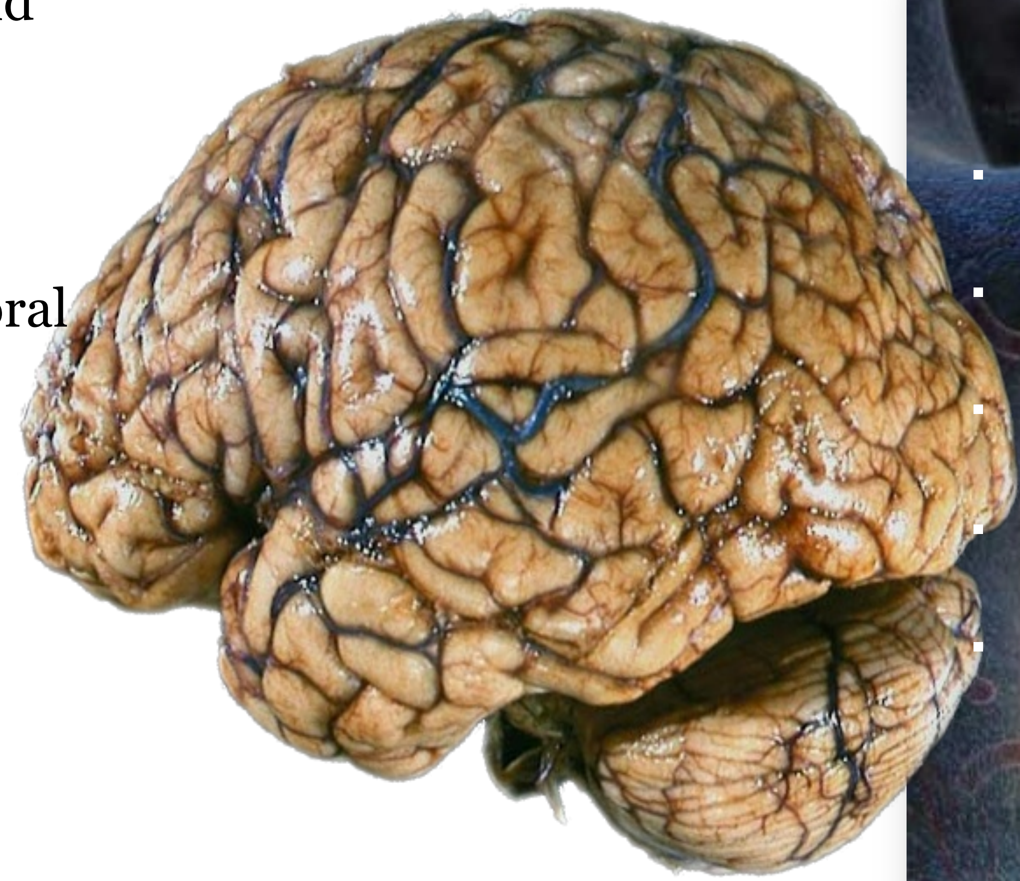
- The human brain – its size and some of its properties
- How we see
- Mis-wiring at birth:  Amazing recovery
- Damage a few years later: Not much recovery
- Putting the parts together: Reading circuitry

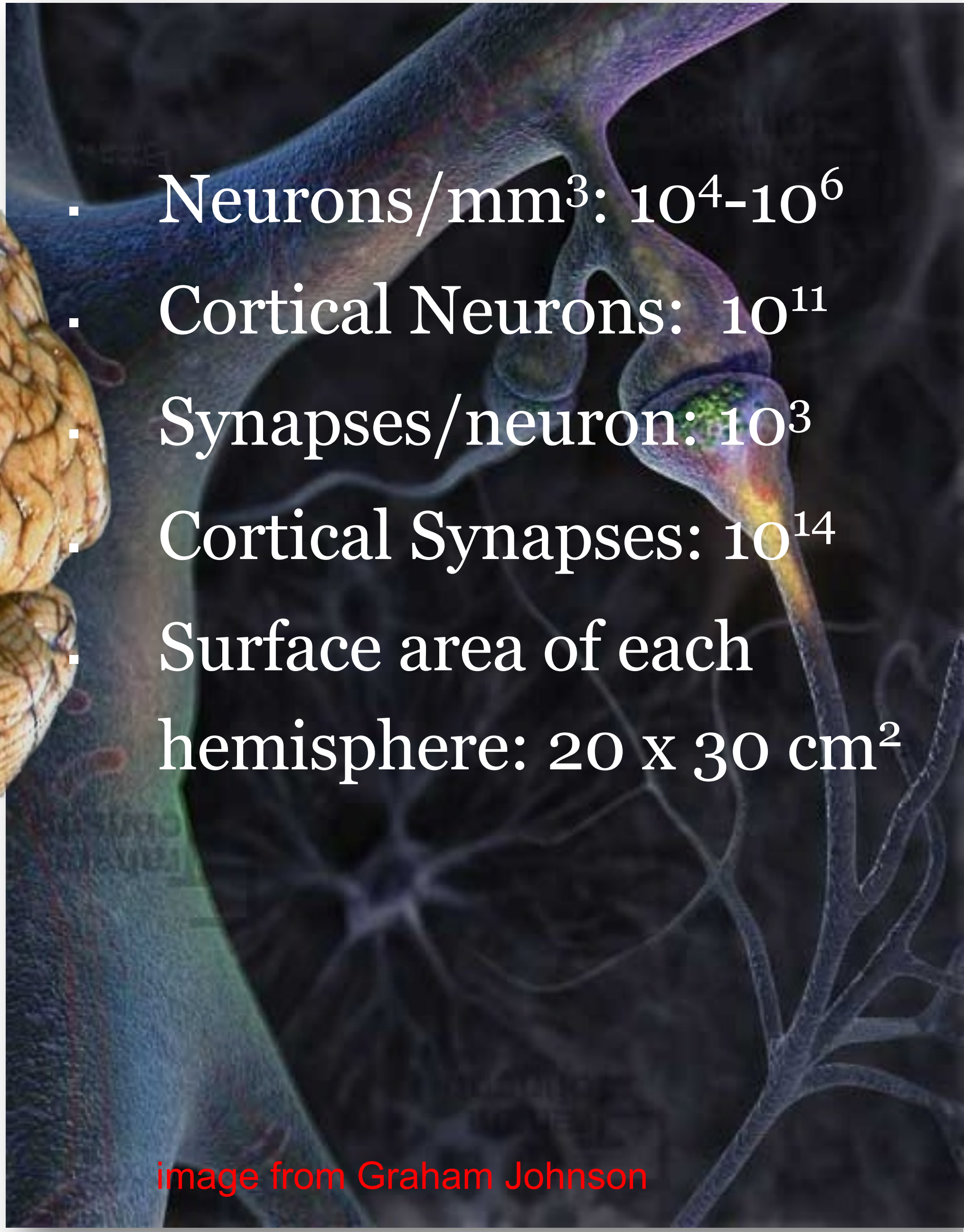


# Cortical computational elements

Brain computations depend on a variety of cells; one important cell type, the neurons, have their cell bodies located in the cerebral cortex (gray matter).

The cortex is a sheet (2-4 mm thick) of tissue that covers the surface of the brain; other subcortical regions and types of cells matter too!





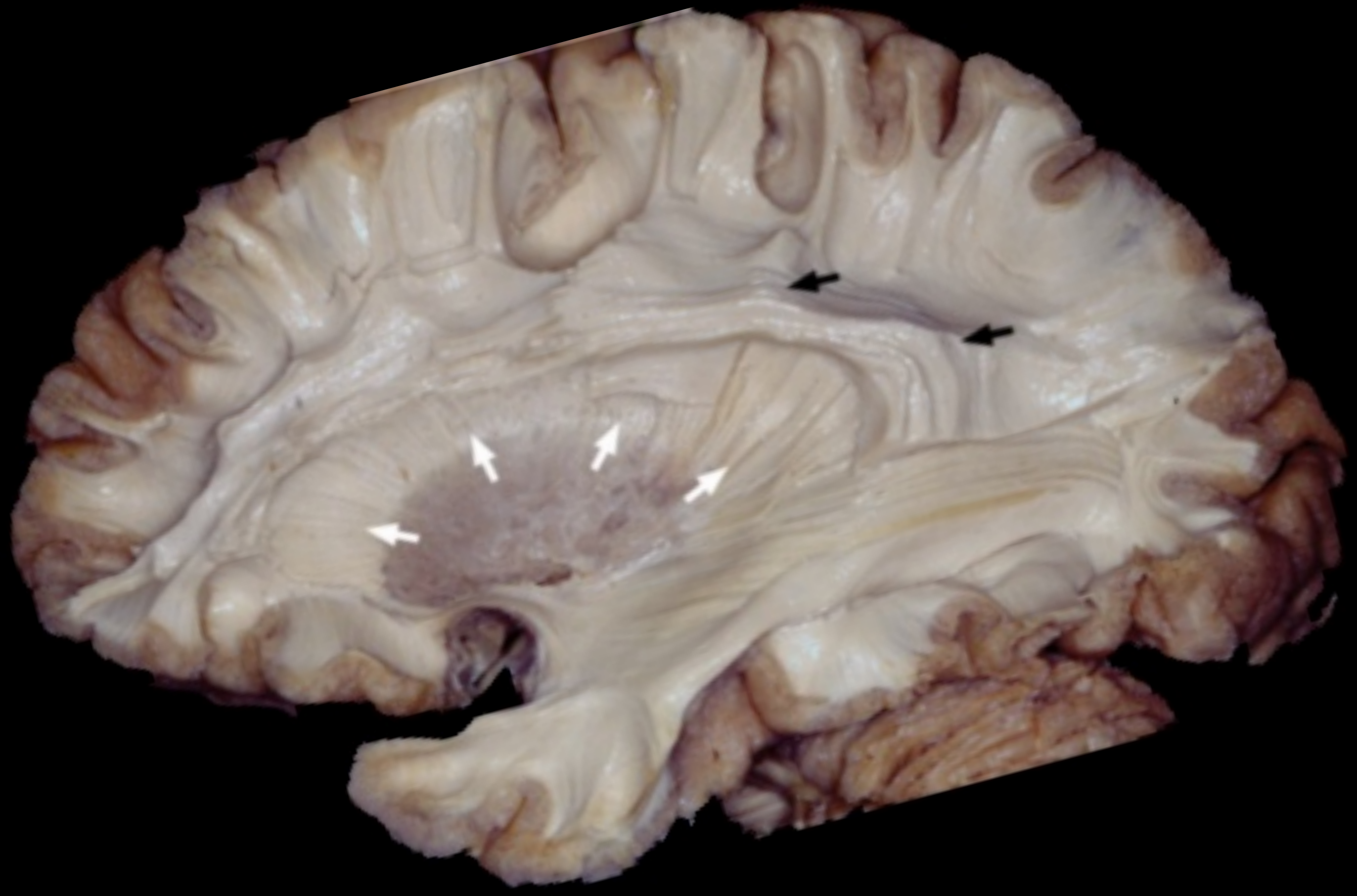
- Neurons/mm$^3$: $10^4$-$10^6$
- Cortical Neurons: $10^{11}$
- Synapses/neuron: $10^3$
- Cortical Synapses: $10^{14}$
- Surface area of each hemisphere: 20 x 30 cm$^2$

image from Graham Johnson

<u>Neuron</u>: impulse-conducting cell; bodies are in the cerebral cortex
<u>Axon</u>: a thin fiber that carries the output impulses from a neuron
<u>Dendrite</u>: a branching process of a neuron that receives impulses from other neurons
<u>Synapse</u>**:** The point of connection between neurons

# Long-range communication architecture (tracts)

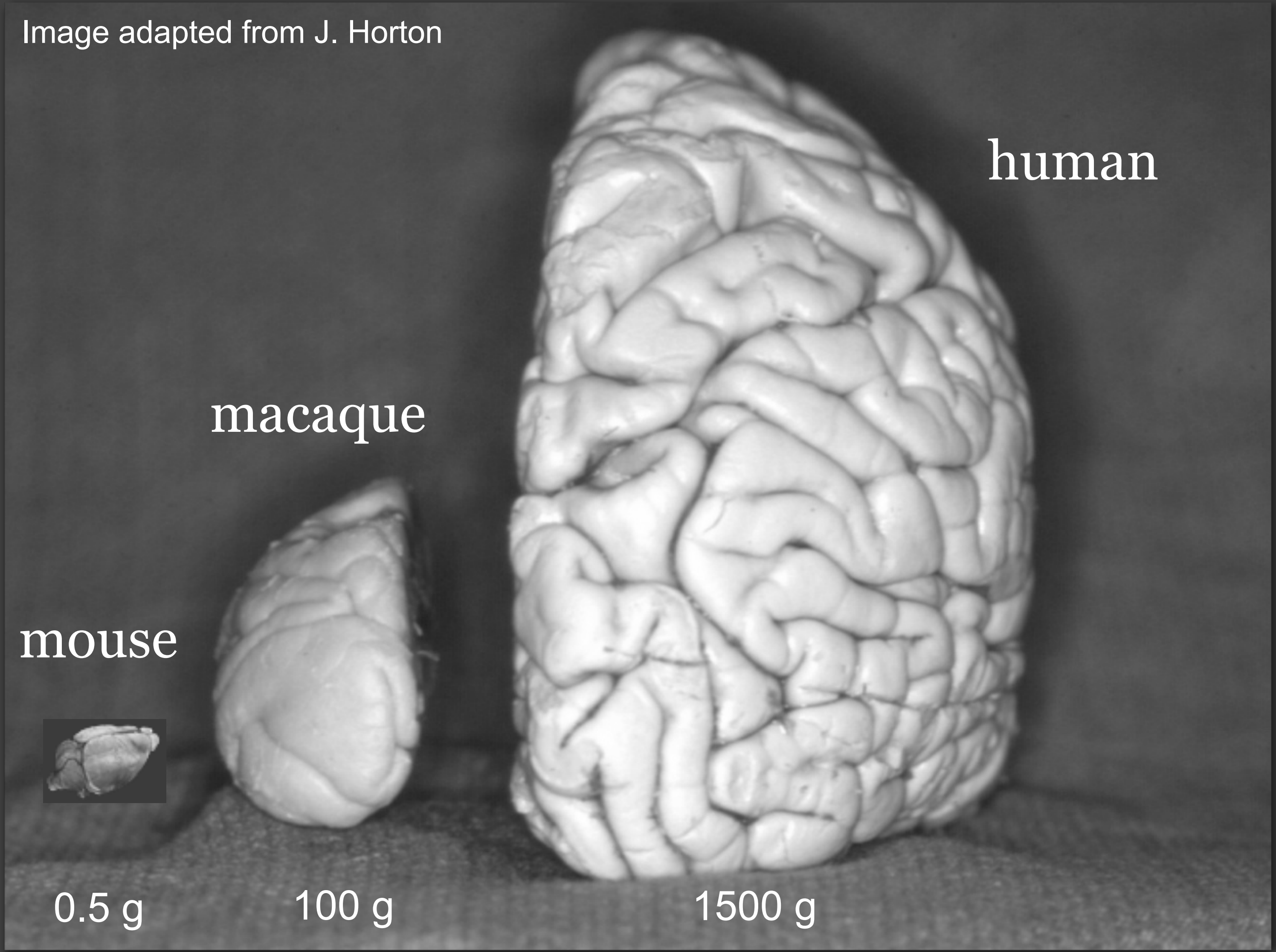
- There are many long-range connections
- These connections are not passive – they change their properties in response to use
- A system with active wires



*Courtesy Professor Ugur Ture*

# The human brain

## 1: 15: 3000 (volume ratios)




- Brains differ
- Check which system was measured

# Human functional and anatomical MRI

- Basic facts about the human brain and how we see

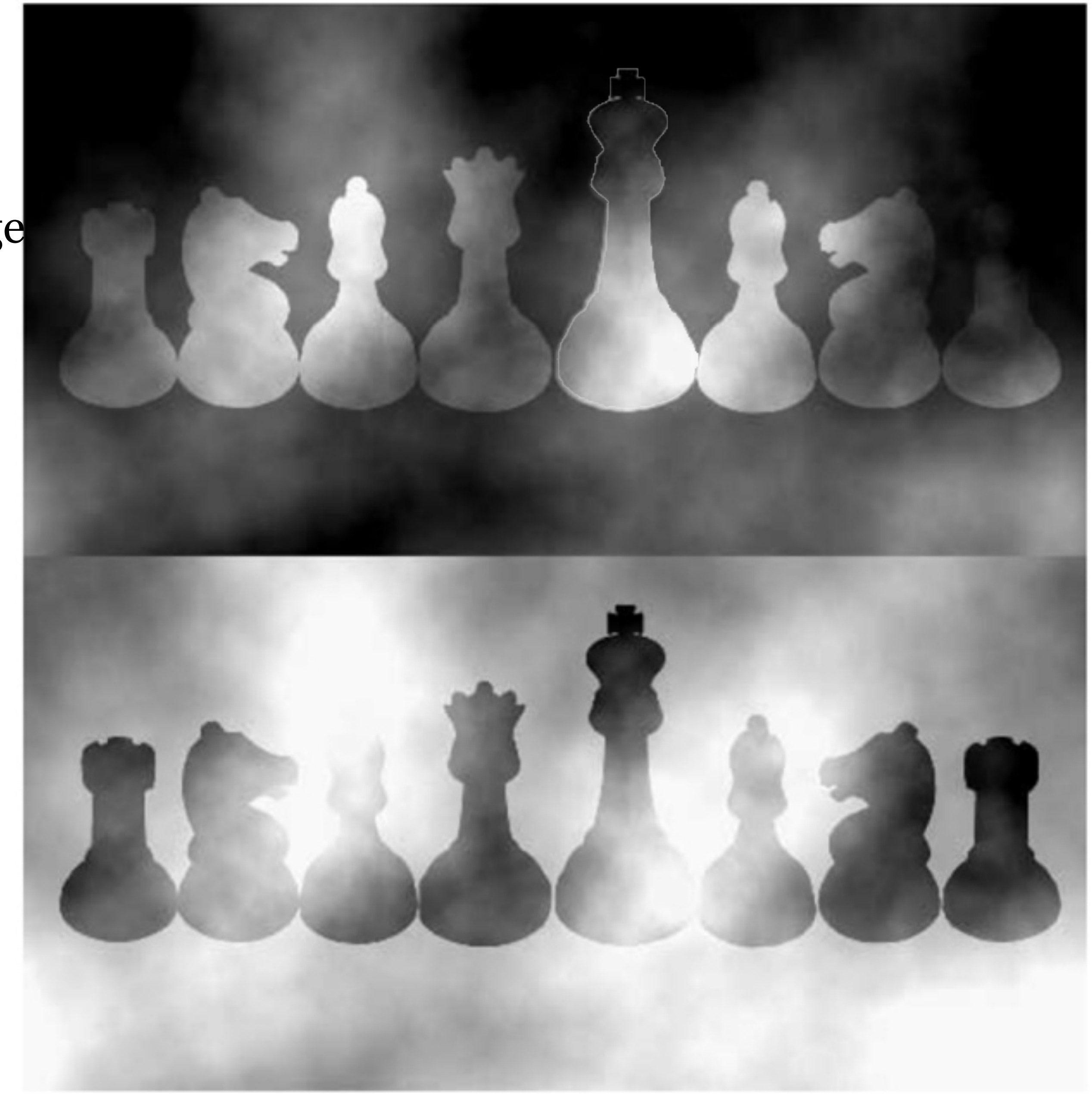
# Vision and computation

- Even simple judgments – such as lightness - depend on substantial interpretation of the image data carried out by brain circuits

- The vision science has been influential in developing principles for other neuroscience fields and artificial intelligence

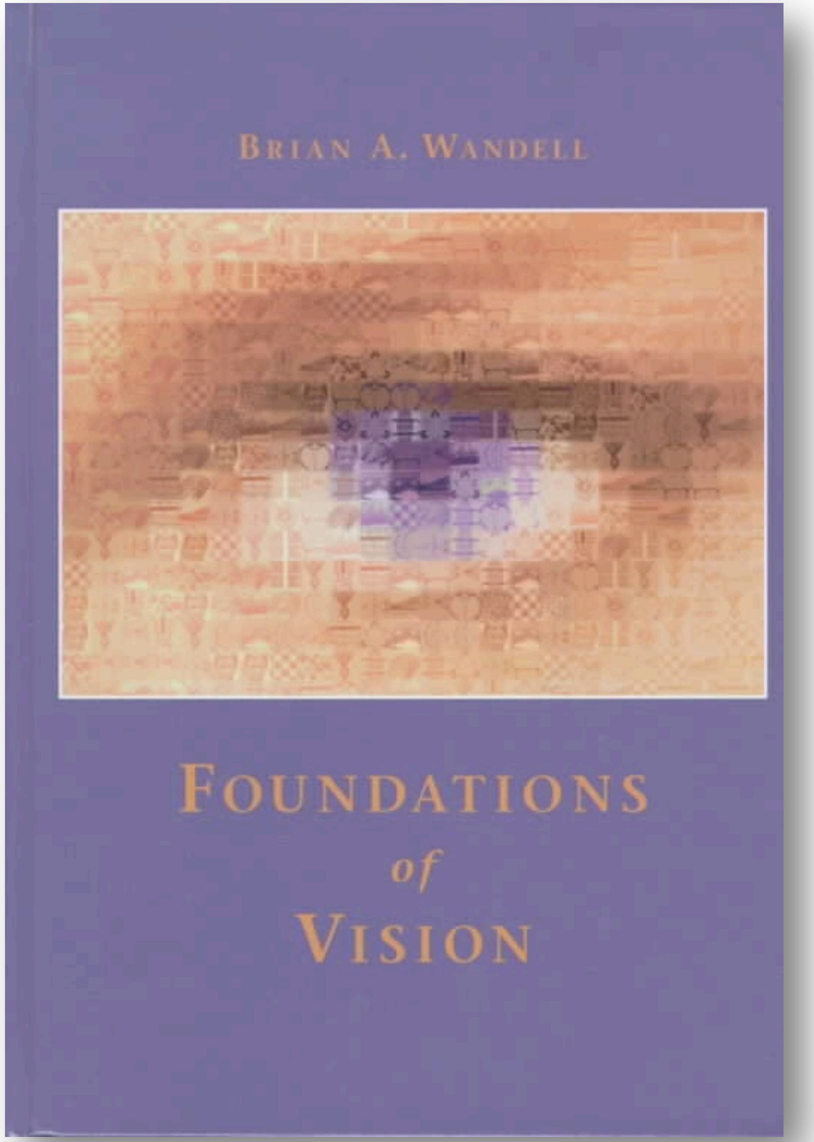
- Vision science fundamentals are important for the entire imaging industry

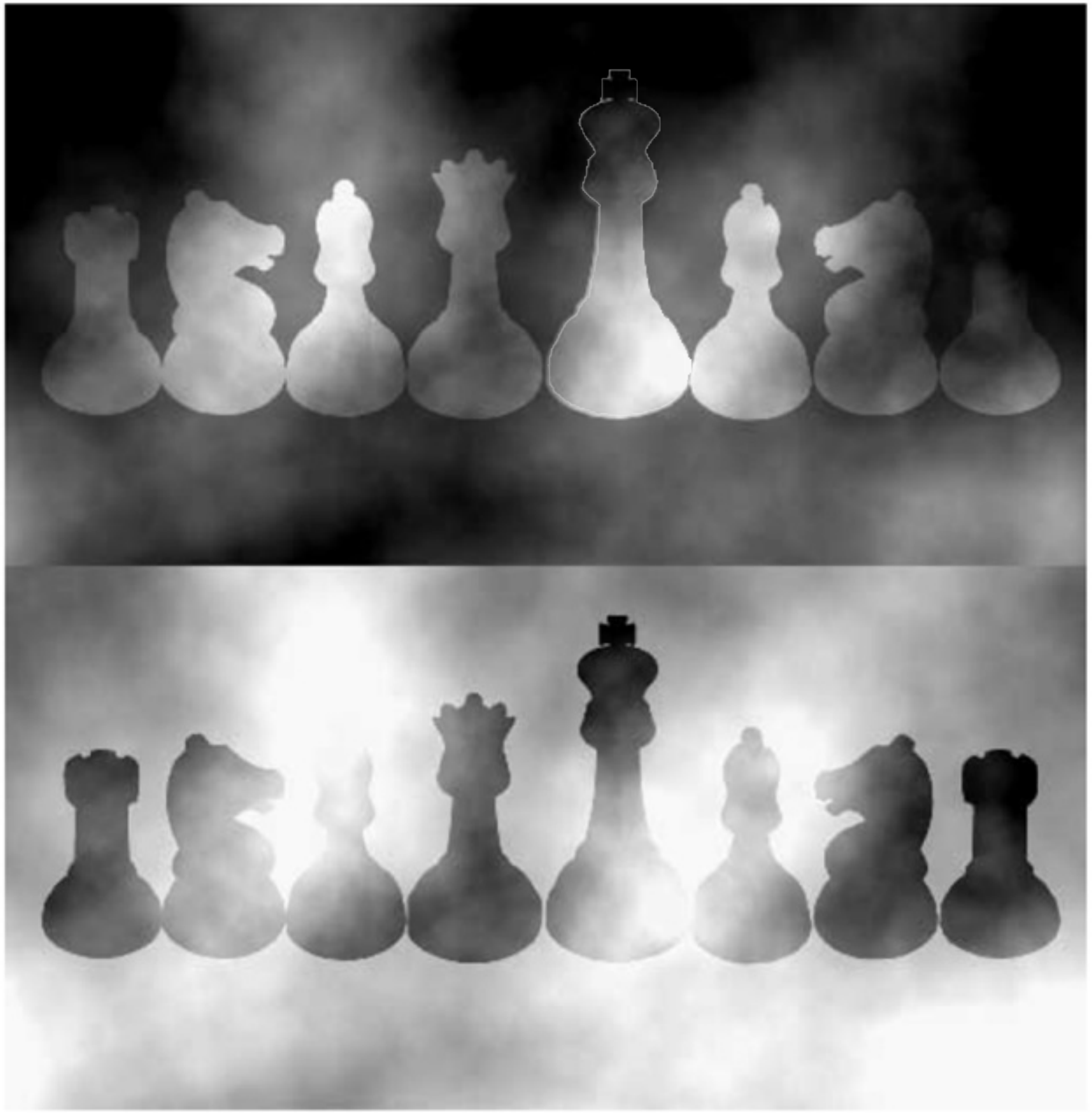
(Anderson and Winawer, Nature, 2005)



# Vision and computation

http://illusionoftheyear.com/

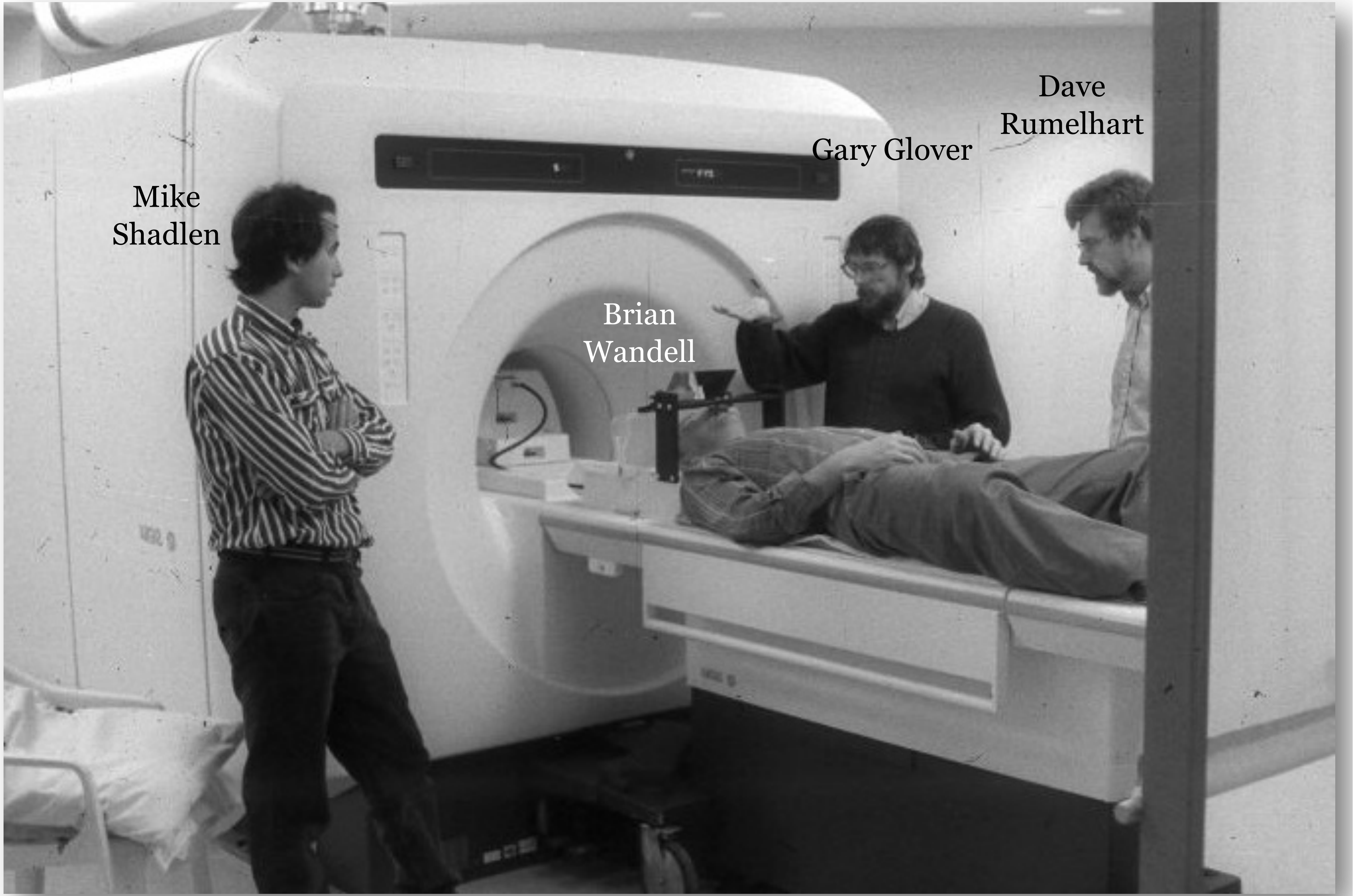


# Early days of MRI

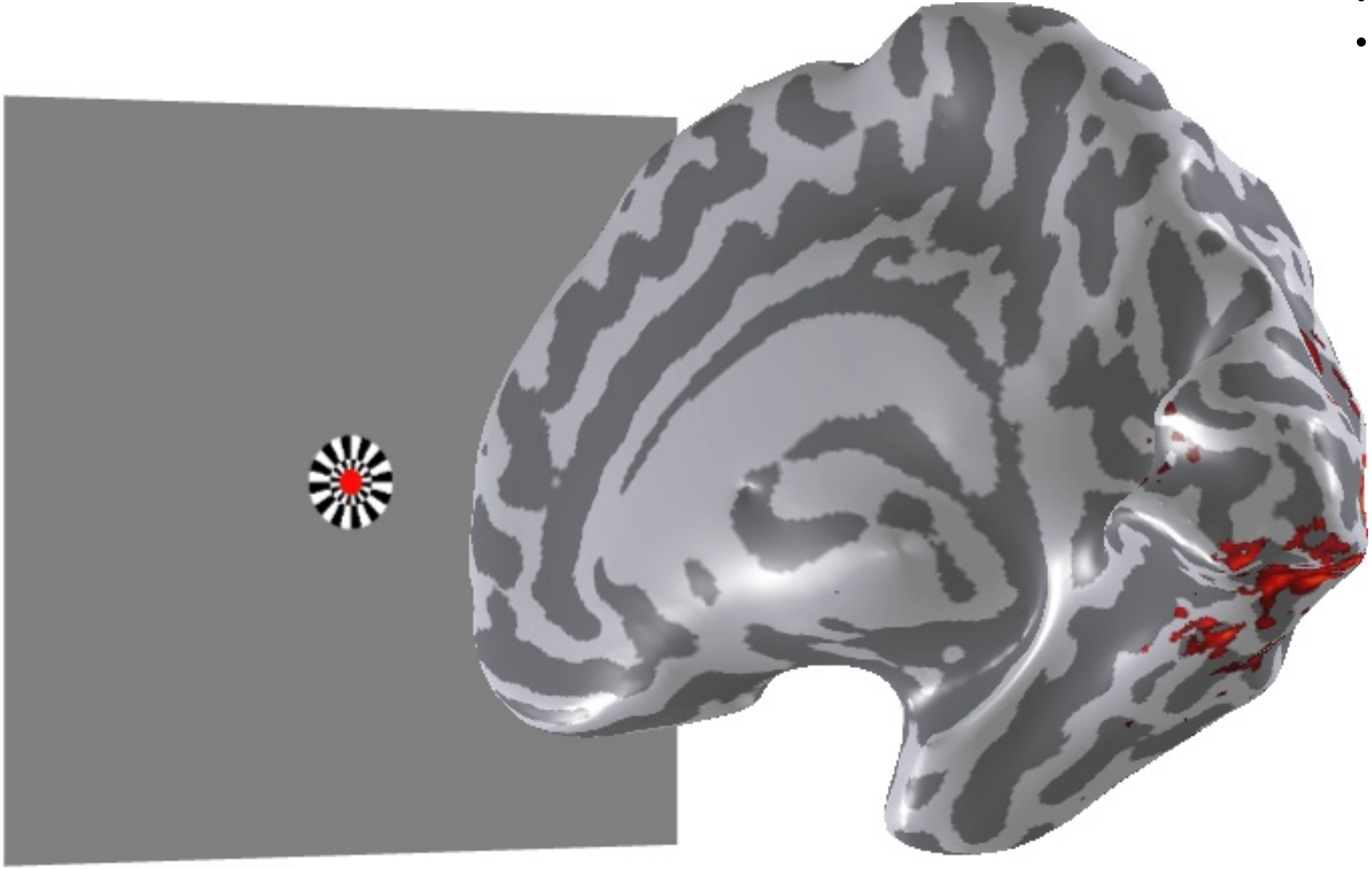
1992

- MRI acquisition methods have become more complex
- MRI computations (reconstruction, data analysis) have become more complex
- Networking and computer technology have advanced



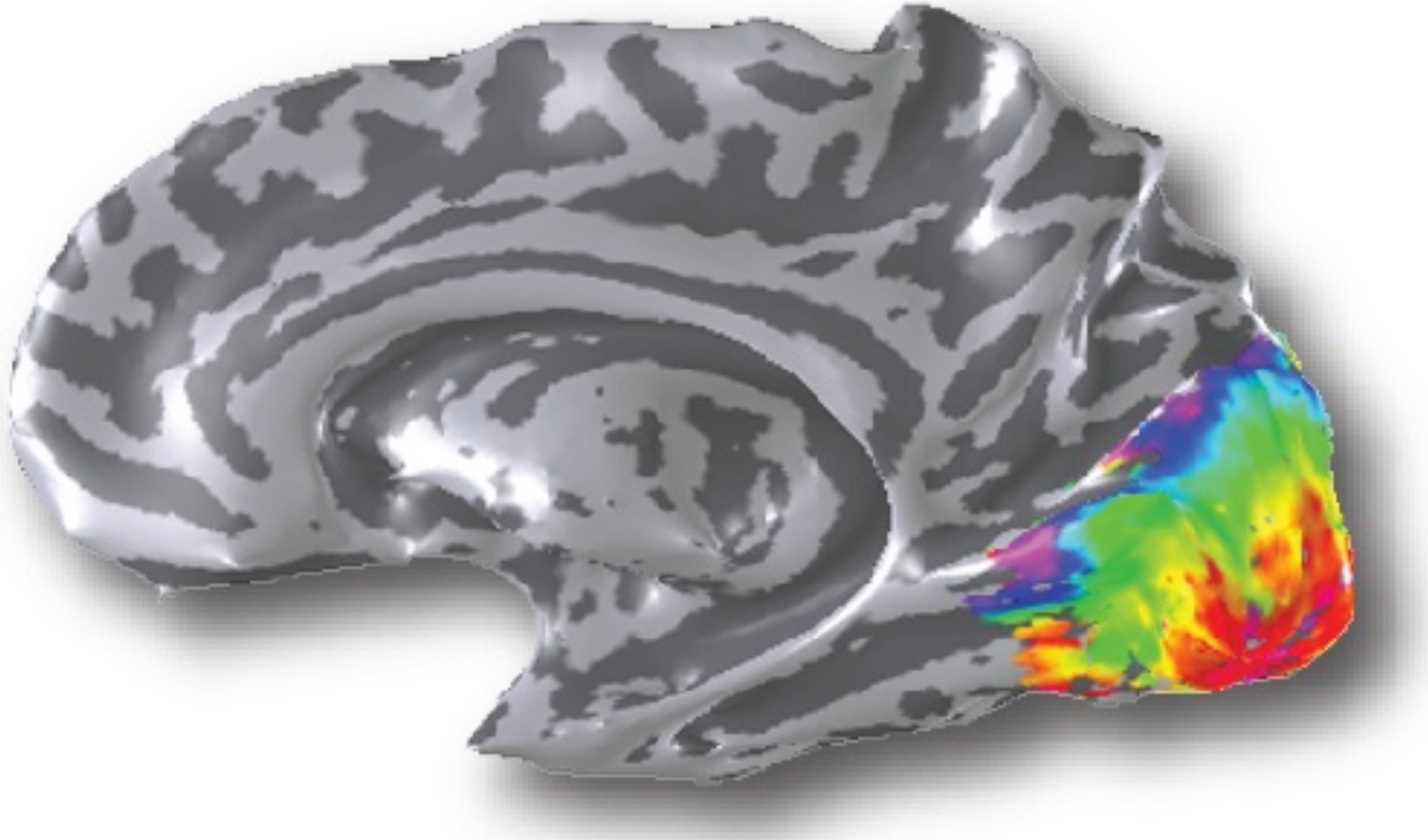
# Human eccentricity mapping with fMRI

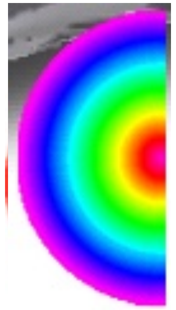
(Engel et al., 1994,1997; Sereno; Tootell, DeYoe; Others)



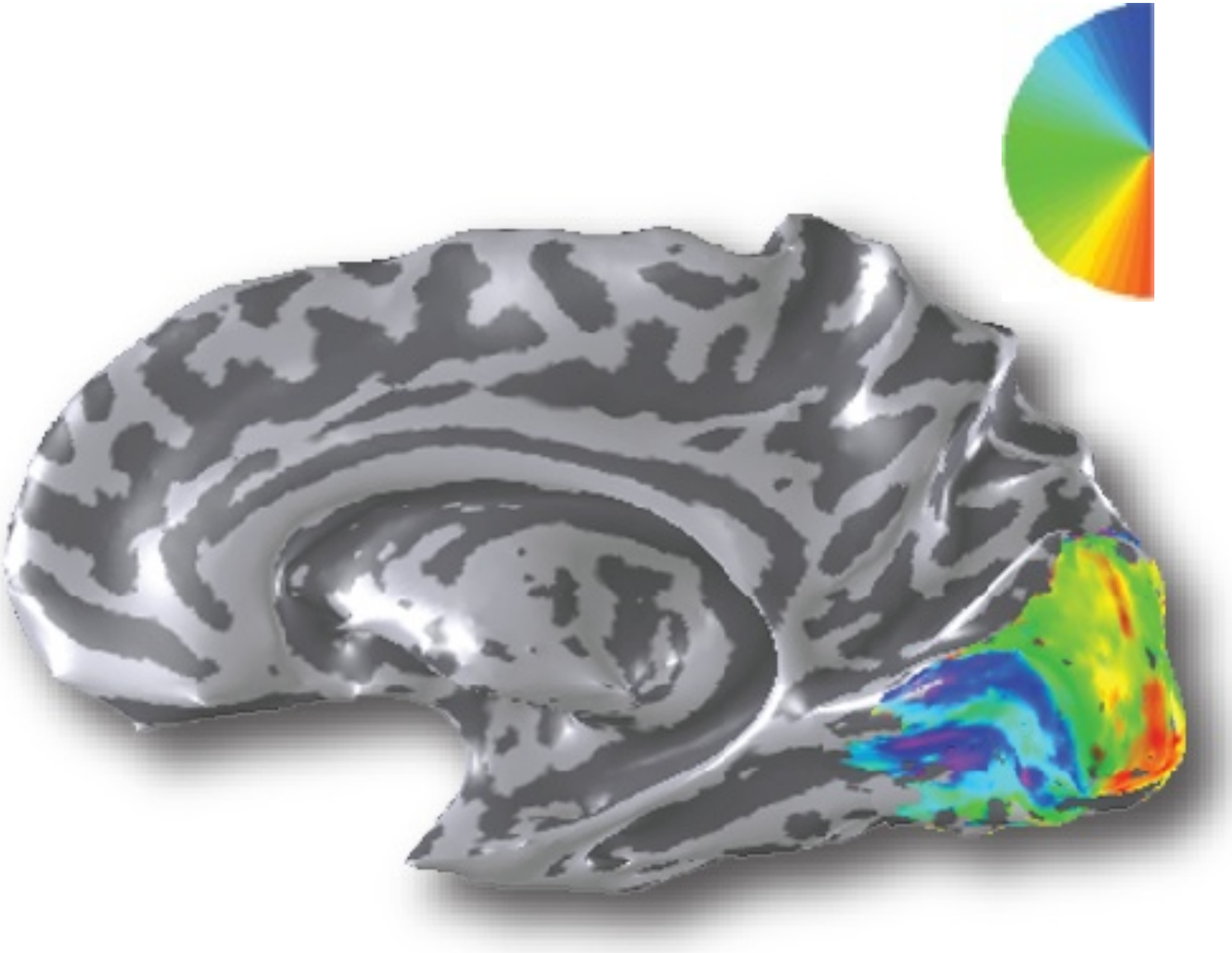
- Inflated brain
- Gray/white are sulci/gyri

# Pseudo-color representation of visual field map

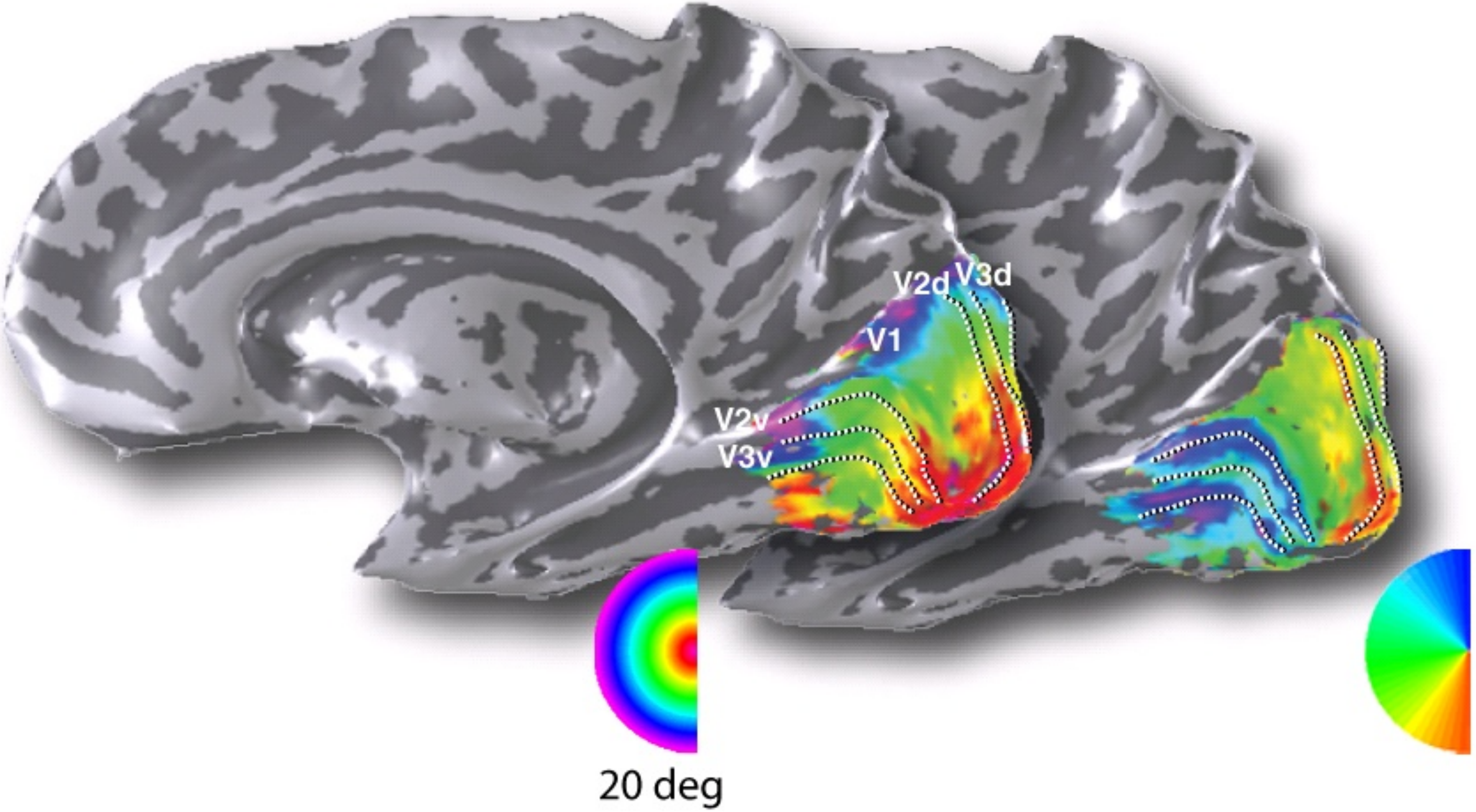




# Angular measurements delineate visual field map boundaries

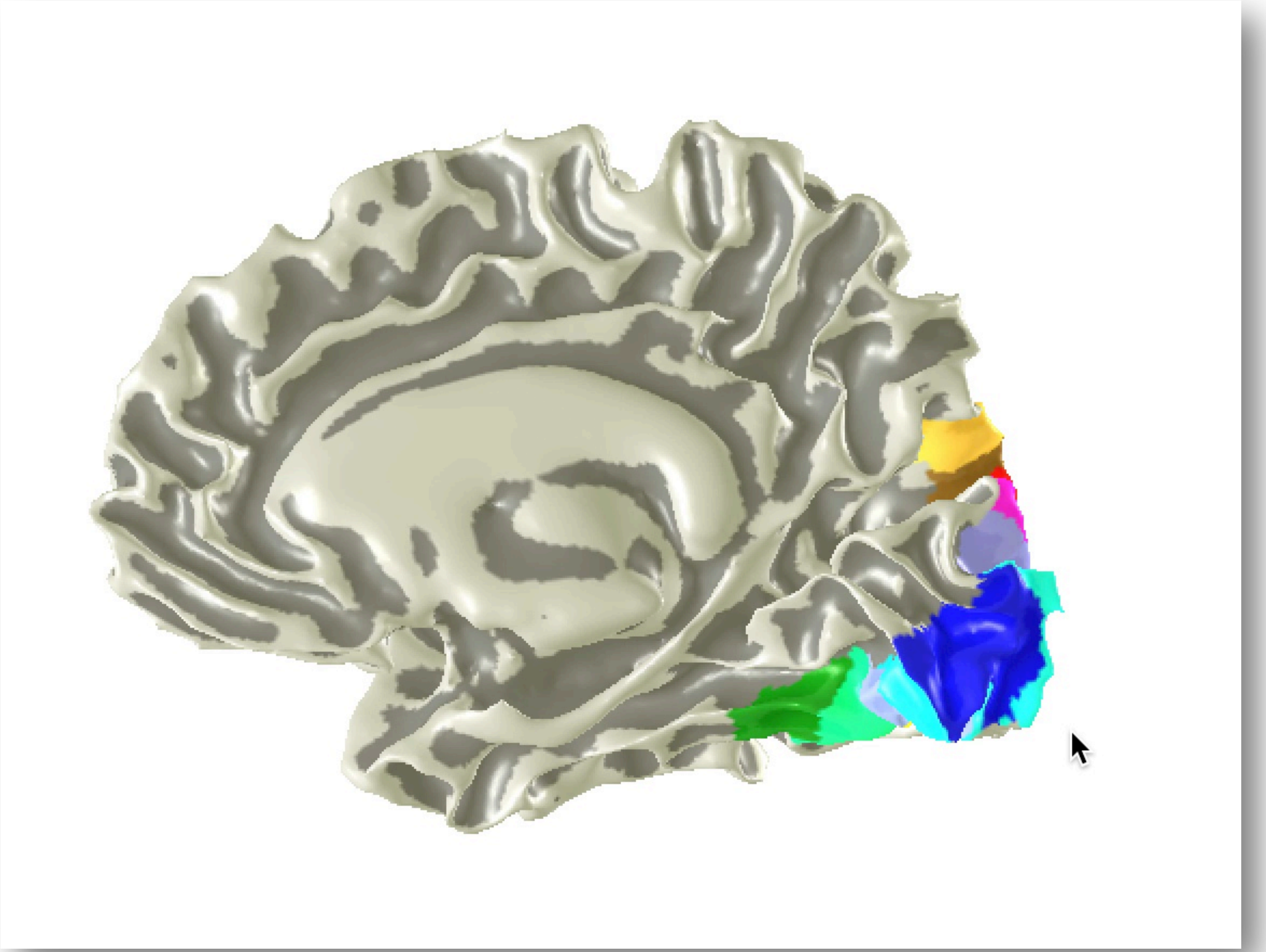


# Combining eccentricity and angle data yields maps



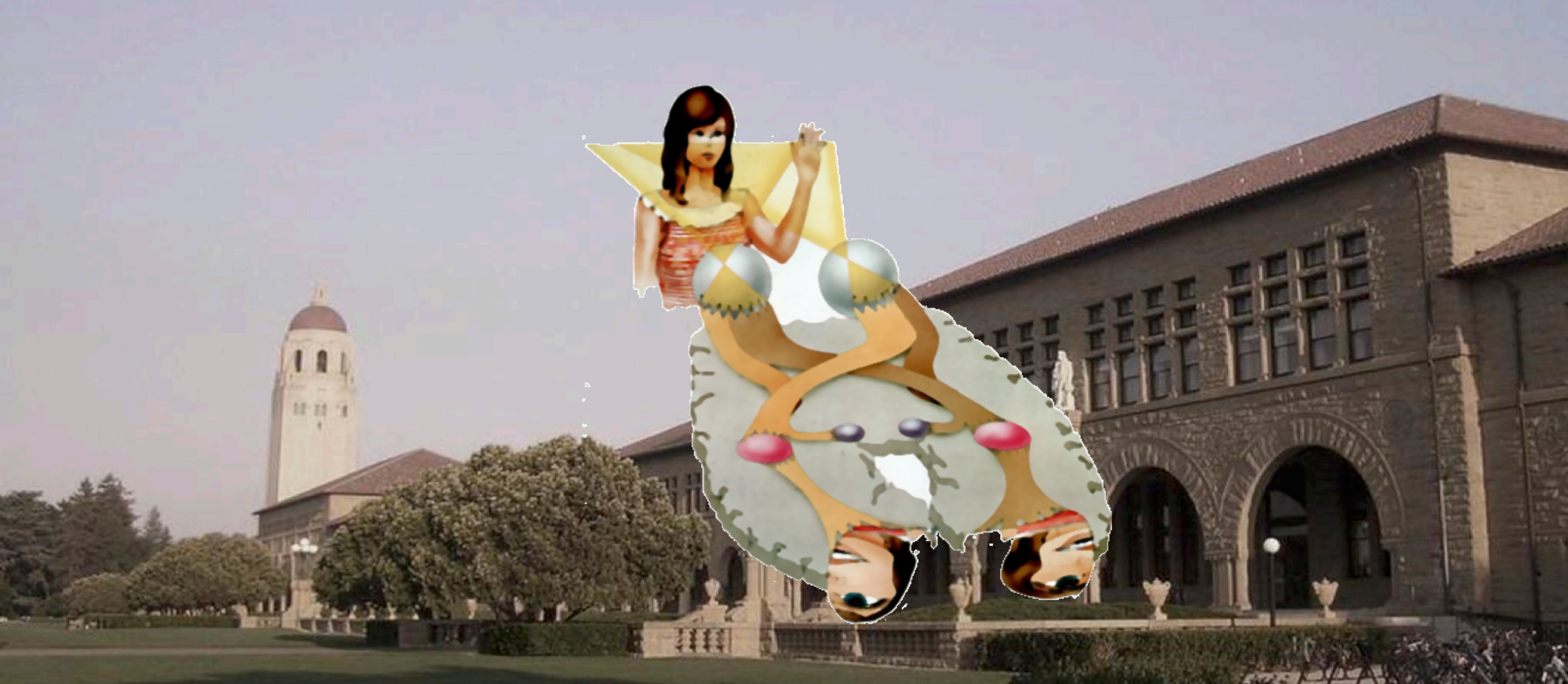
# Visual field map reviews

- Maps tile a lot of the back part of the brain
- The maps appear to be specialized for important stimuli – motion, depth, faces, navigation
- We have learned how to find the positions to within a couple of millimeters just from the anatomy



# Mis-wiring at birth

The case of a missing optic chiasm
(Hoffman et al., 2012)

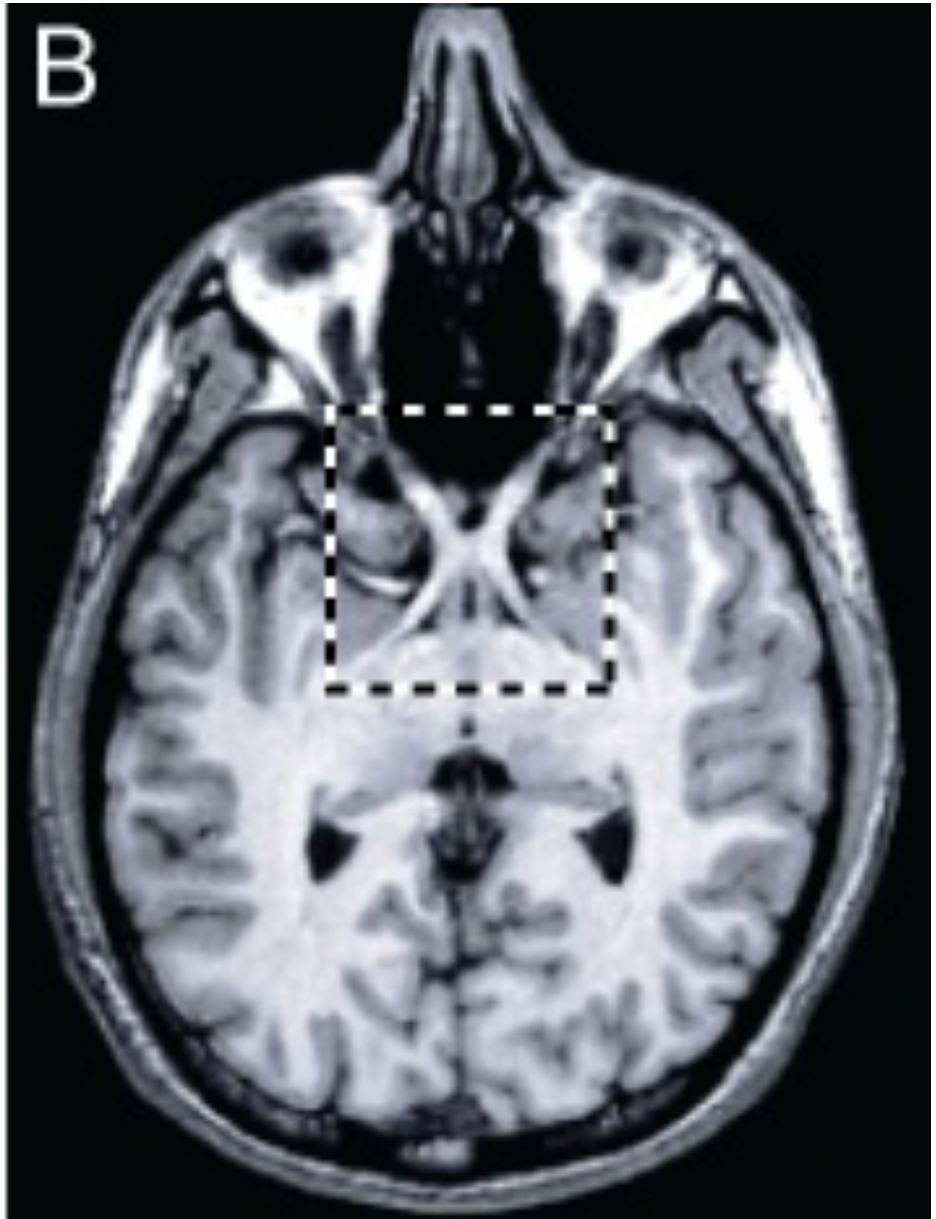


# The axonal pathways from the eye to brain

- The optic nerve from each eye meets in the optic chiasm
- Half the fibers cross to the other side of the brain
- In the typical brain to the right of fixation drives activity left hemisphere activity; and conversely

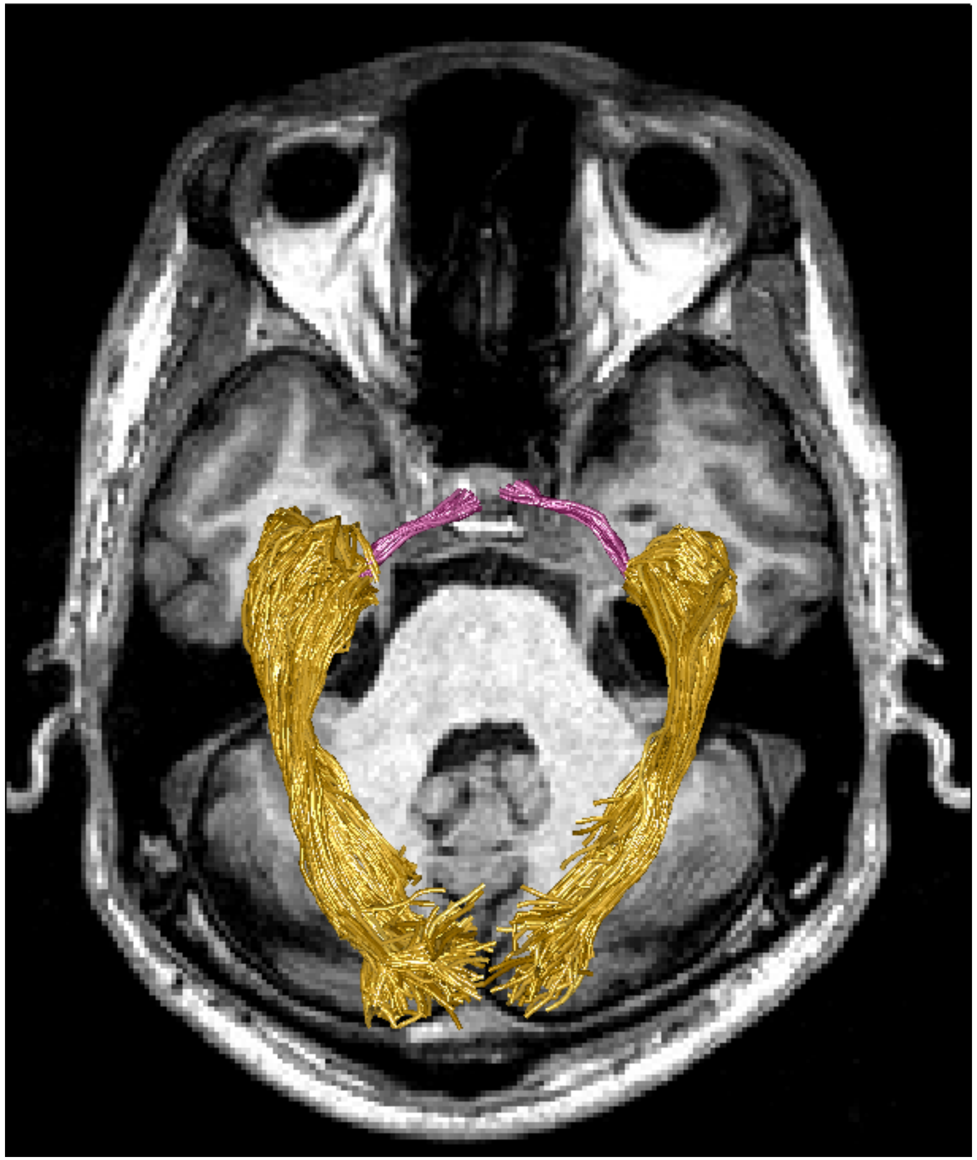
# The optic chiasm

- The chiasm is visible in a standard anatomical image



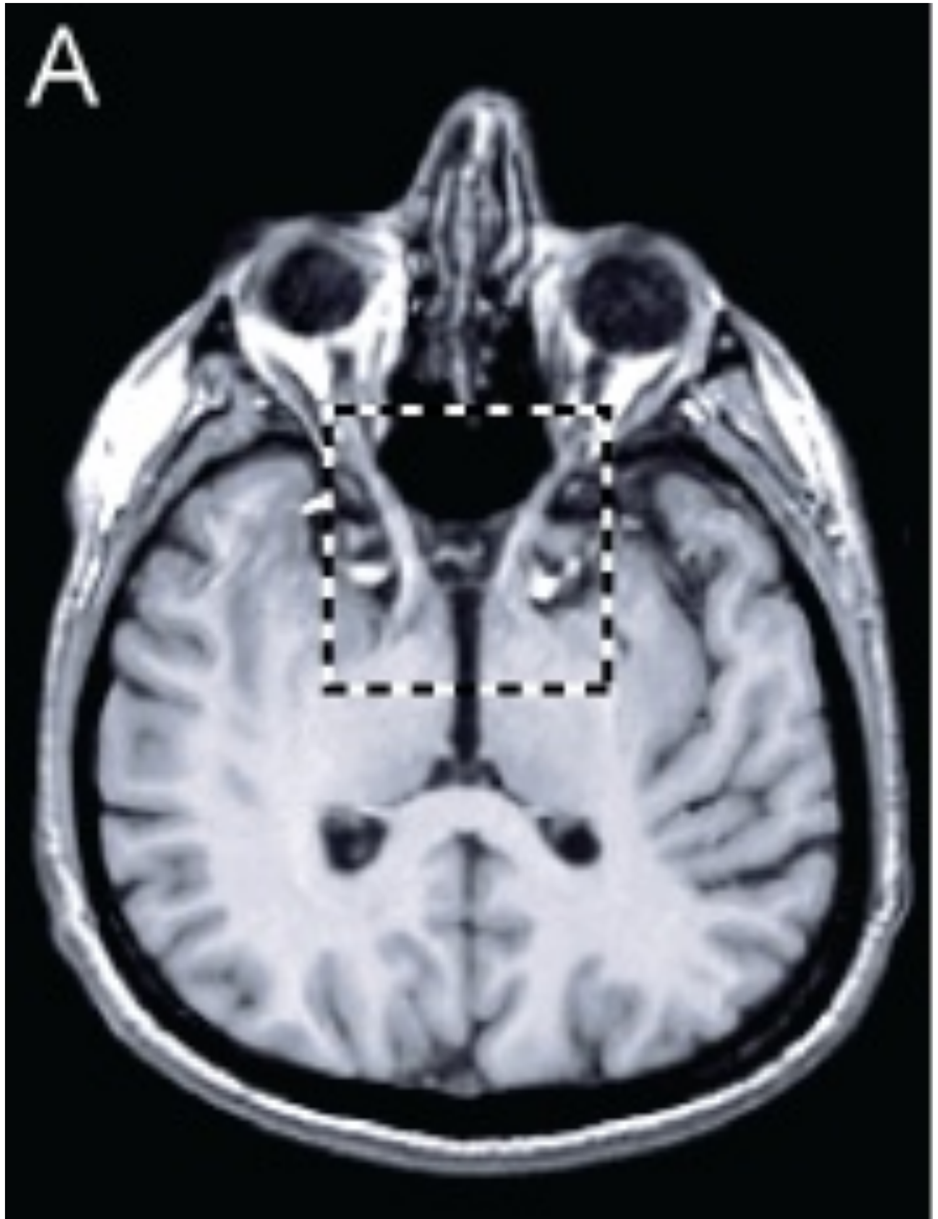
# Diffusion MRI (dMRI)

- We can measure the axonal pathways using another MRI modality, diffusion MRI (dMRI) coupled with computational algorithms (tractography)



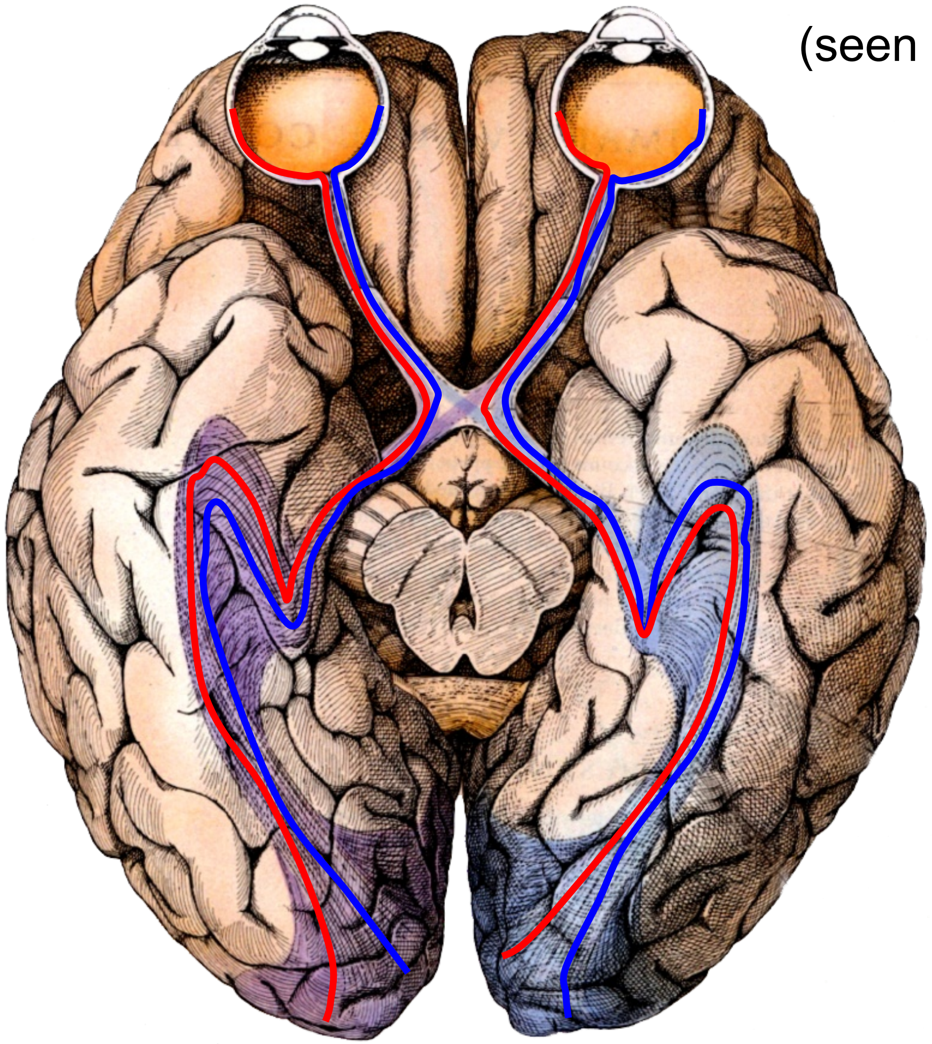
# A subject without a chiasm (Achiasmic)

- Eye movement (nystagmus)
- Discovered during routine testing for nystagmus
- Resolved after a few weeks

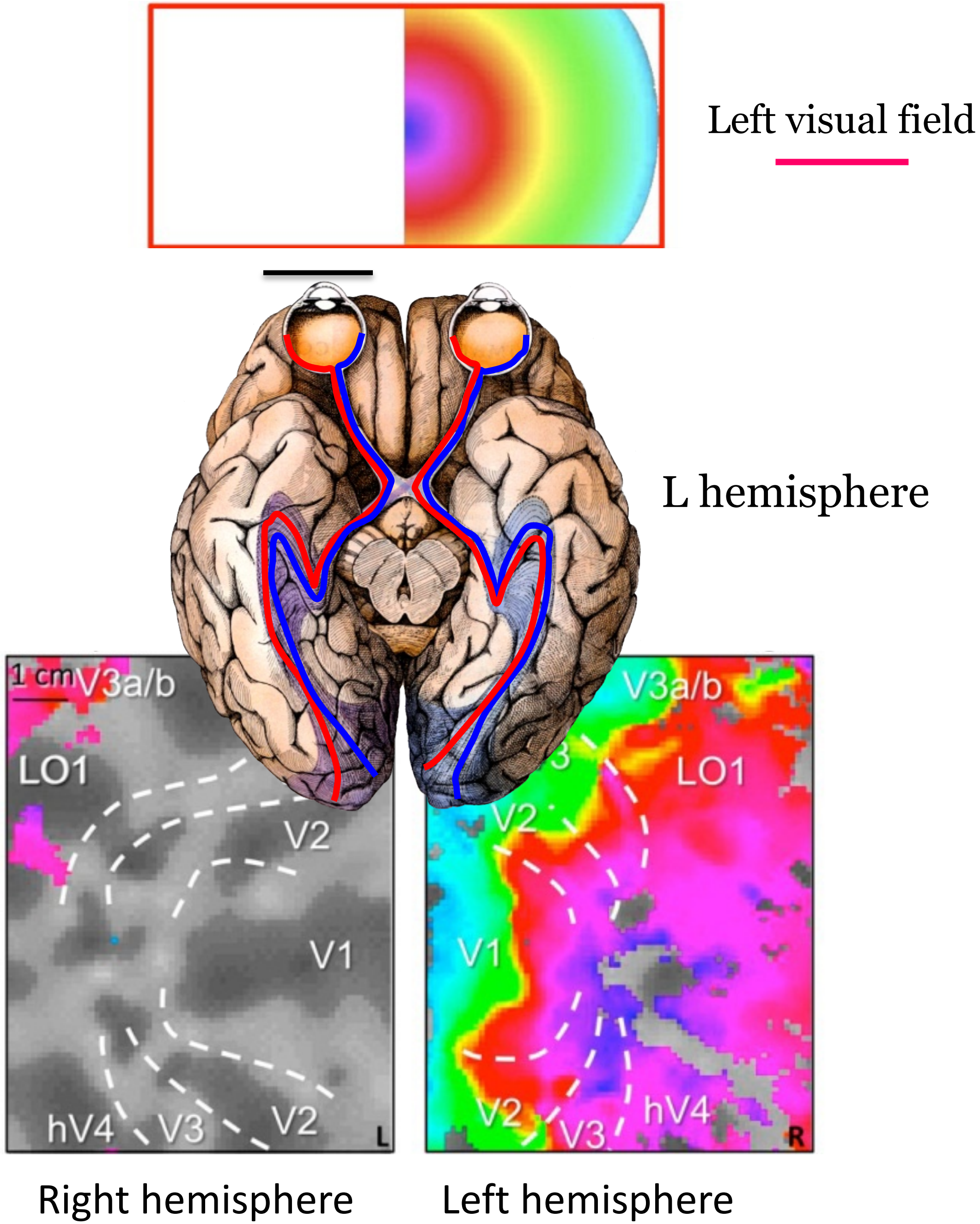


# Achiasmic axonal pathways from the eye to brain

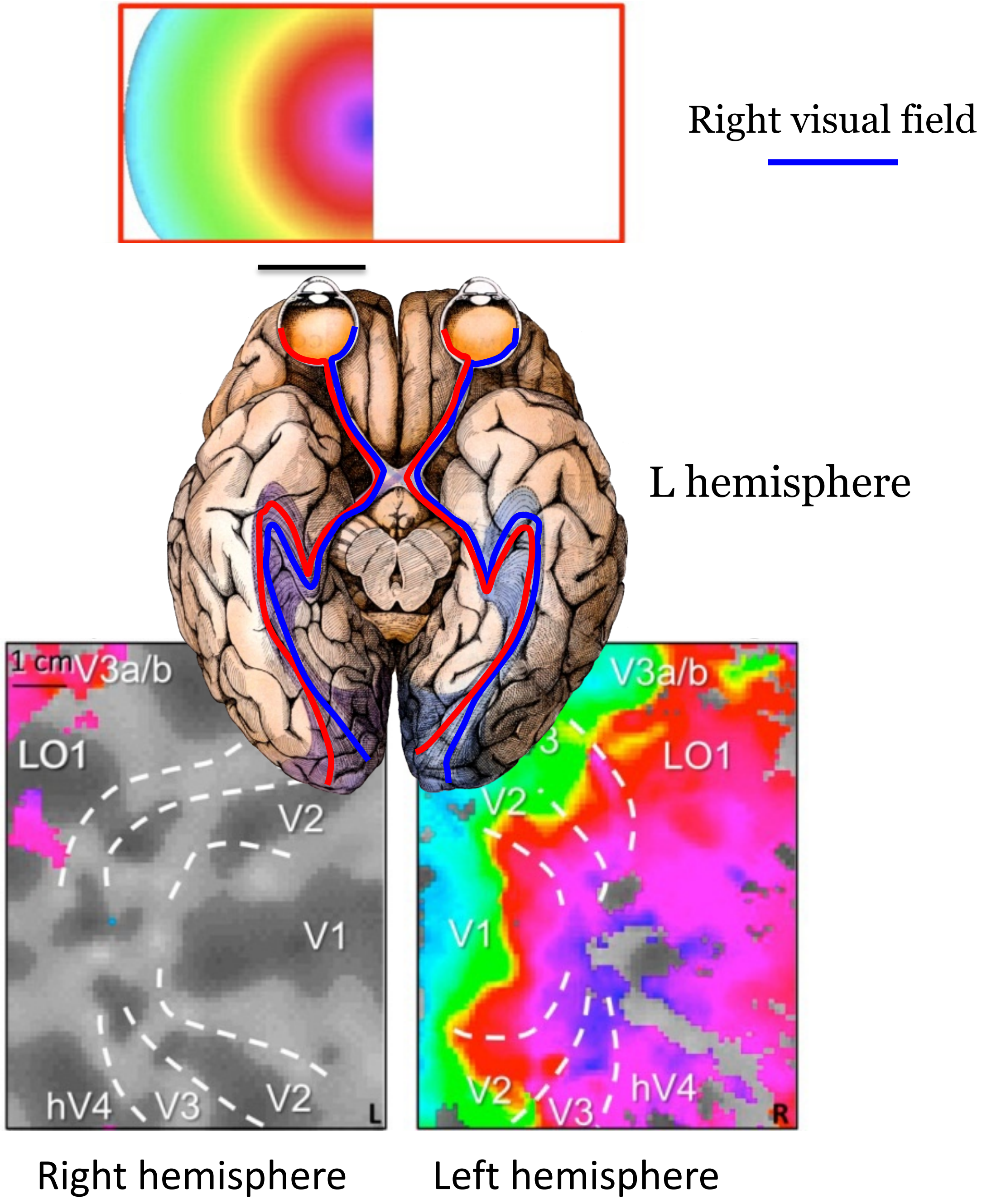
- For this subject, the optic nerves do not cross!
- The right eye sends signals only to the right brain, and the left eye only to the left brain



# FMRI confirms that in this person's brain the right and left visual fields are overlaid in cortex



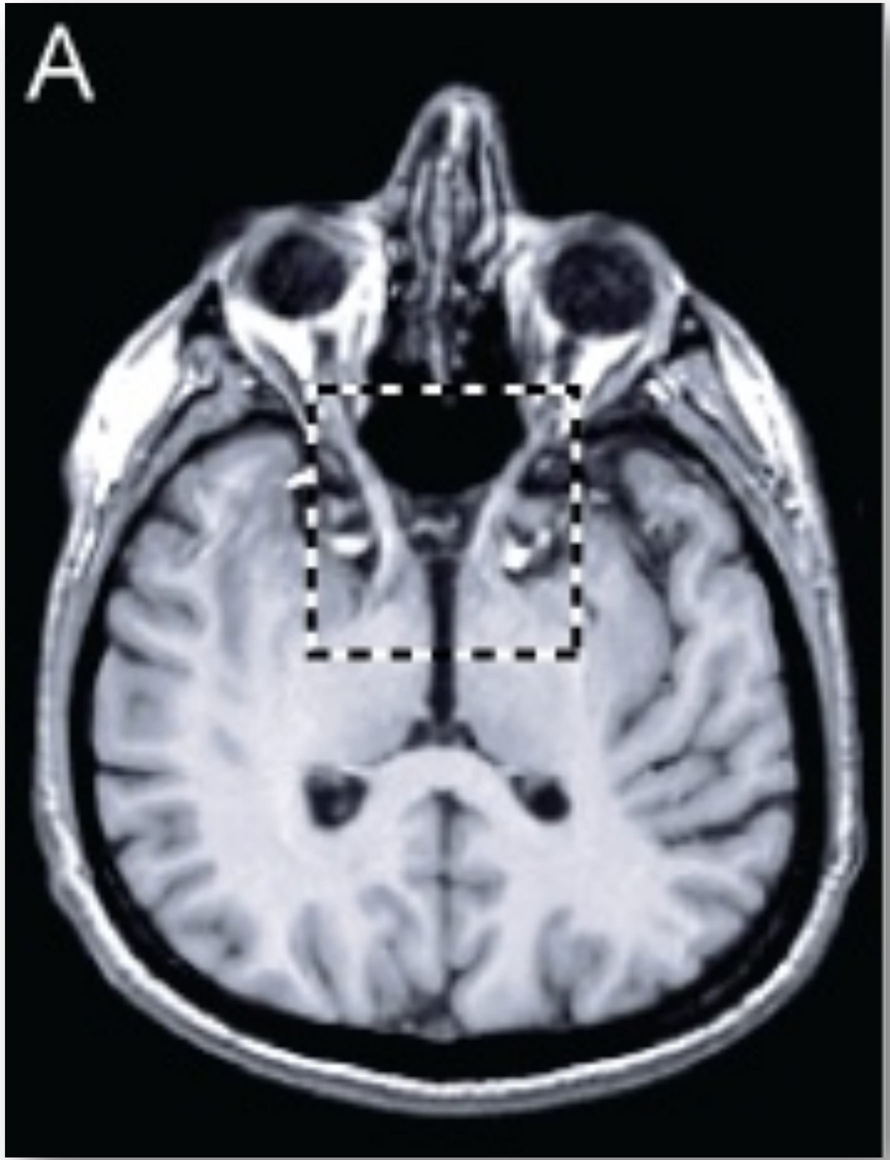
# FMRI confirms that in this person's brain the right and left visual fields are overlaid in cortex



# Summary – the system view

1. A genetic defect that disrupts crossing at the chiasm signaling causes a developmental reorganization in visual cortex.

2. **Despite the profoundly disrupted maps, the rest of the brain figures out what to do.**



# First point

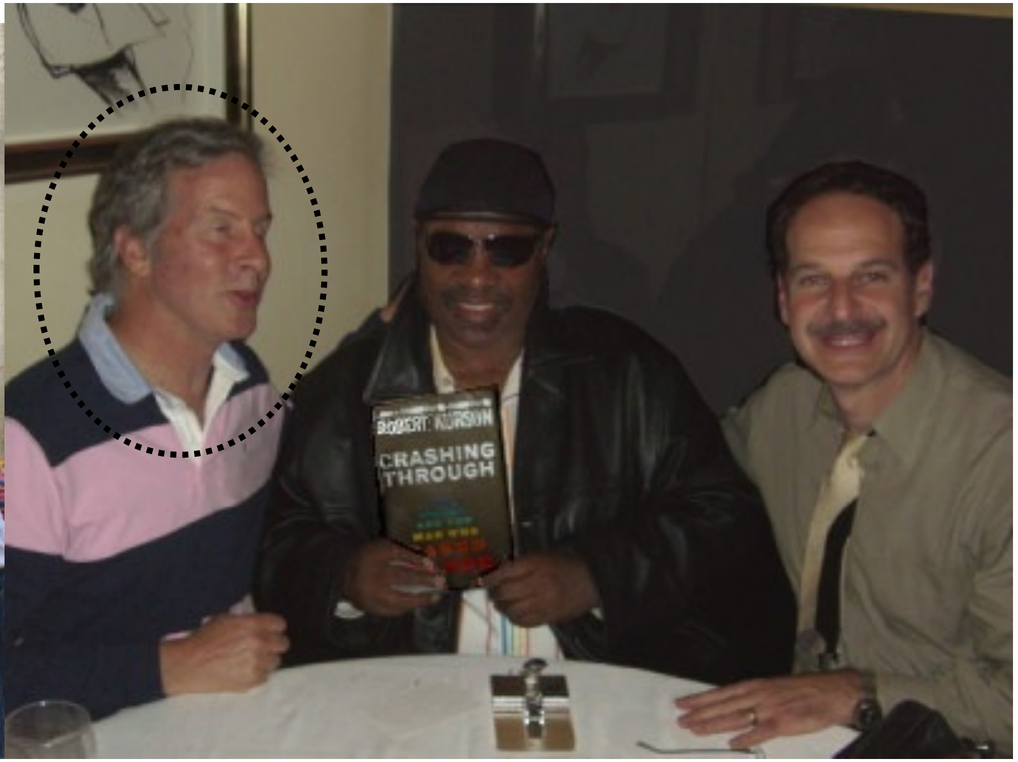
In some cases, when a child is born with a very unexpected pattern of brain connections, during development the brain can compensate and the system can still function

There are probably millions of people in the world functioning with these types of natural brain experiments

# Brain plasticity and stability

# Michael May

- Chemical explosion (3 yrs old)
- One eye lost; other cornea (and limbic stem cells) destroyed
- Blind (no contrast or form) from age 3 through 46

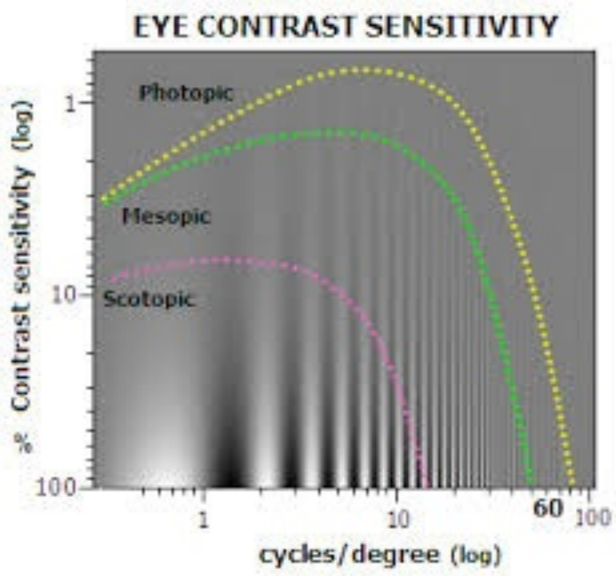


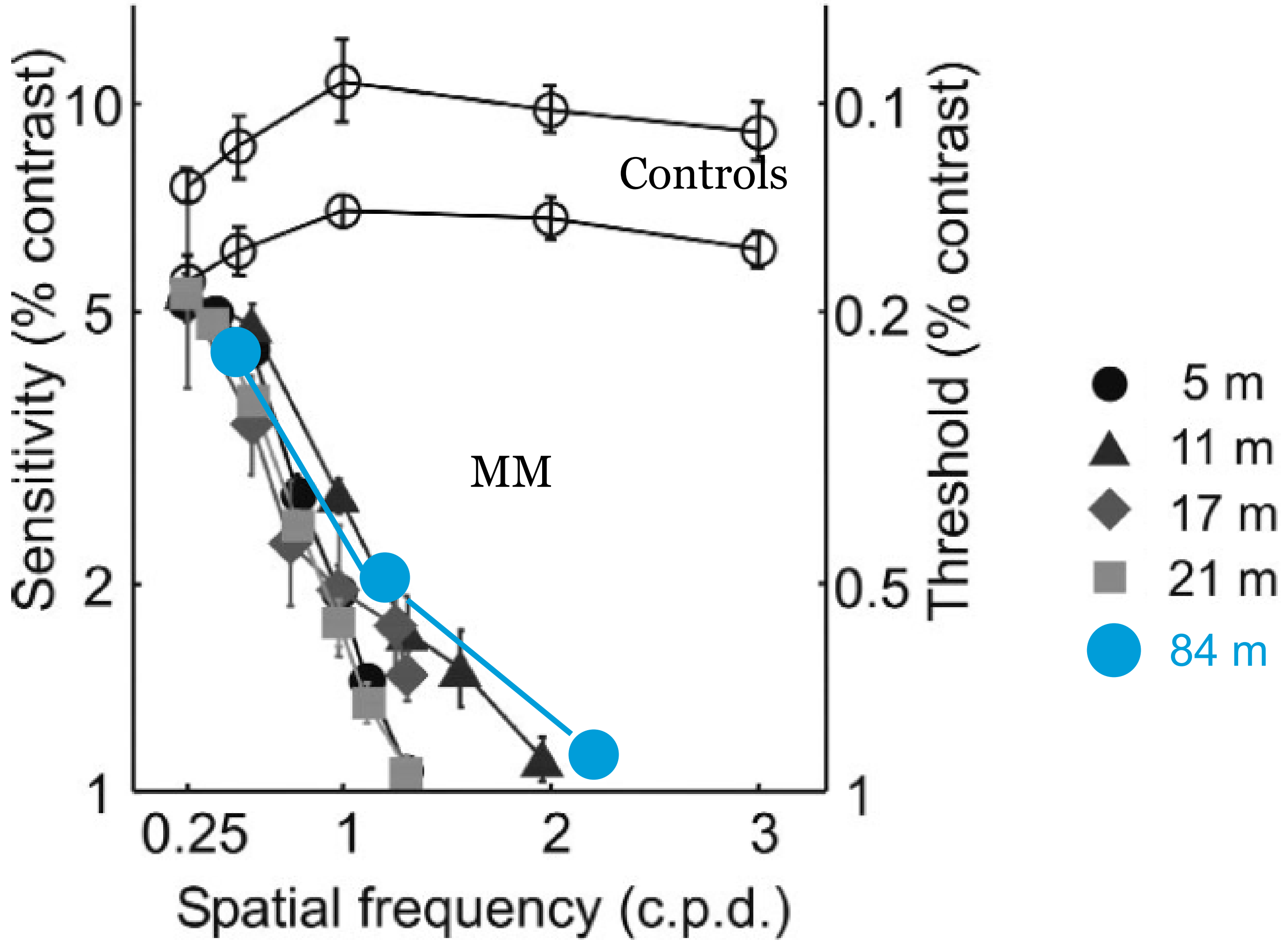

*Images courtesy of Michael May, Sendero Group*

# Recovered sight?
(images courtesy Michael May)

Limbic stem cells and corneal replacement

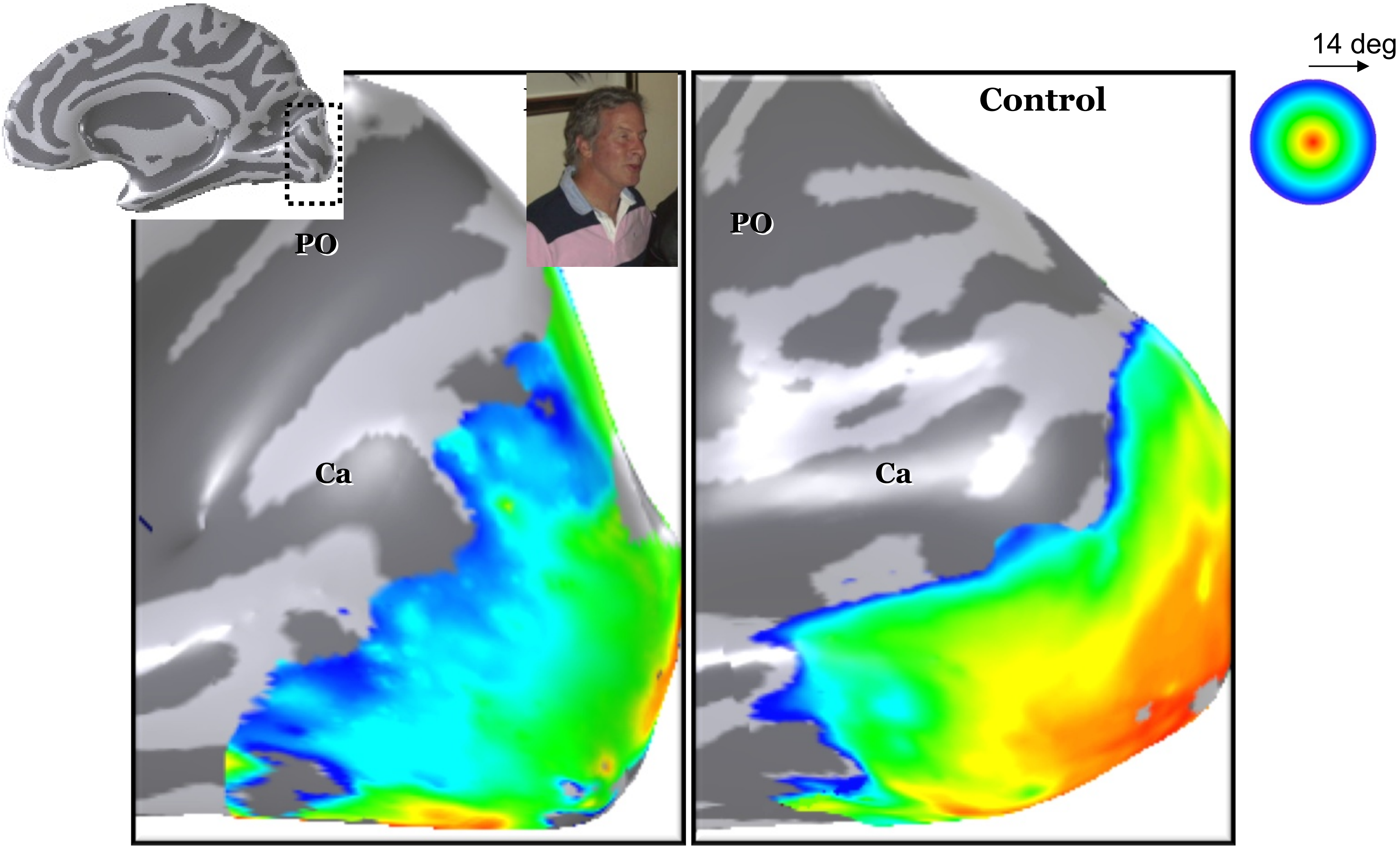
# Perceptual contrast sensitivity functions




- Similar to controls at low spatial frequency
- Substantially worse above 0.25 cpd
- Constant for the 7 years following surgery

# MM has an unusual cortical map

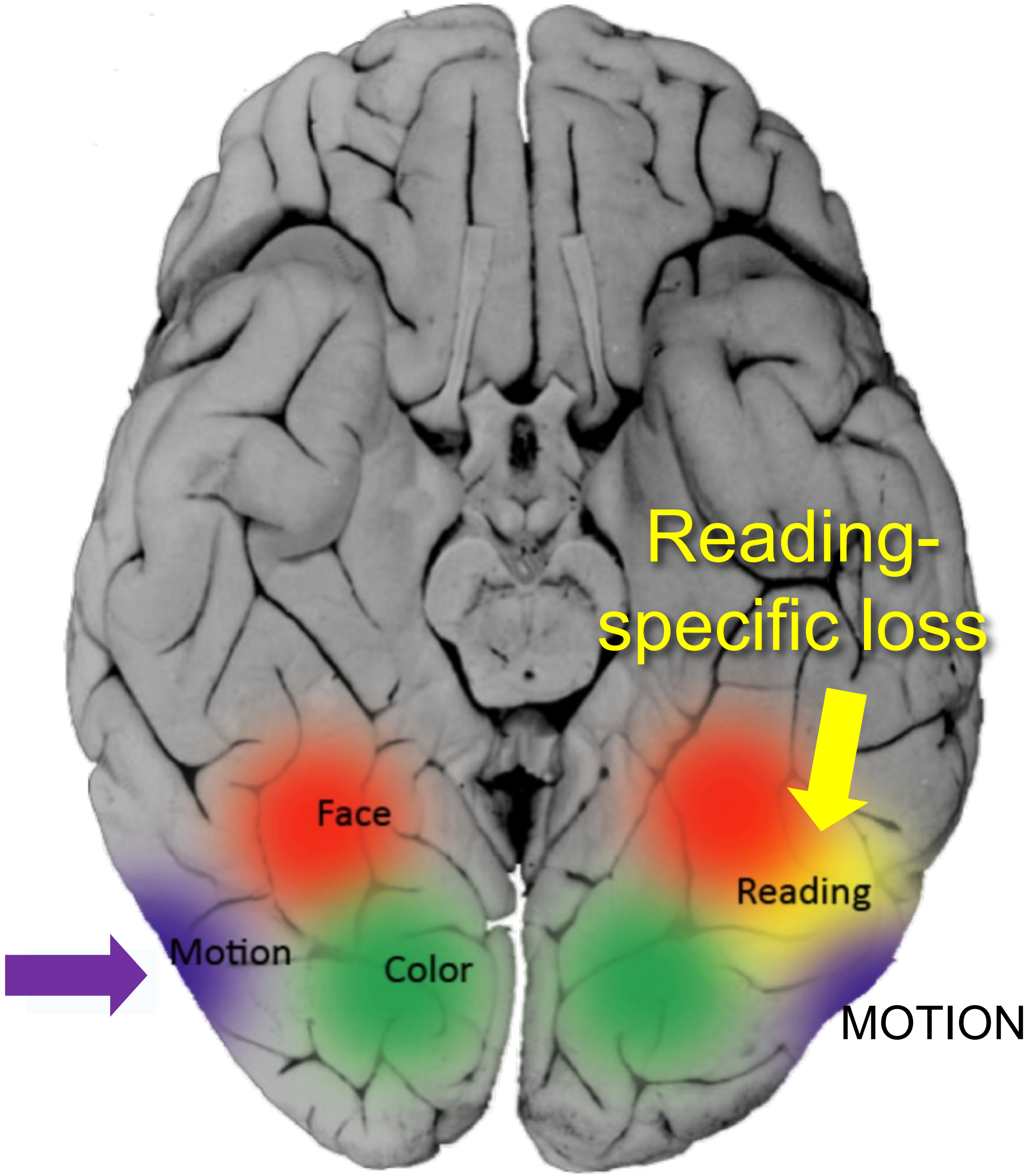


# Specializations in the human brain

# Specializations of brain function

Damage to small regions of gray matter can produce very specific cognitive problems, such as face-blindness, loss of color vision, loss of motion perception, **or loss of reading ability**

Motion perception loss

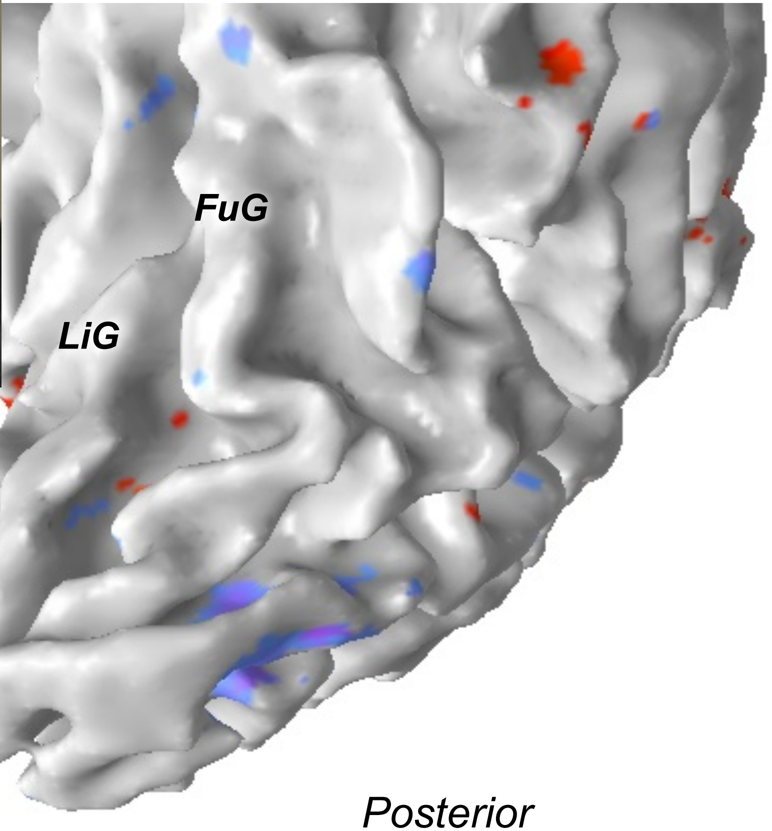


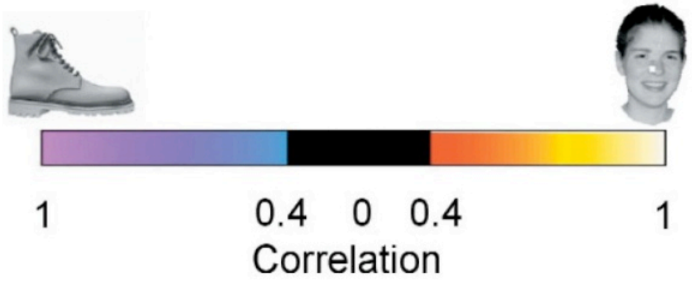

Wandell et al. 2007, New Encyclopedia of Neurosciences

# Motion selective cortex

- Responds powerfully
- Is organized as a map
- Has the same size as in controls


# Object and face-related responses



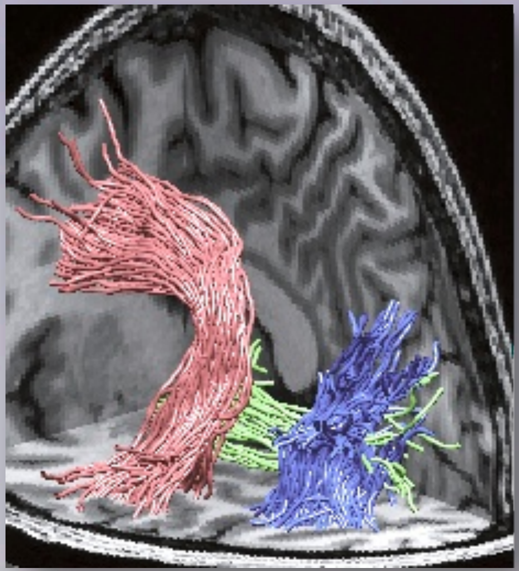
# Second point

In some critical systems repairing damage after development requires that neuroscientists learn more about restoring plasticity.

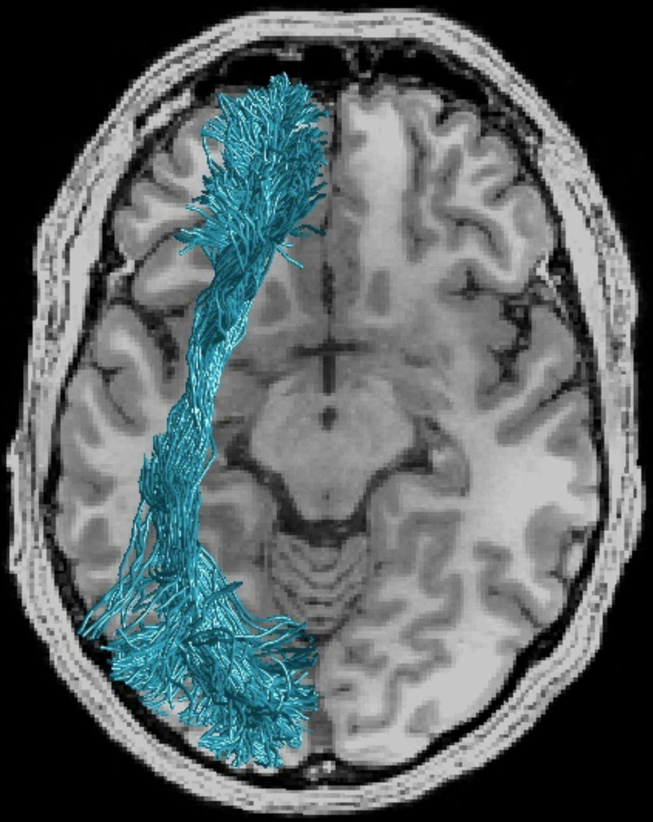
Restoring plasticity in the adult is a research goal; it is a dangerous and uncertain path.

# Brain connections: Diagnosing the reading circuitry

The what matter connections for reading



# White matter fascicles are generated by step-wise sampling of local diffusion information



Left
IFOF

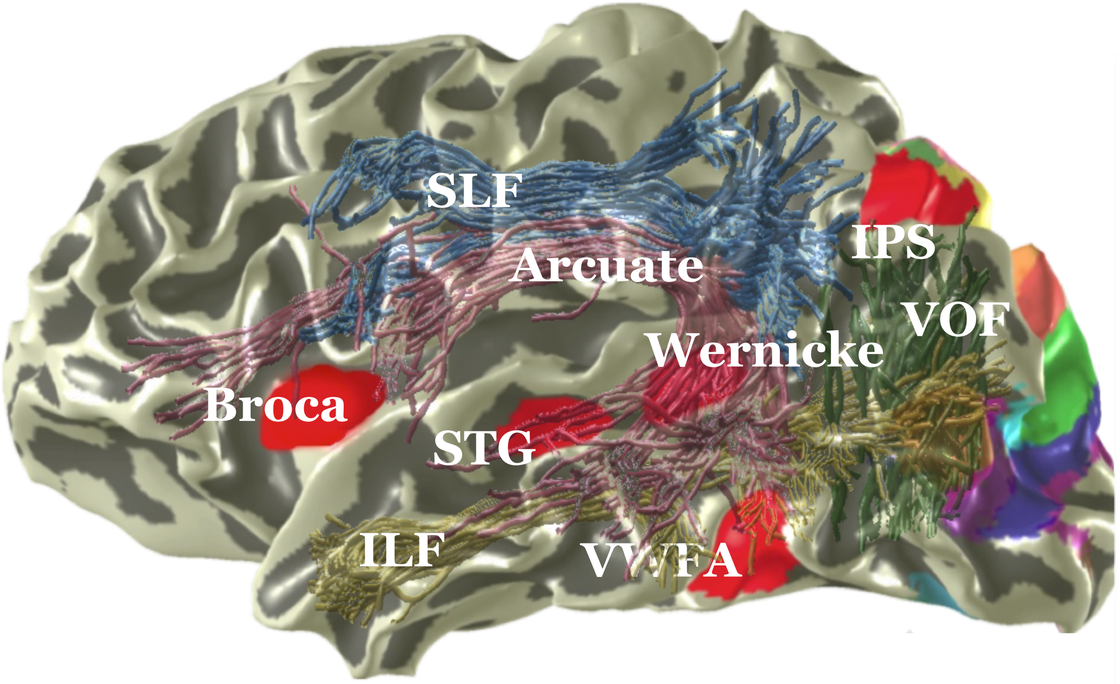
150 Directions, 2 $mm^3$, B=2000 projected on a 1 $mm^3$ T1 anatomical image

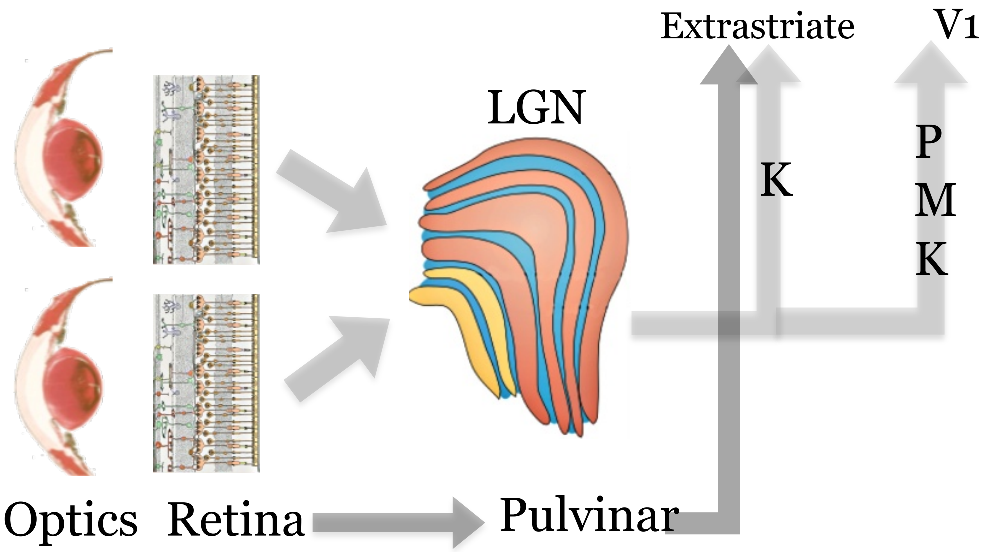
# Major components of the reading pathway

Wandell and Le (2017)

**The goal: Diagnosis**

Identifying the locations and responses in a poor reader that differ significantly from measurements in good readers

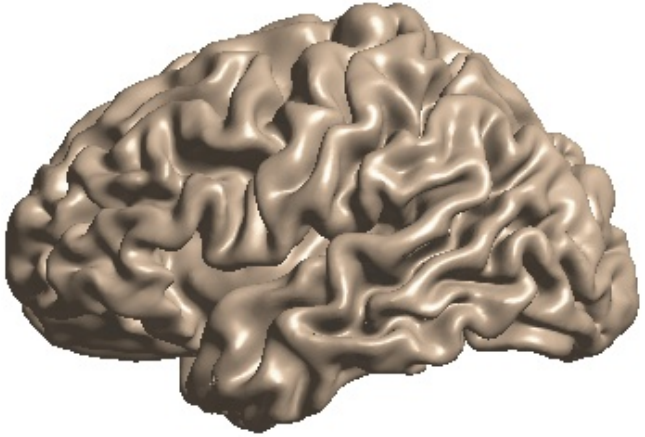


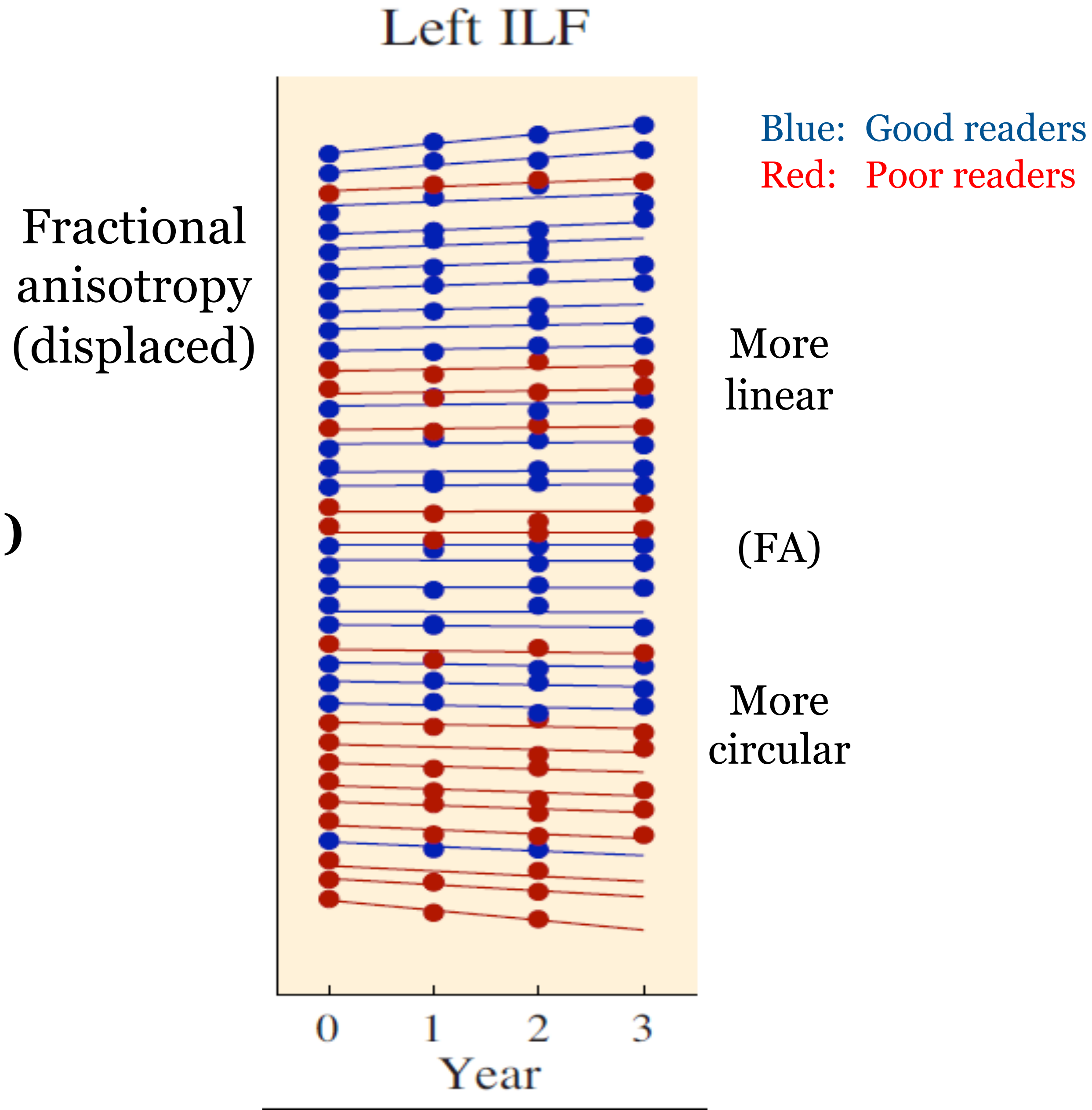


Learning to See Words
B.A. Wandell, A. Rauschecker and J. Yeatman (2012).
**Annual Review of Psychology** Vol. 63, pp.31-53.

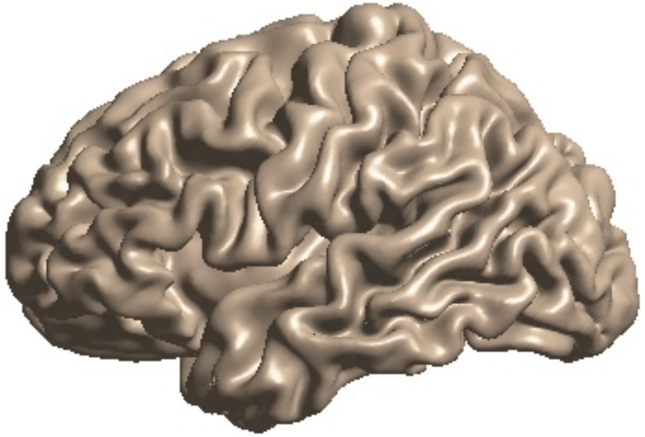
# Diffusion (FA) changes differs between good and poor readers



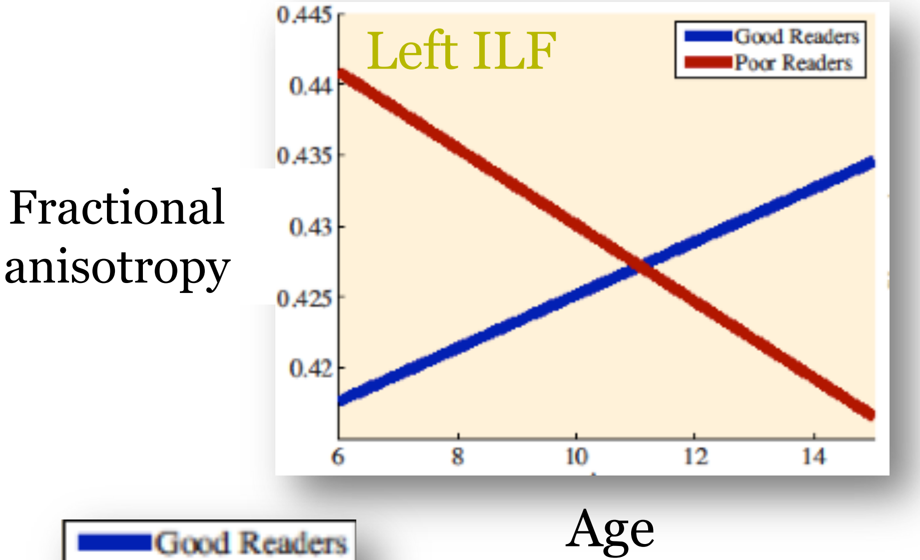
- Measured brain and behavior at 4 time points **(data management!)**
- The first measurements predict reading over the next few years
- The rate and direction of FA development differs between good and poor readers in both the Arcuate and the ILF

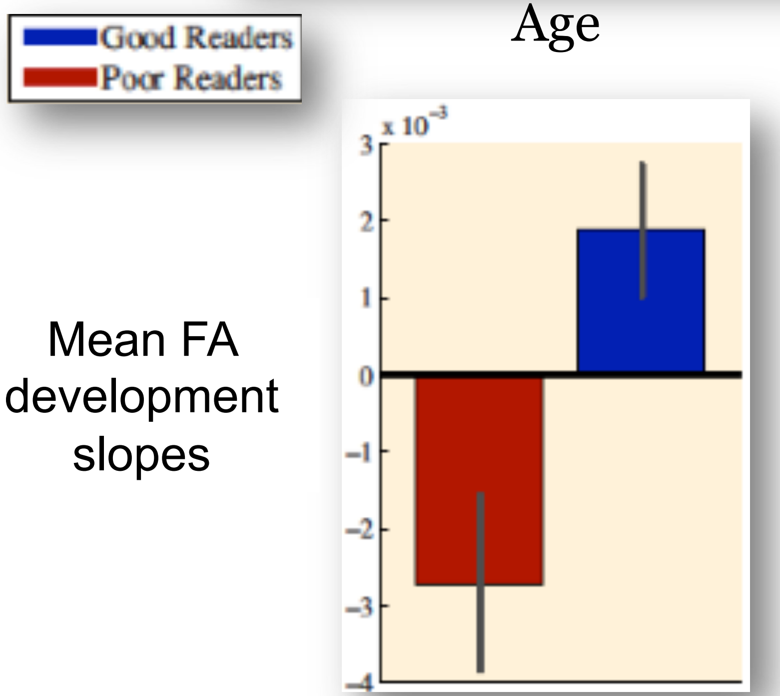


# Diffusion (FA) changes differs between good and poor readers



- Measured brain and behavior at 4 time points **(data management!)**
- The first measurements predict reading over the next few years
- The rate and direction of FA development differs between good and poor readers in both the Arcuate and the ILF



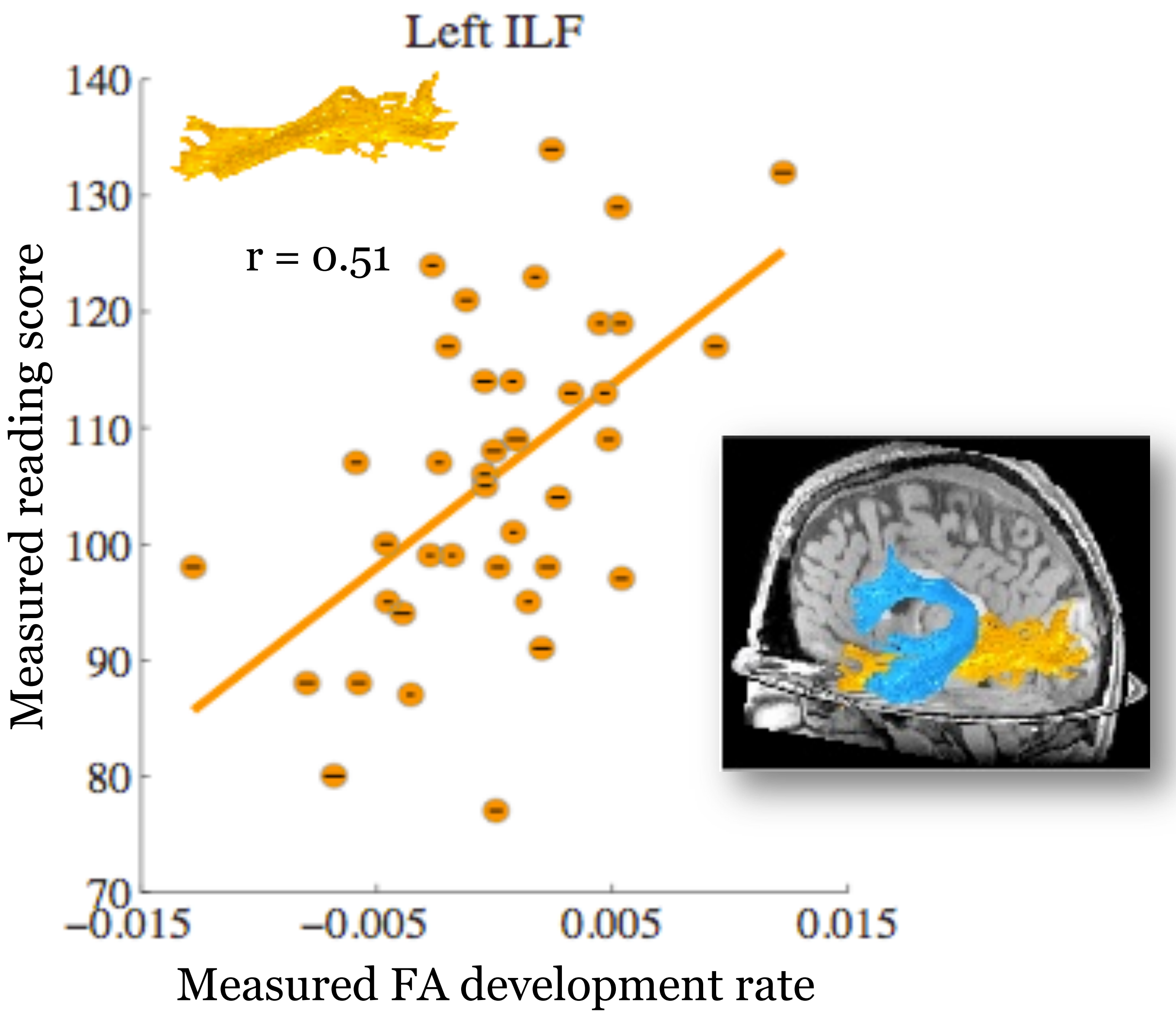
# Correlations between tract diffusion change and seeing words

(Yeatman et al., 2012, *PNAS*)

- Development measured by dMRI in the ILF and Arcuate, but not others tracts, correlates with the ability to rapidly see words

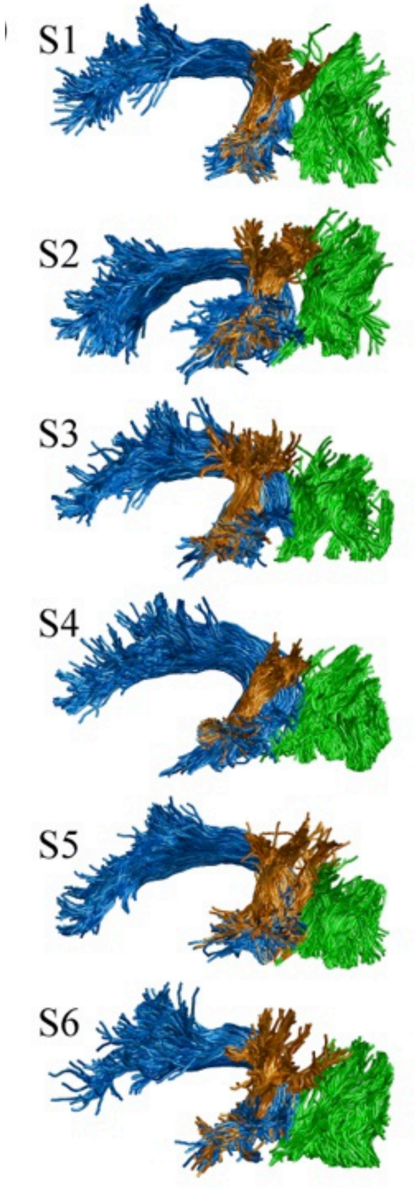
- This is one reason we think that the wires are active, changing in response to learning and memory

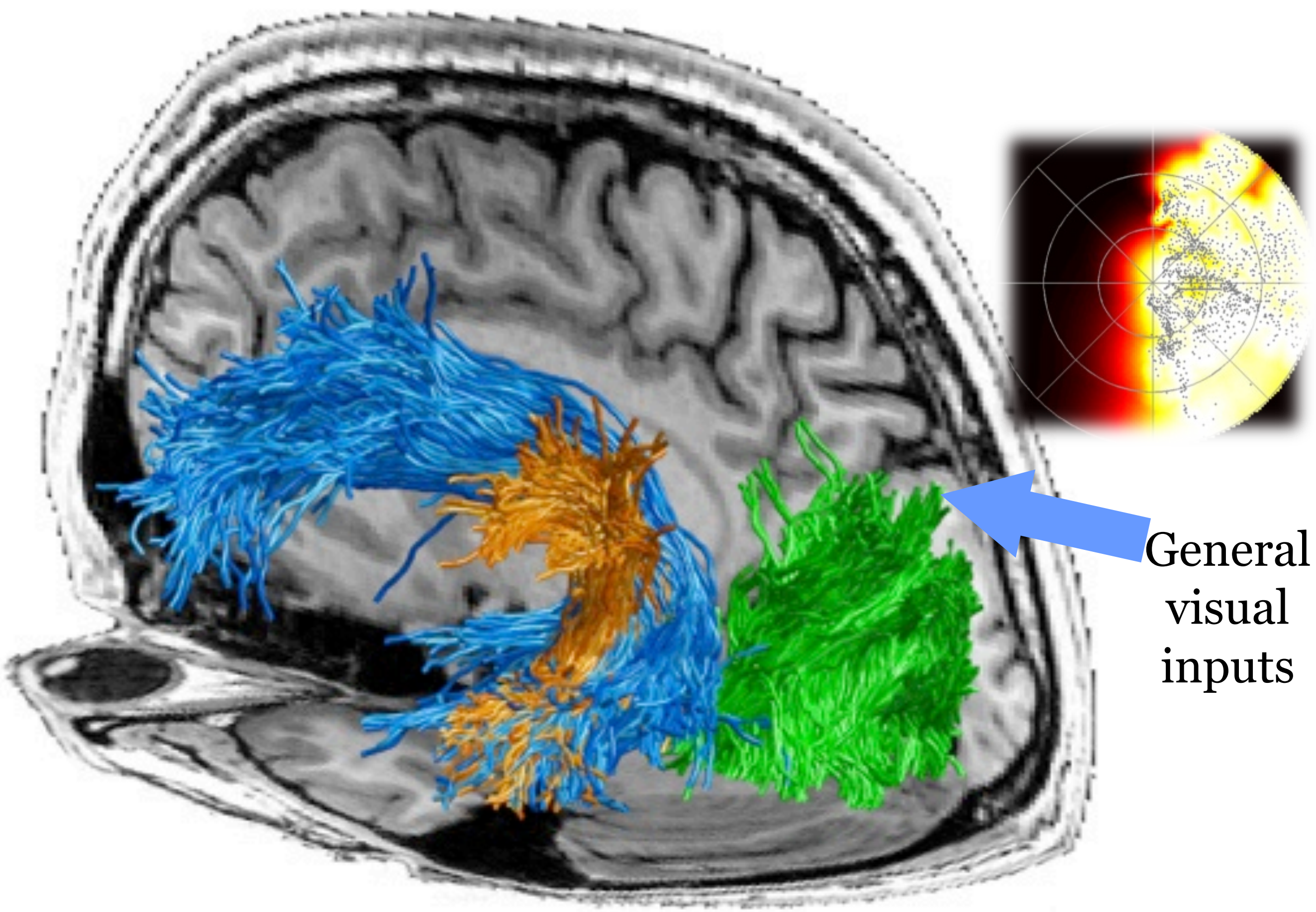
- The predictions are not yet useful; they are statistically reliable



# **The future:** Modeling the biological networks that carry visual signals for reading

Car analogy

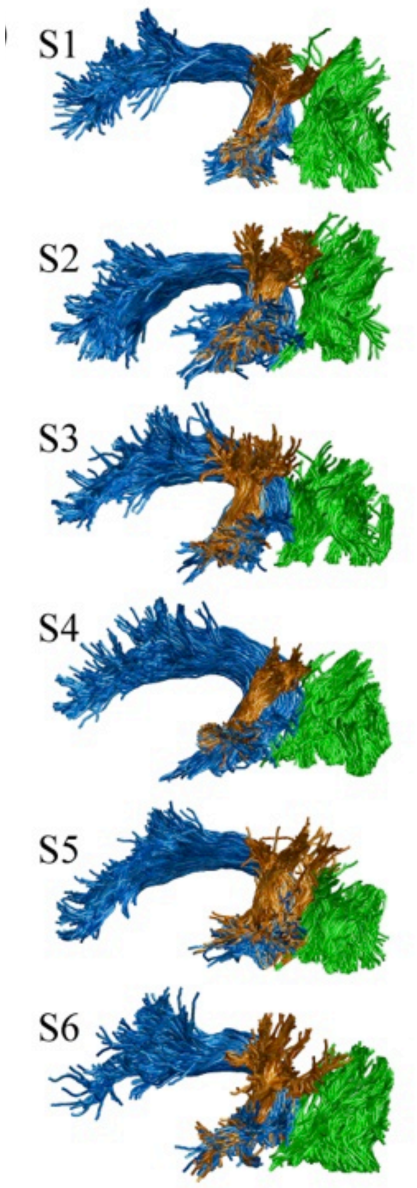


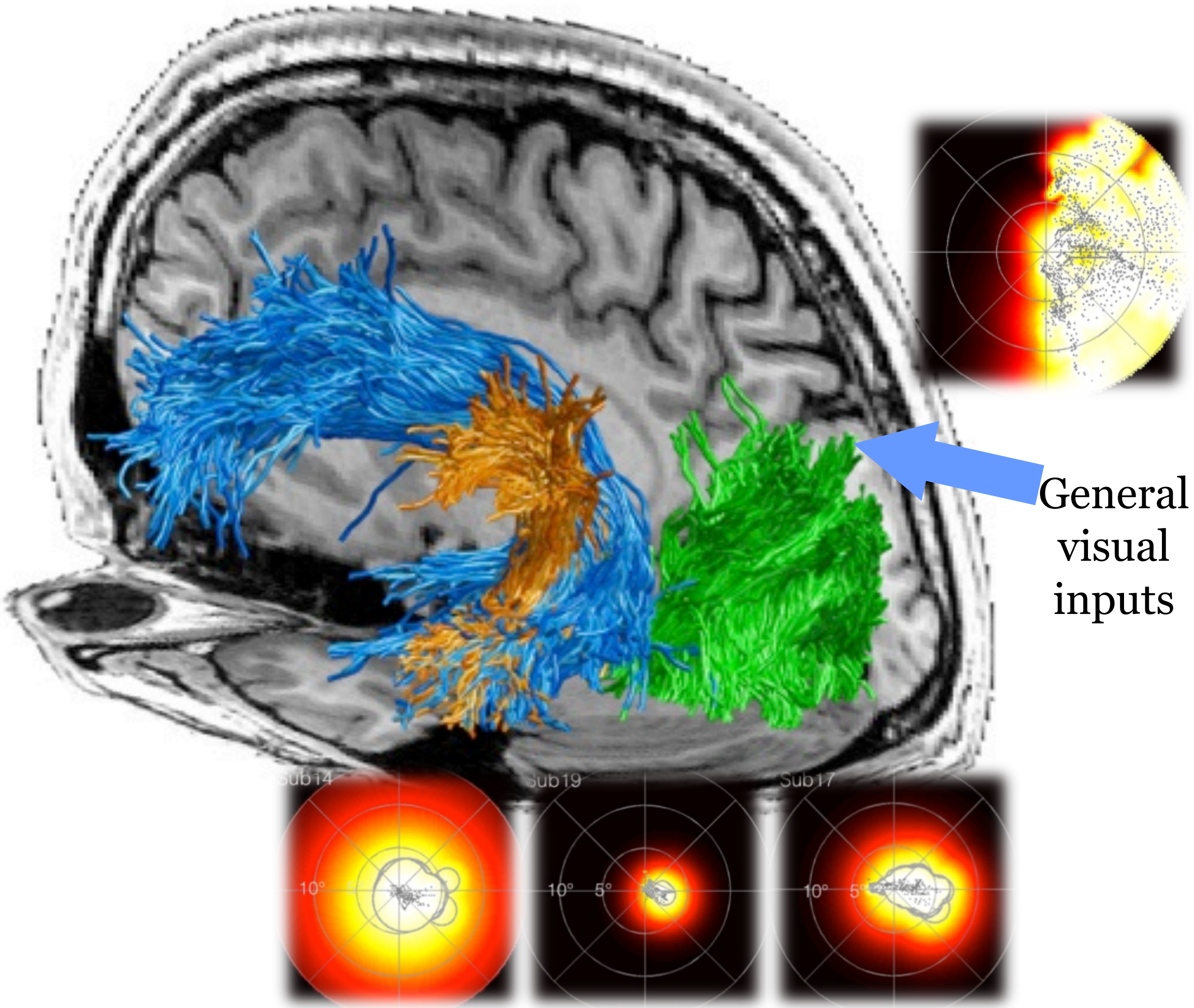




VOT
Specialized processing for
faces, words, other things

# **The future:** Modeling the biological networks that carry visual signals for reading

Car analogy




General visual inputs

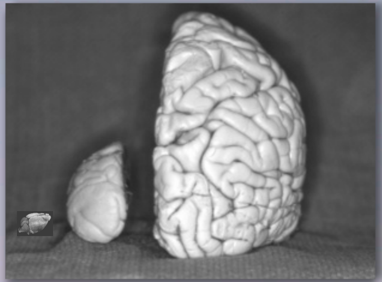
# Third point

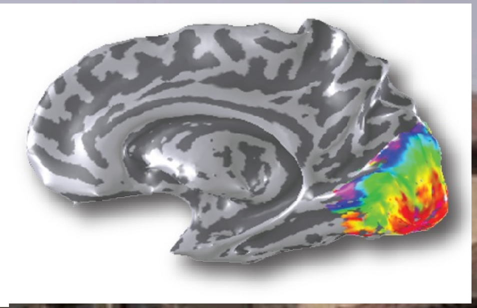
Most newspaper reports about clinical diagnoses describe a single factor – a place in the brain, a type of cell, or a type of molecule.

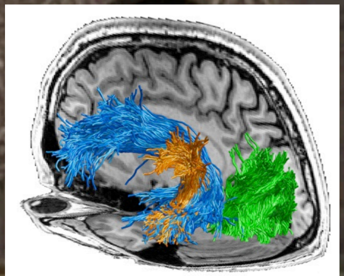
I am urging students and colleagues to think about how the parts of the system work together, not about a single critical object.

# Main points

- The human brain has unique properties
- We have learned much about the visual parts of the brain
- Mis-wiring at birth:  Amazing recovery
- Damage a few years later: Not much recovery
- Future: studying reading the circuitry





# The brain is studied at an enormous range of spatial scales

- There is no reliable theory or model that relates measurements at different scales

- This doesn't stop scientists from speculating or speaking hopefully about relationships