Lecture 2.5: Brain Imaging

1. **X-rays (computer assisted tomography (CAT)),**
2. **Oxygen and Glucose utilization by the Brain**
3. **Positron emission tomography (PET)**
4. **Magnetic Resonance Imaging**

Houpt 1-11-08

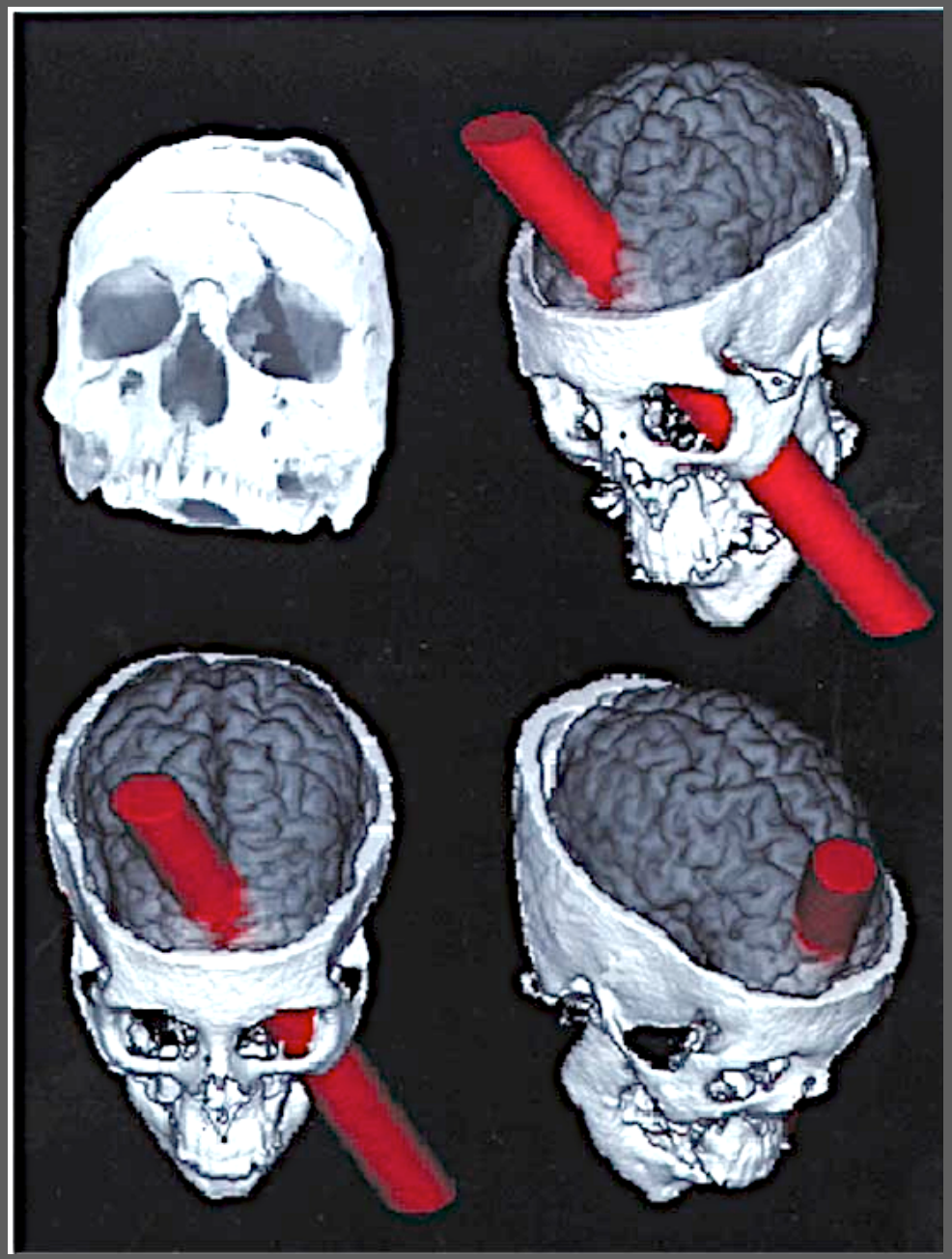
The most famous case of brain damage that causes a change in morality remains that of Phineas Gage, a railroad laborer in Vermont who, one day in the fall of 1848, suffered a horrific on-the-job injury. Gage, the foreman of a crew laying track outside the town of Cavendish, was tamping black powder into a hole drilled in rock when he apparently struck a spark. In a flash of explosion, the tamping iron, a three-and-a-half-foot-long bar an inch in diameter, blew through his left cheek and clean out the top of his head, landing some 30 yards behind him. "It essentially severed the front third of his brain," Eslinger says. "The surgeon who came to the scene described that he insert a could finger through either side of the wound and actually touch them. It was just this clean hole."

www.rps.psu.edu/ indepth/brainscans1.htm

Phineas Gage's skull and life mask

Credit Warren Anatomical Museum, Francis A. Countway Library of Medicine

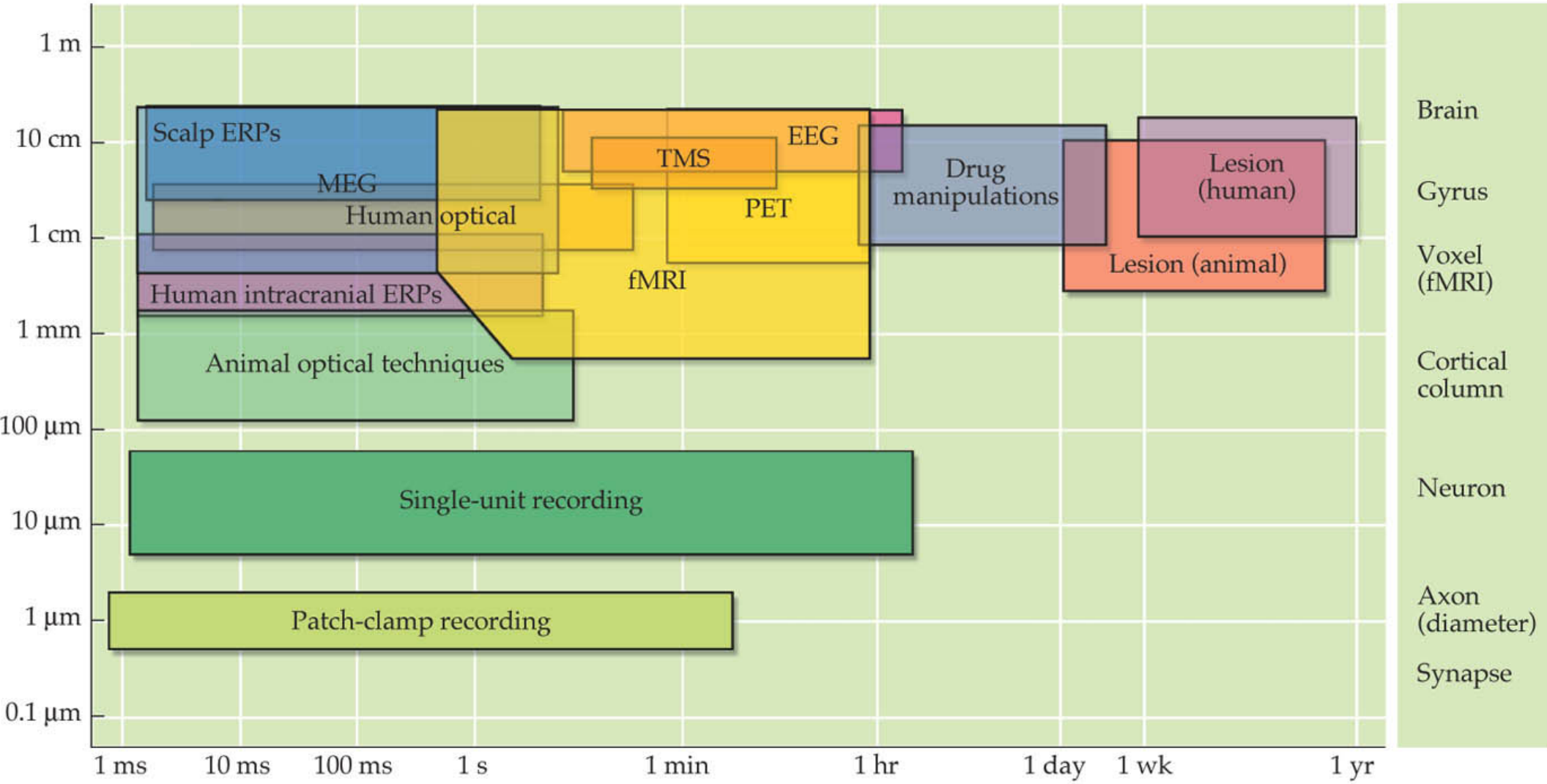
X-rays (computer assisted tomography (CAT)



Reconstruction of the lesion incurred by Phineas Gage, in which an iron bar was driven through his prefrontal cortex as a result of a blasting accident.

Amazingly, Gage survived, and was in fact strong enough to resume work in less than a year. His basic mental faculties—motor skills, memory, speech—were essentially intact. What had changed, profoundly and irrevocably, was his personality. Where before the accident, Gage had been regarded as an excellent foreman, thoughtful, shrewd with money, and well-spoken, afterward he was described as "fitful, irreverent, and grossly profane," and acting with little regard for others. His friends said he was "no longer Gage."

www.rps.psu.edu/ indepth/brainscans1.htm



Methods for analyzing brain function: spatial and temporal resolution

FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 1.7

Two ways to detect change in brain activity (without using electrodes):

1. **Change in blood flow:**
   more active brain regions have increased blood flow

2. **Change in glucose utilization:**
   more active regions use more glucose

(note: both these approaches are **relative** changes, measured against some baseline)

Glucose is energy source for the brain

Brain = 2% of body weight

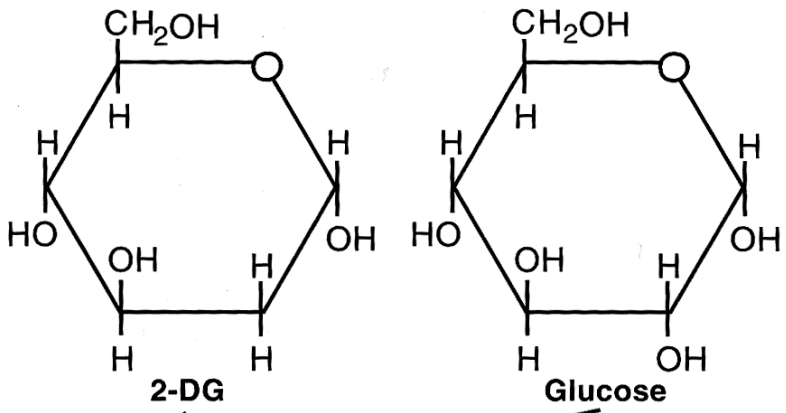
Brain uses 25% of glucose & 20% of oxygen

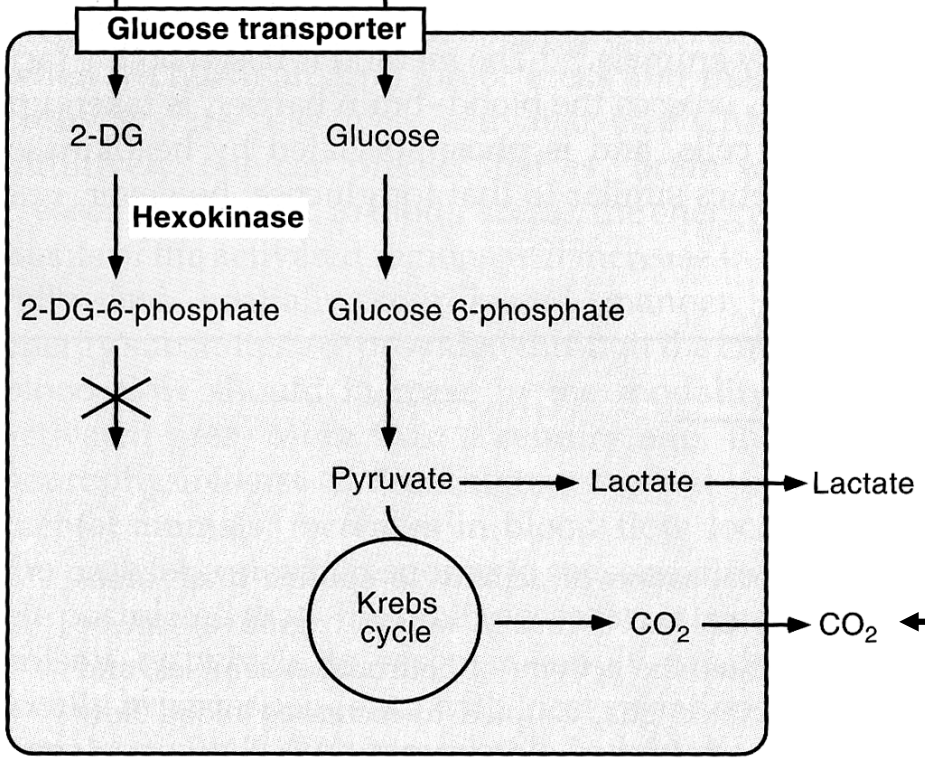
glucose and oxygen used to generate ATP to drive most cellular processes

Can track increased neural activity by increased glucose and oxygen utilization.

2-Deoxy-Glucose (2DG) can track metabolic activity…

label with radioactive 13C





So accumulated 2DG means cell (trying) to use glucose

Can't label plain glucose, just get radioactive CO_2

To detect metabolism with 2DG:

post mortem

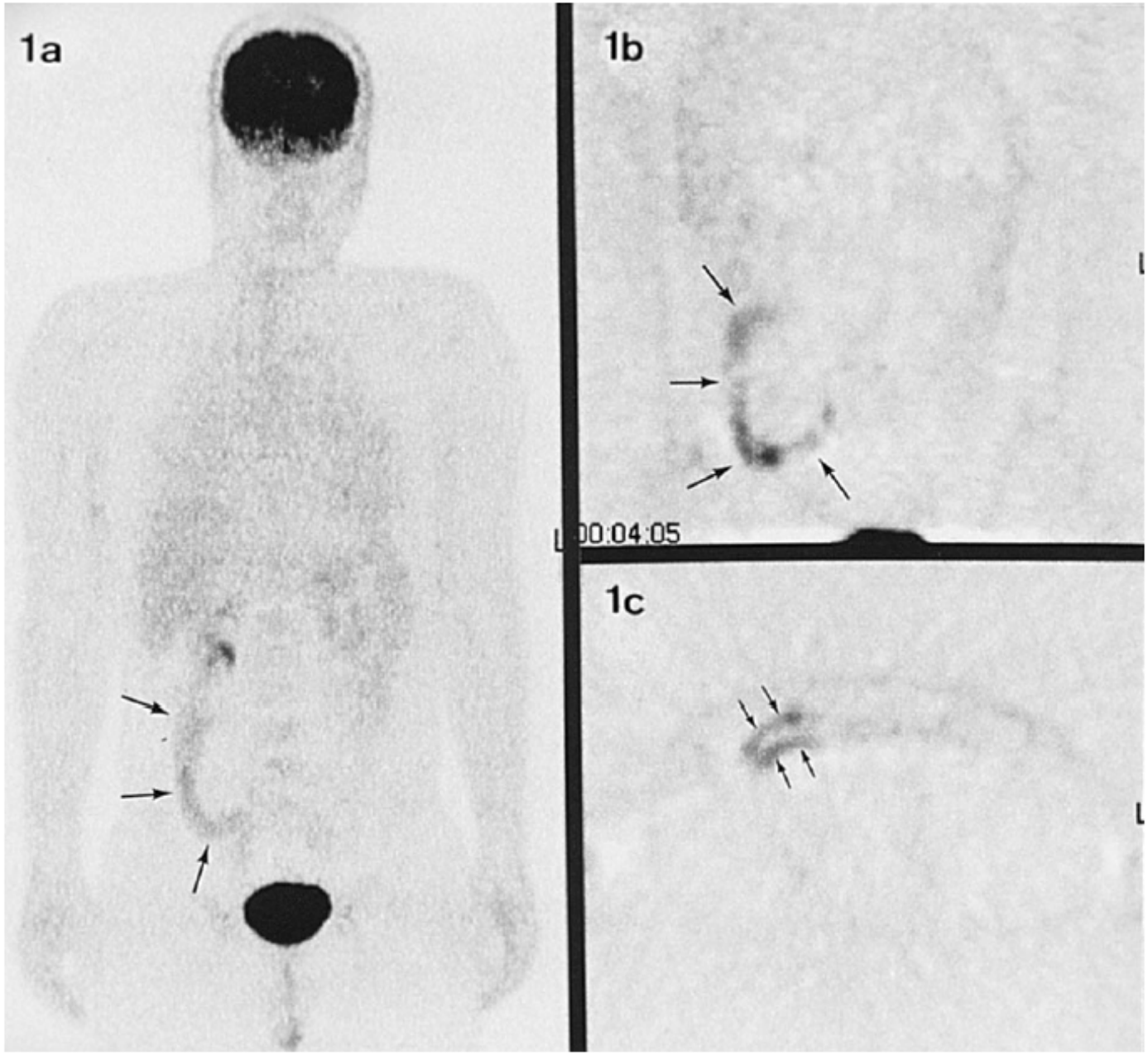
radioactive ^{13}C-2DG is administered, the brain is removed, and tissue sections are apposed to film; an autoradiogram is created when the radiation exposes the film.

in vivo

radioactive fluro-2DG is administered intravenously. 2DG sequested in metabolically active regions is detected with Positron Emission Tomography (PET scan) to make 3D images of the brain.

PET Scan
(in vivo example)

accumulation of radioactive 2DG in living person



FDG-PET image of a patient with Crohn's disease
(a) antero-posterior and (b) coronal projections showing increased FDG uptake in ileum and ascending colon (arrows); (c) axial view at level of transverse colon showing FDG uptake in colonic cells.

Autoradiogram example (Postmortem)

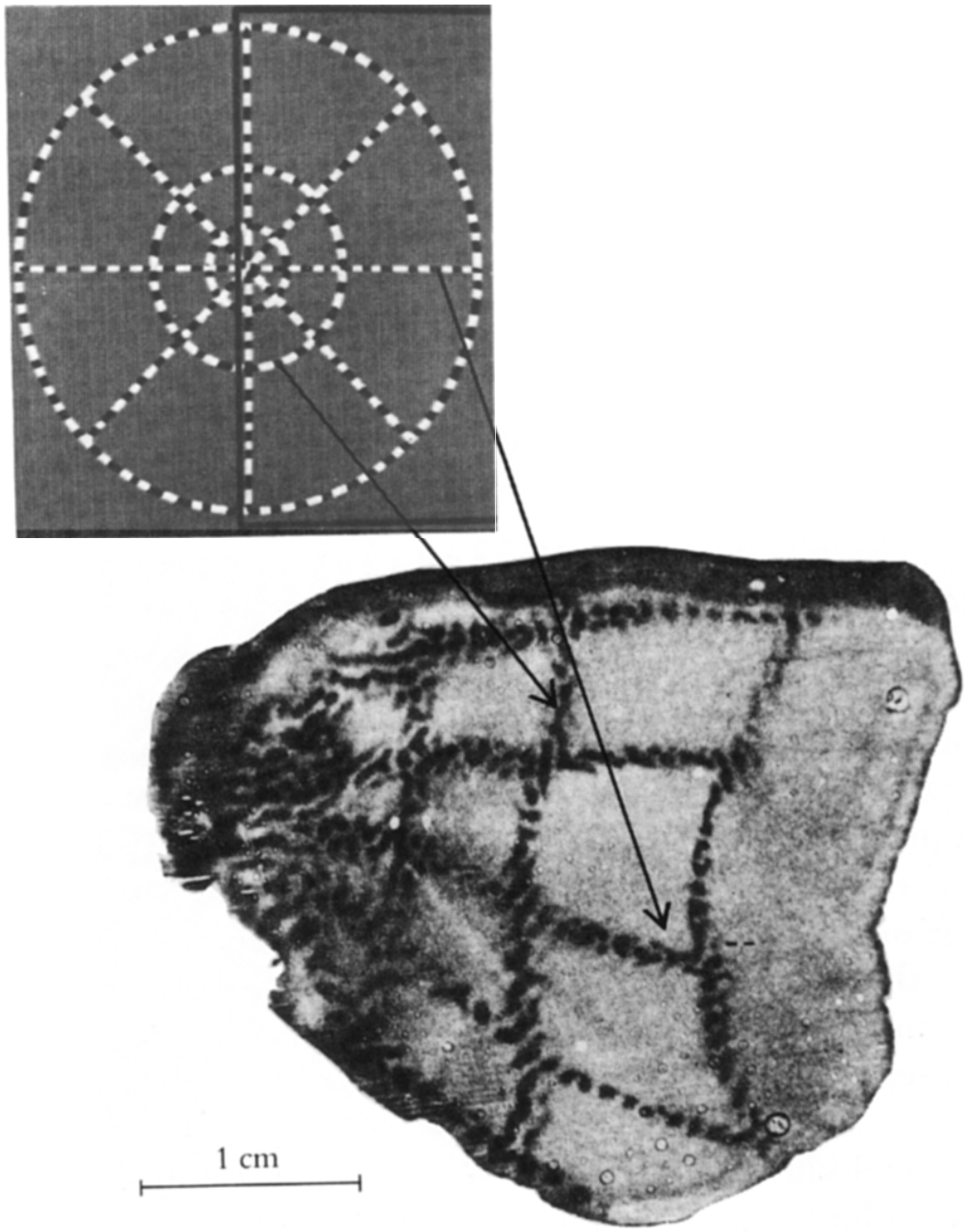
1. Inject monkey with ^{13}C-2DG

2. Project pattern onto screen in front of monkey

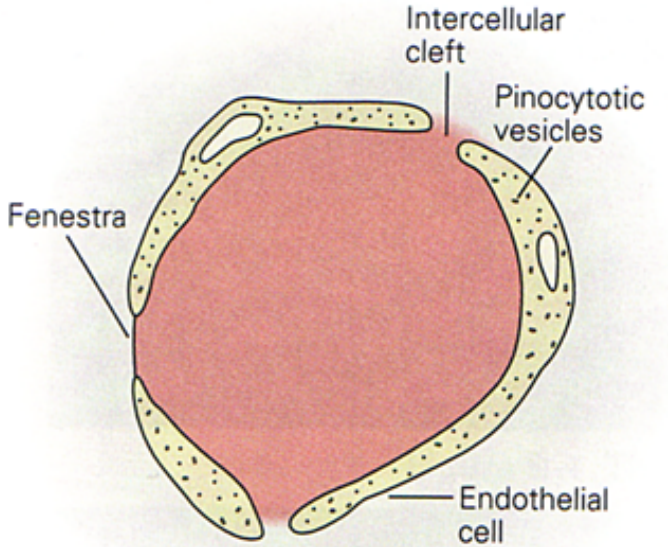
3. Let monkey watch screen for 1 hour

4. Remove brain and expose visual cortex to film

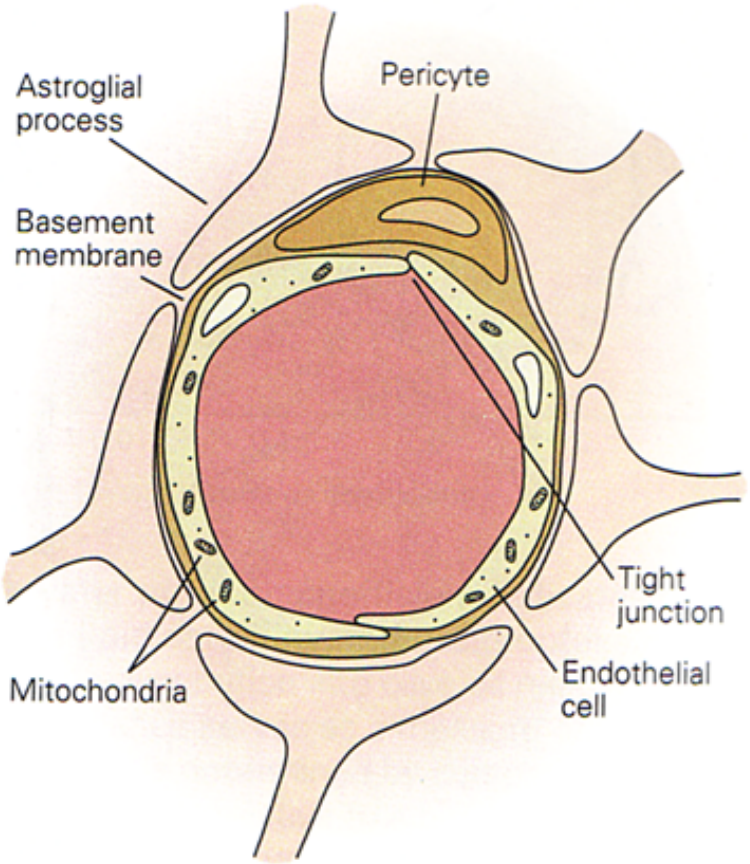
So, are these neurons that respond to visual input?



Blood brain barrier prevents diffusion of glucose into brain



General Capillary



Brain Capillary

How does Glucose get to neurons?

1. **Blood-brain barrier (BBB) prevents diffusion of large, polar molecules like glucose from the blood to the extracellular space of the brain.**

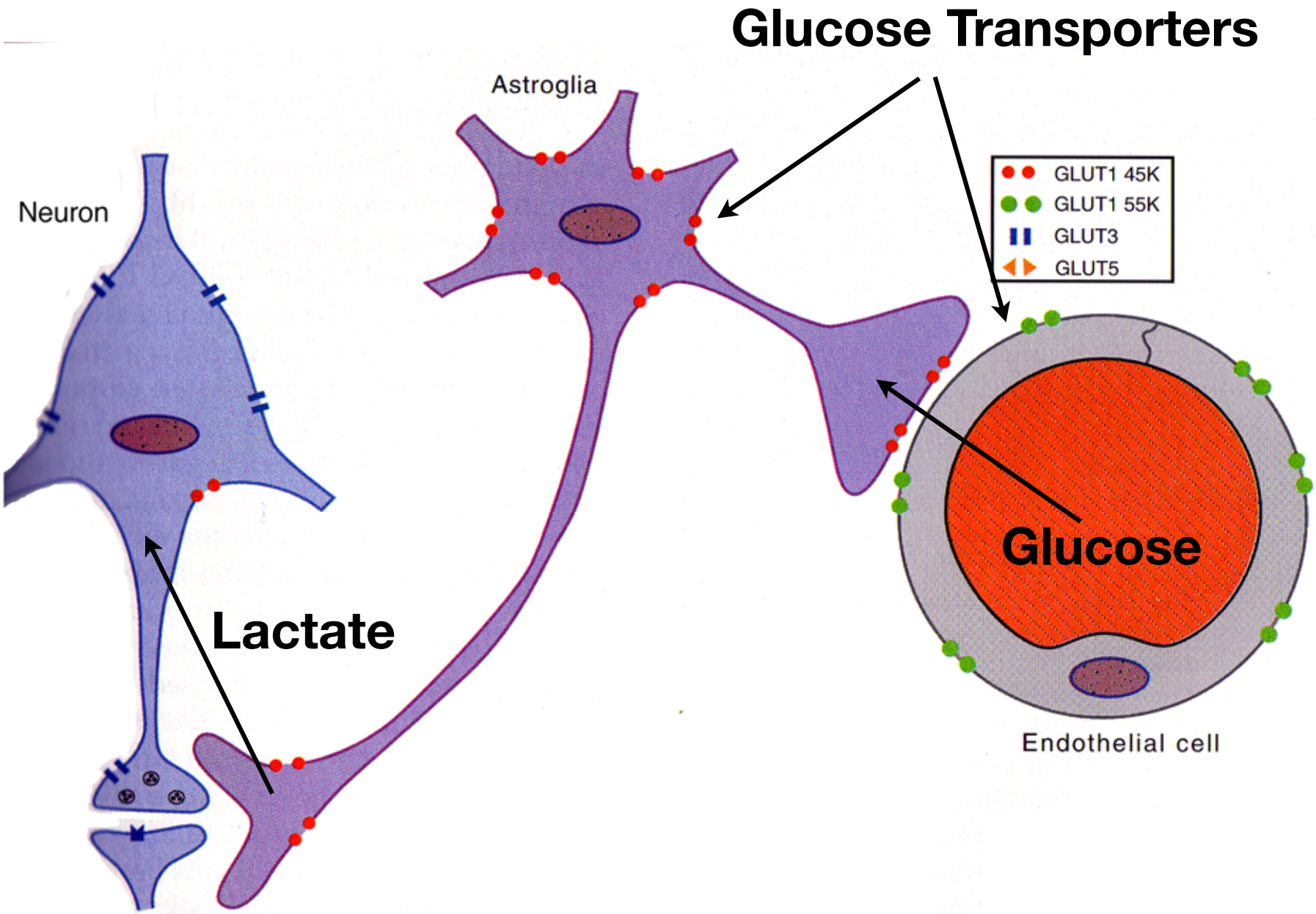
2. **There are glucose transport proteins (GLUTs) in the endothelial cells that move glucose by facilitated transport across the BBB.**

3. **The astrocytes have a large number of GLUTs to take up glucose.**

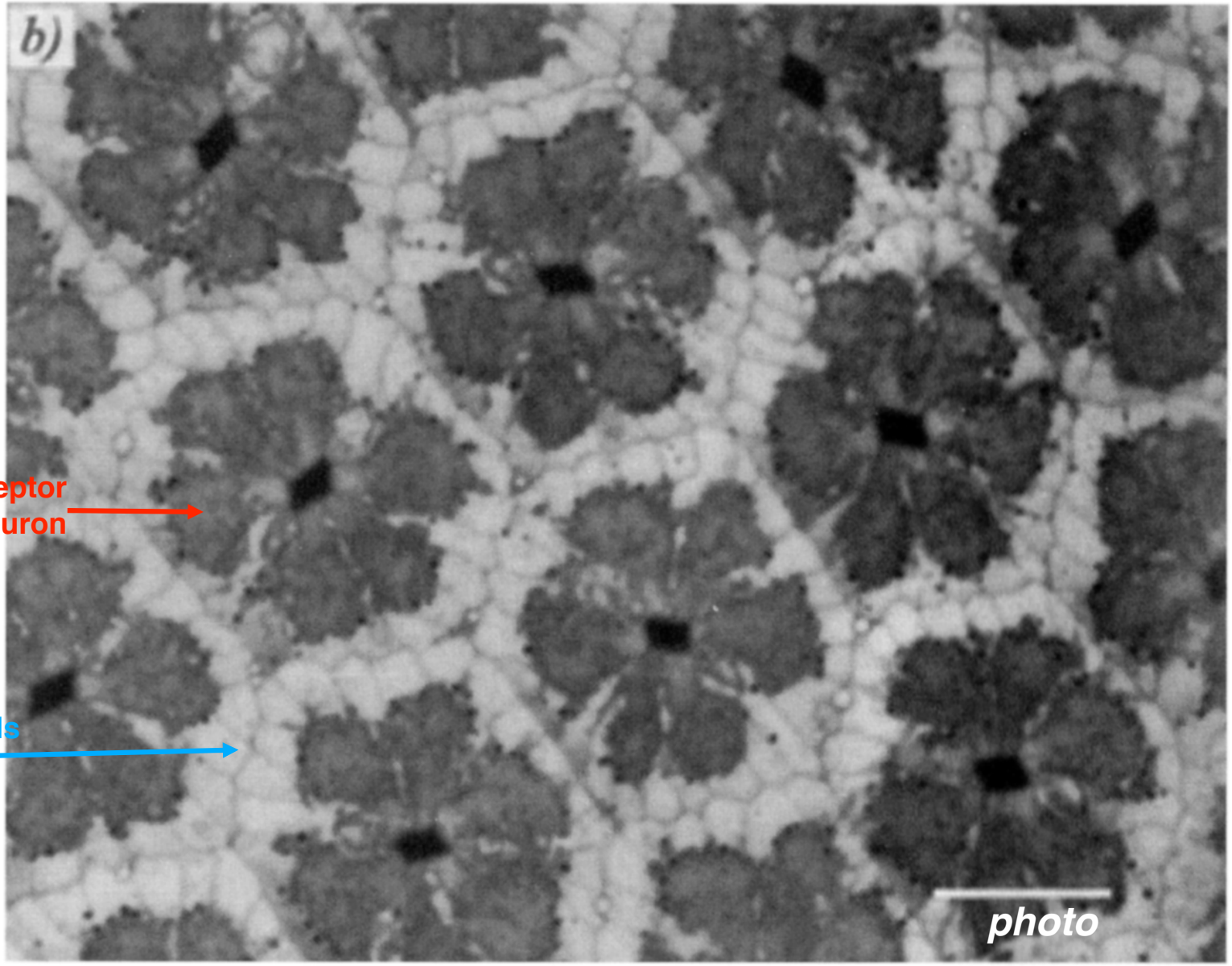
4. **Neurons have a specific GLUT-3 to take up some glucose.**

5. **Astrocytes metabolize glucose to lactate, which is released and taken up by neurons.**

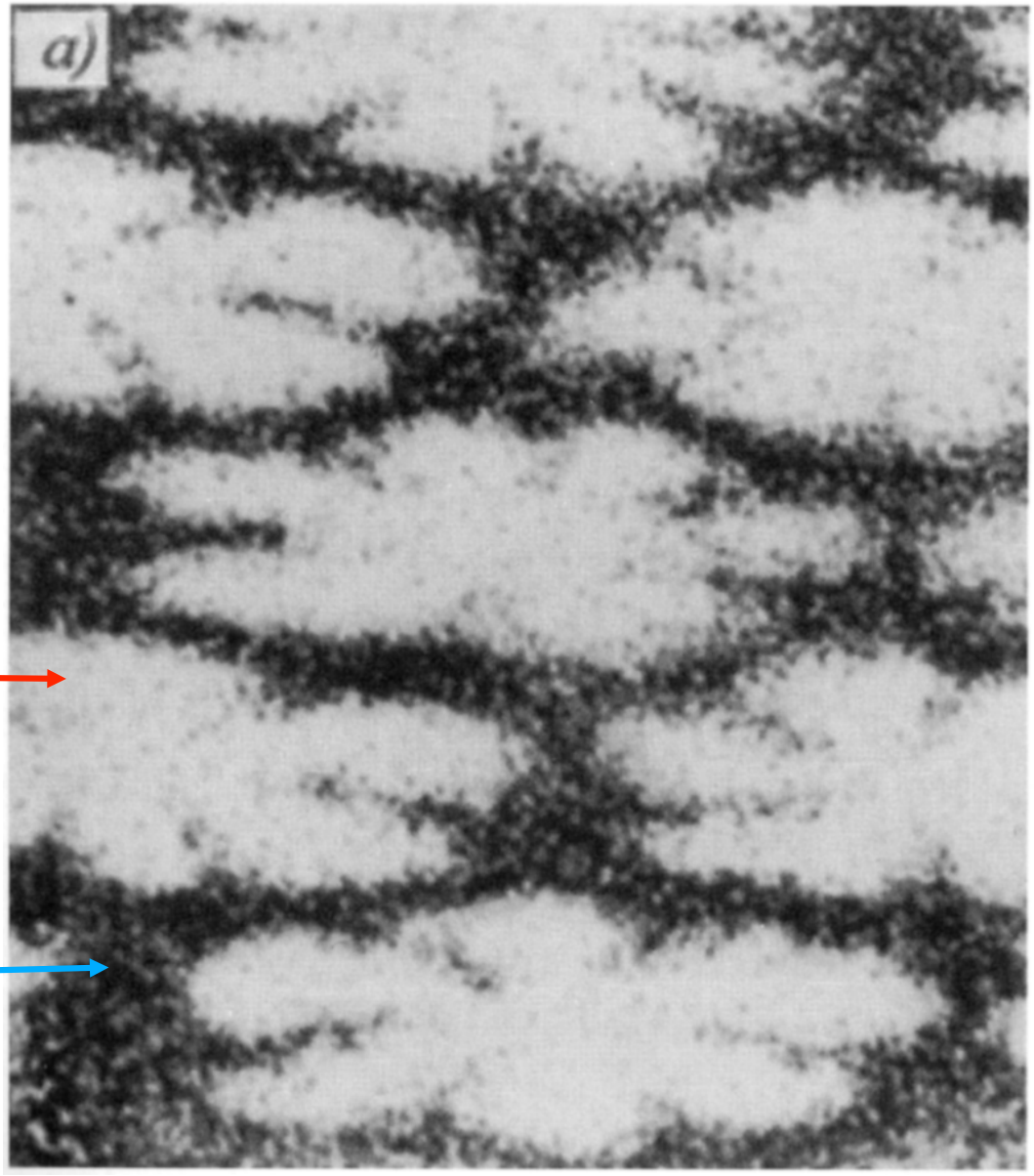
   (Neurons and astrocytes in the feeding centers of the hypothalamus have GLUT-2 transporters, like the pancreas, to monitor glucose levels).


Glucose Transporters
Astroglia
Neuron
GLUT1 45K
GLUT1 55K
GLUT3
GLUT5
Glucose
Lactate
Endothelial cell

Test in a system with clean separation of glia and neurons:



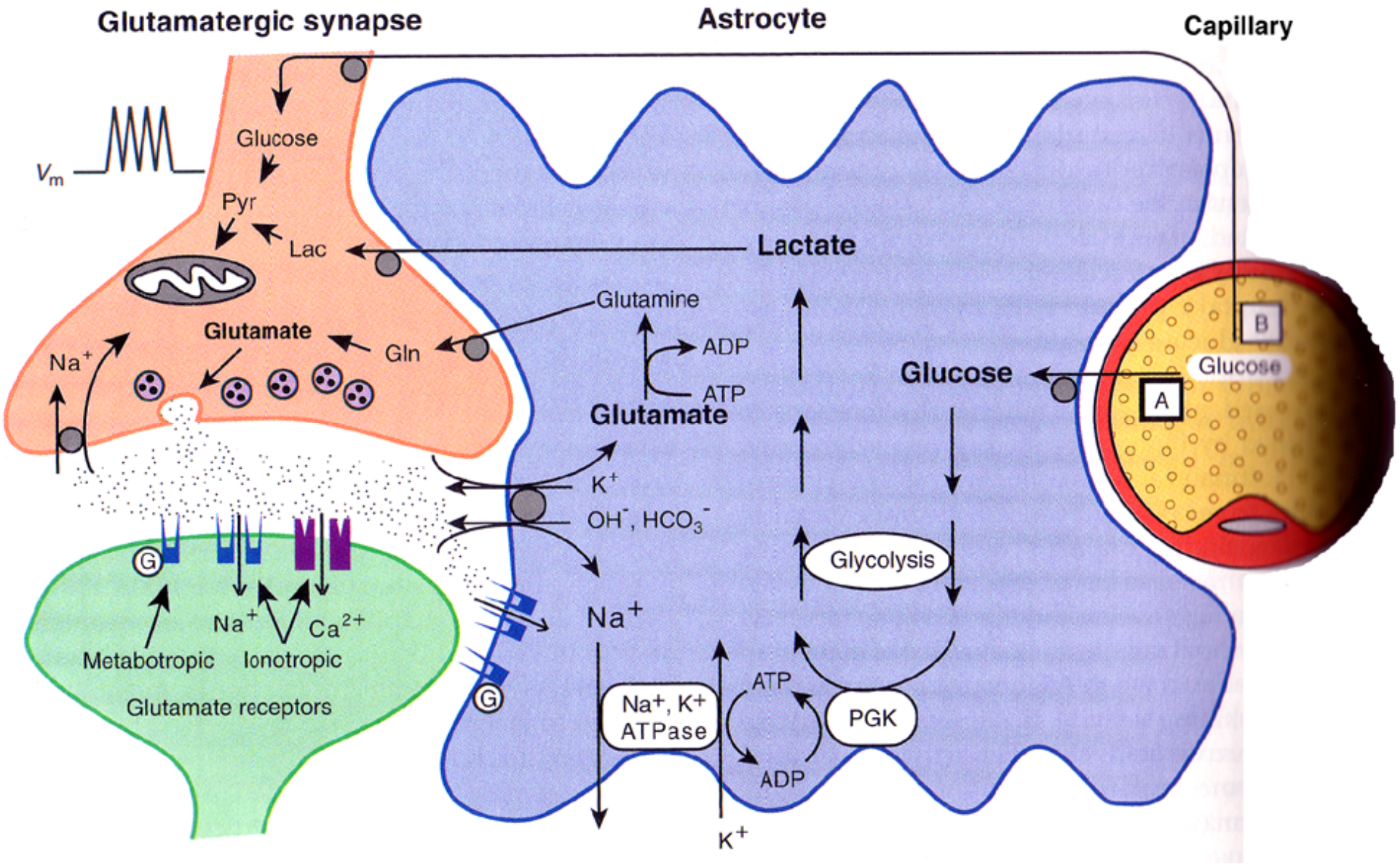
Honey bee photoreceptor neurons are arrayed in hexagonal “rosettes”, surrounded by glial cells.



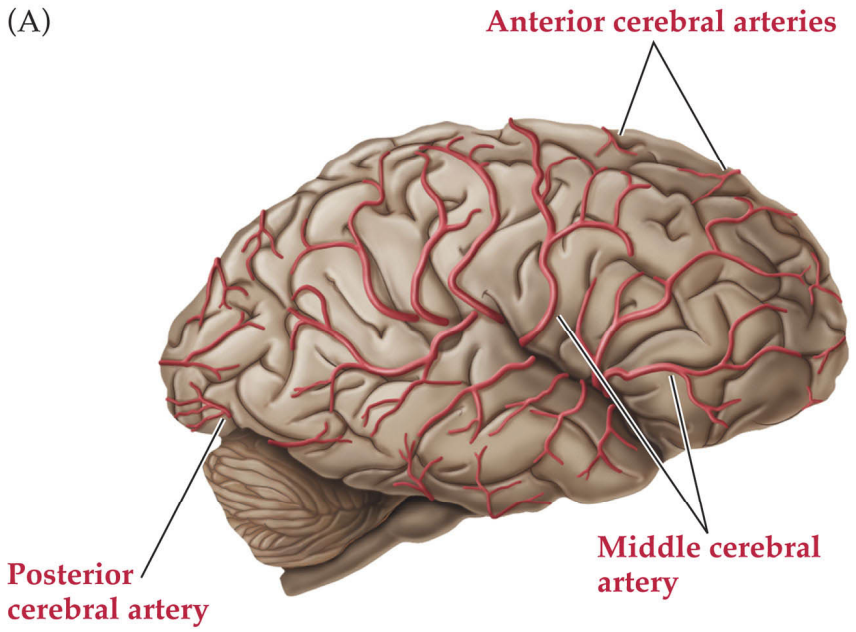
autorad

After incubation with 2DG, the neurons accumulate almost no glucose, but surrounding glia cells are heavy users of glucose.

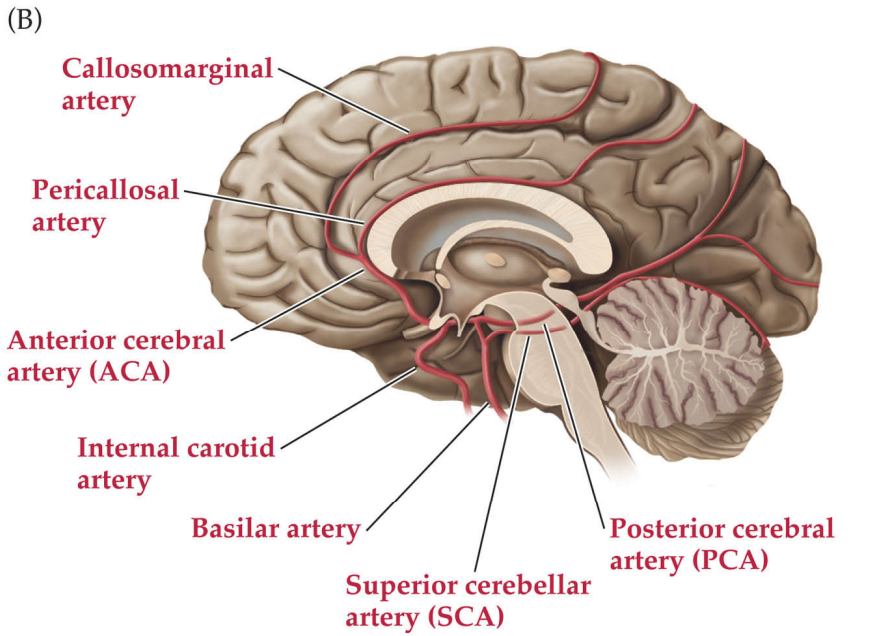
Glial cells partially metabolize glucose -> lactate -> neurons



Blood Flow to Active Brain Regions



FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 6.11 (Part 1) © 2004 Sinauer Associates, Inc.



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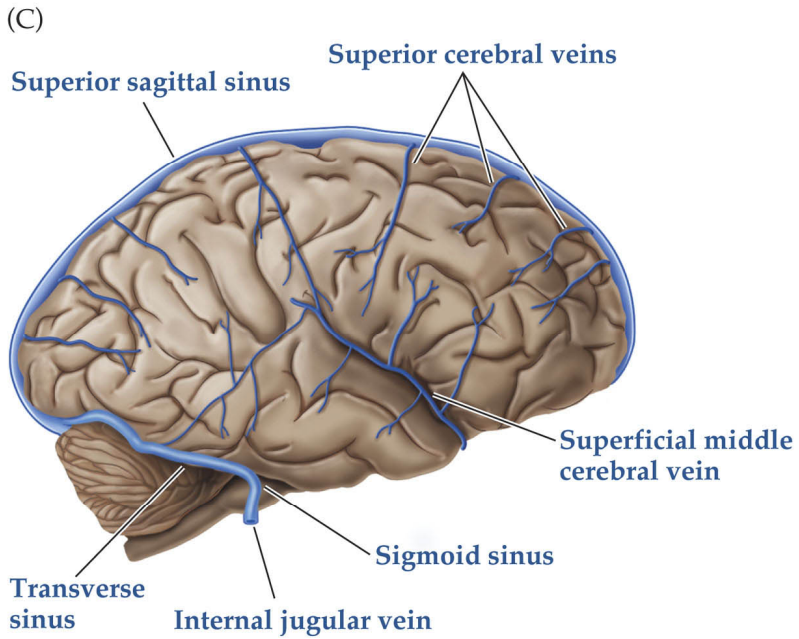

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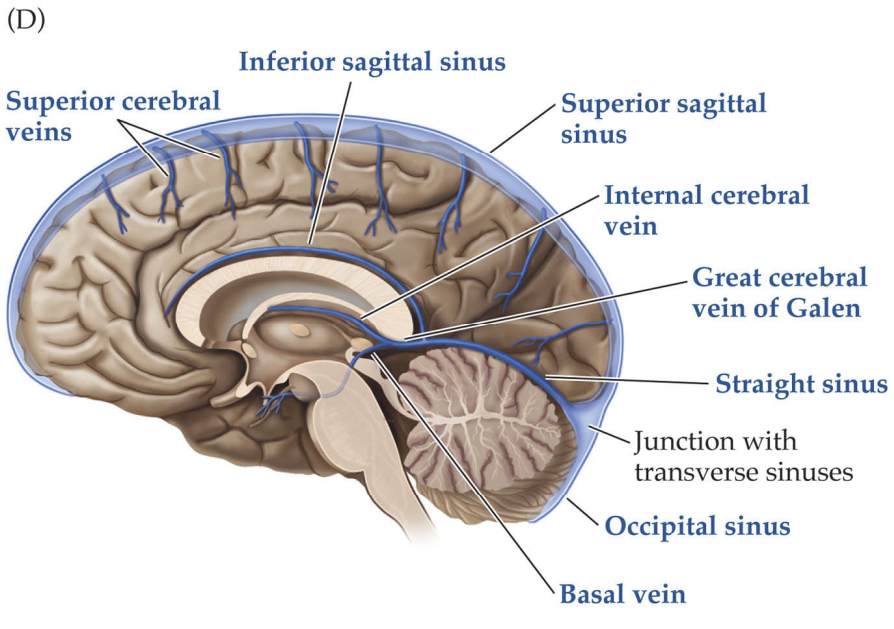

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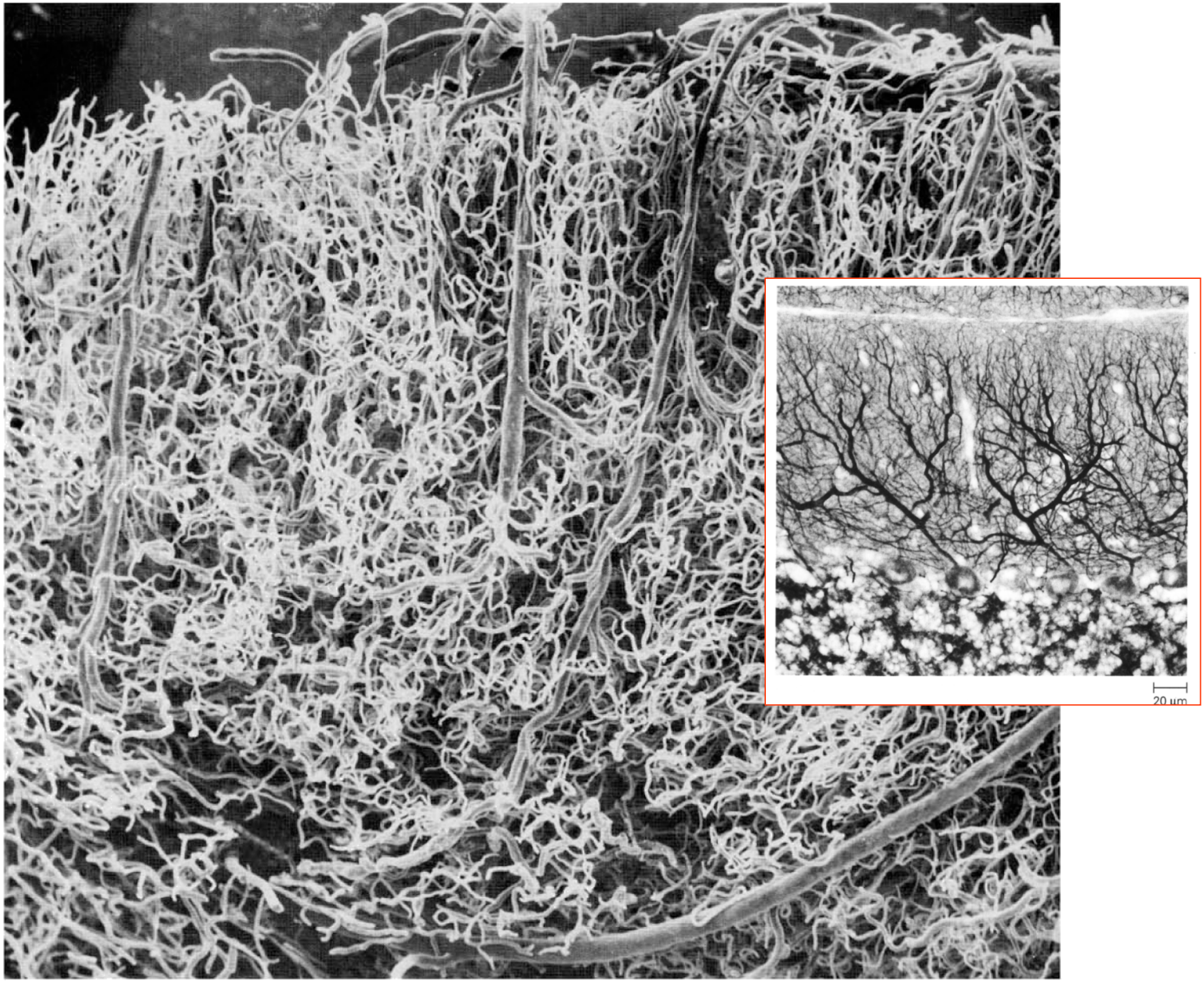
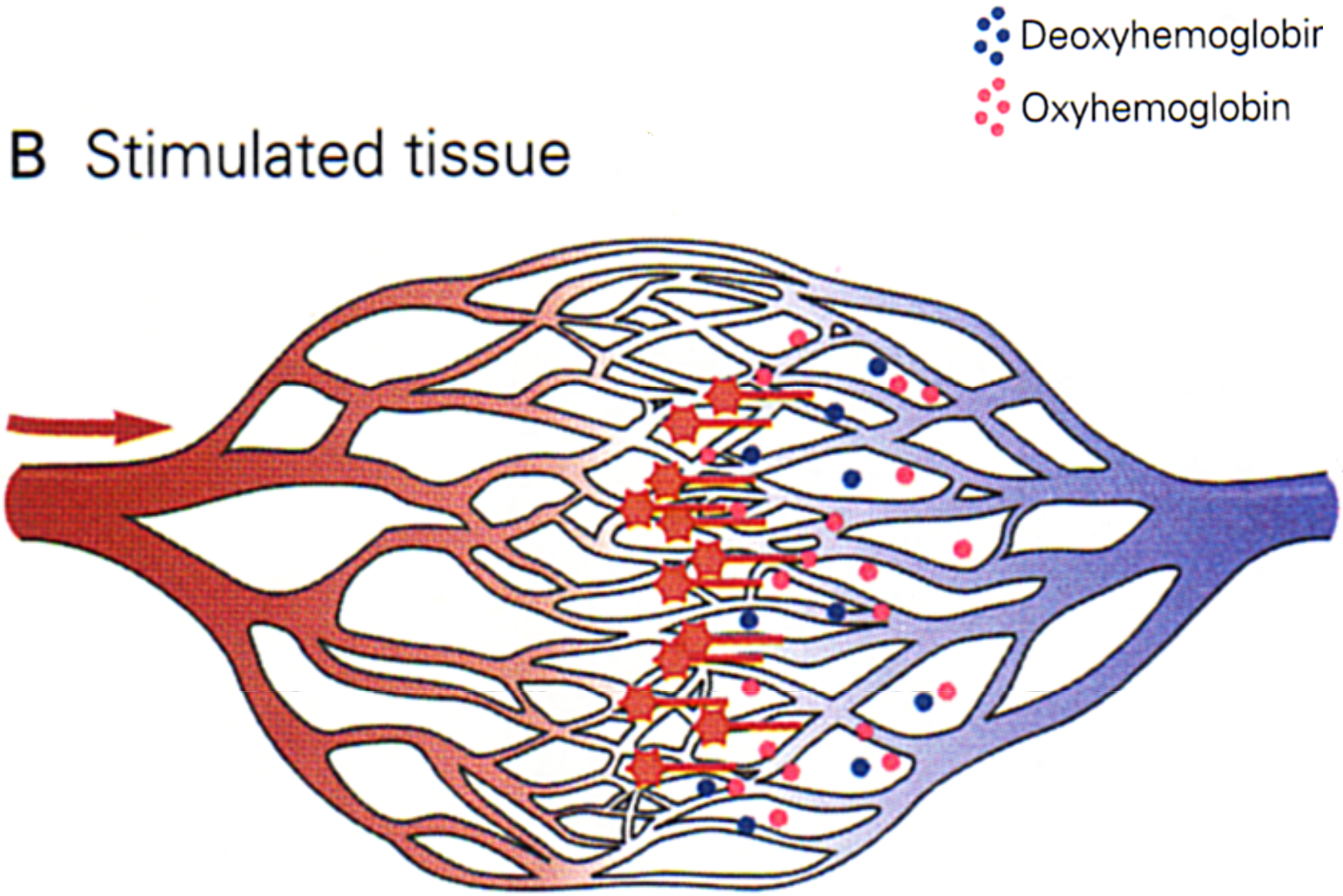
(A)

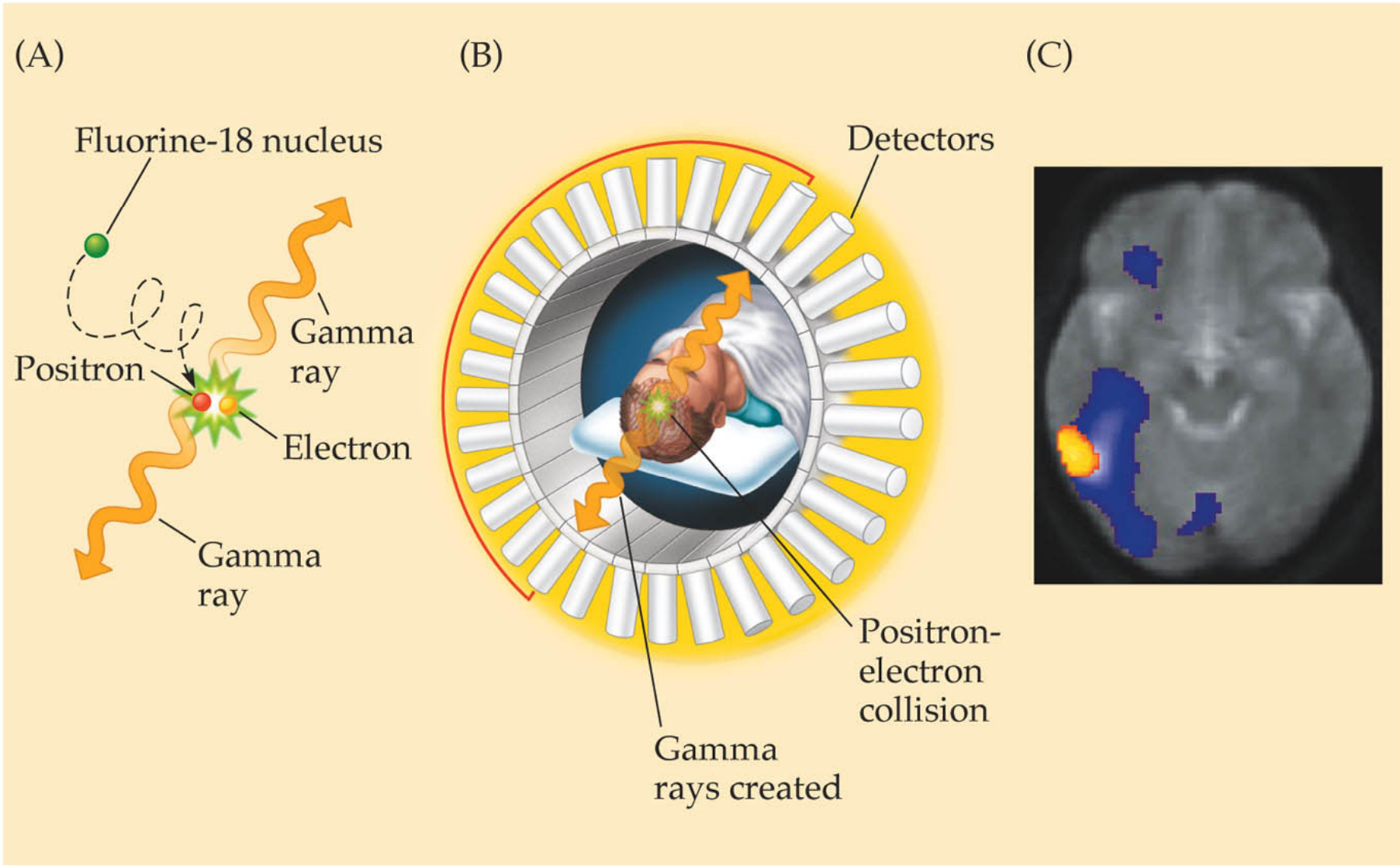
(B)


20 µm



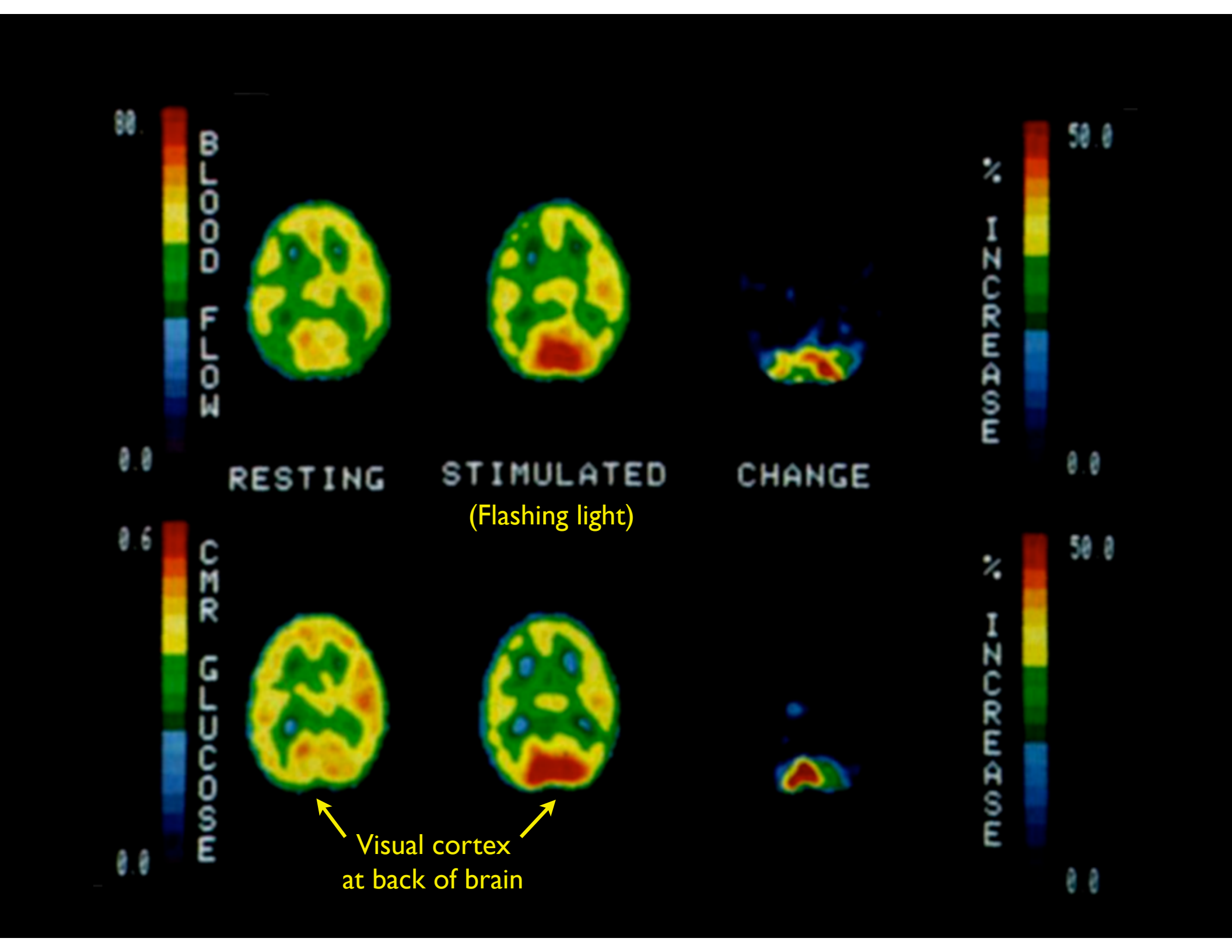
Release of K+, adenosine, lactate and nitric oxide by neurons and glia causes local vasodilation and increase in oxygenated hemoglobin

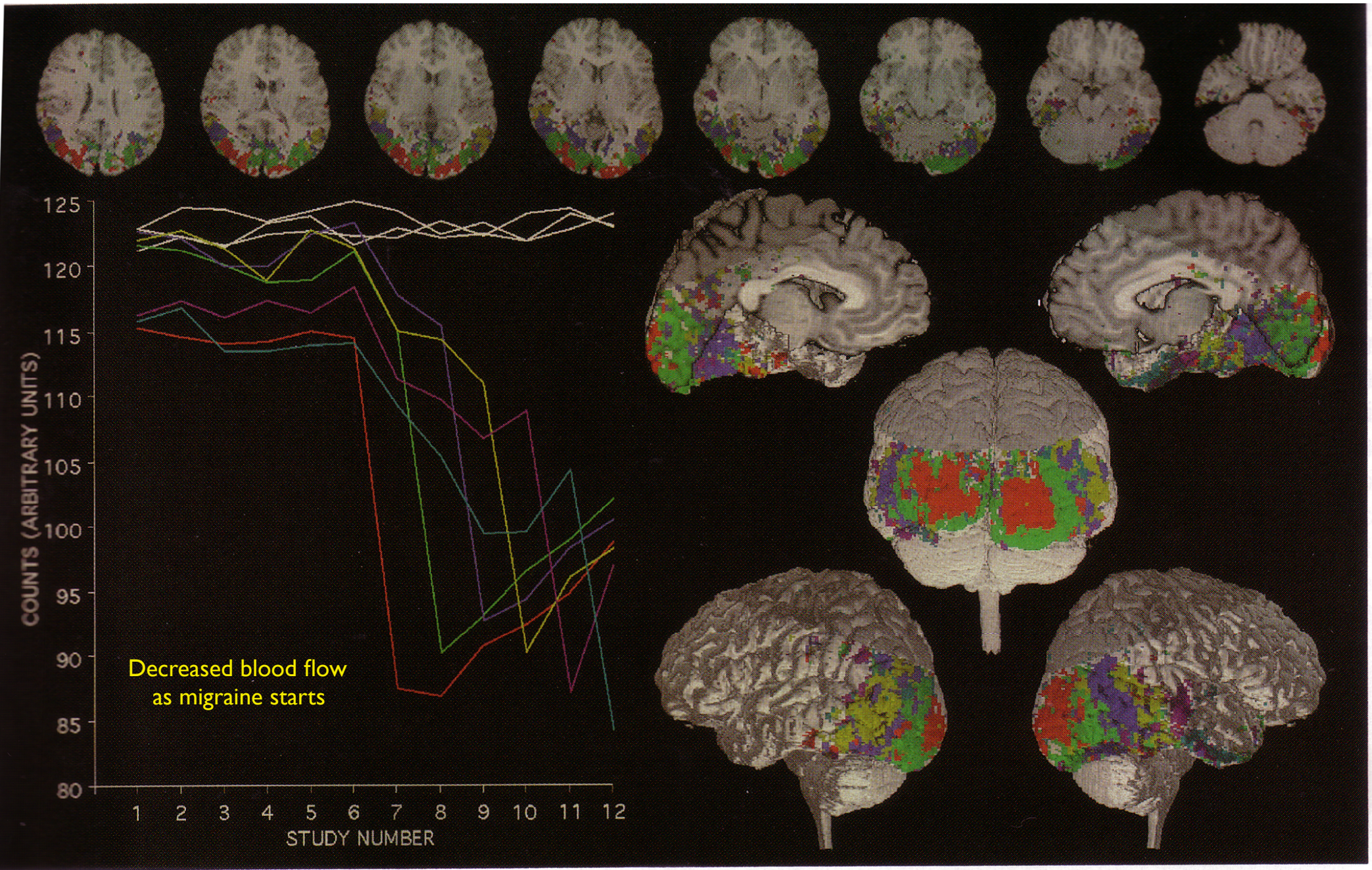
PET scan



Different isotopes can be used for different measures:
e.g, ^{18}F-deoxy-Glucose for metabolism, or ^{15}O-water for blood flow

FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 7.4**


80.
BLOOD FLOW
0.0
RESTING
STIMULATED
CHANGE
50.0
% INCREASE
0.0
(Flashing light)
0.6
CMR GLUCOSE
0.0
Visual cortex
at back of brain
50.0
% INCREASE
0.0



igure 24 [^{15}O]water PET activation study (3D acquisition) from a subject during a migraine headache. Color-coded PET subtraction udies are shown superimposed on rendered MRI data. The migraine started shortly after study number six and continued for the duration f the imaging session. Hypoperfusion starts in the occipital lobes (red) during study number seven and spreads anteriorly into temporal nd occipital lobes during studies 8–12. From Woods *et al.* (1994).

MRI

Synopsis of MRI

1. Put subject in big magnetic field
2. Transmit radio waves into subject (2-10 ms)
3. Turn off radio wave transmitter
4. Receive radio waves re-transmitted by subject
5. Convert measured RF data to image

James Voyvodic, Ph.D

Hydrogen atoms are best for MRI

- Biological tissues are predominantly ^{12}C, ^{16}O, ^{1}H, and ^{14}N
- Hydrogen atom is the only major species that is MR sensitive
- Hydrogen is the most abundant atom in the body
- The majority of hydrogen is in water (H2O)
- Essentially all MRI is hydrogen (proton) imaging

Two types of MRI image

T1 image:

H atoms in non-aqueous environment

Bone, white matter, fat looks bright

T2 image:

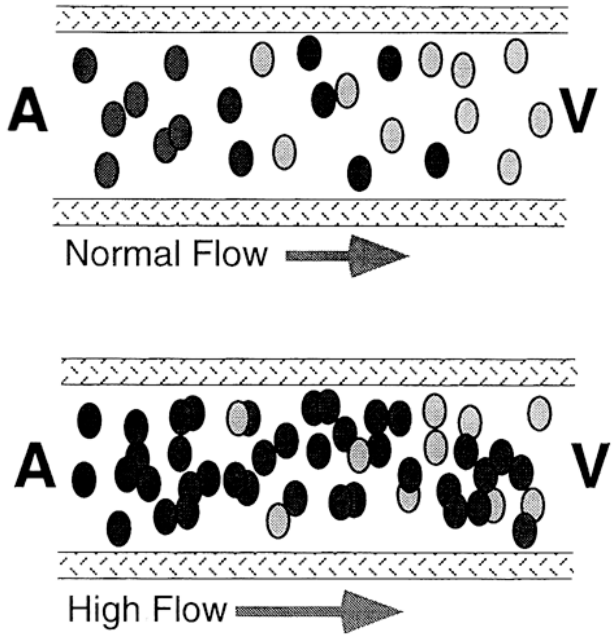
H atoms surrounded by water

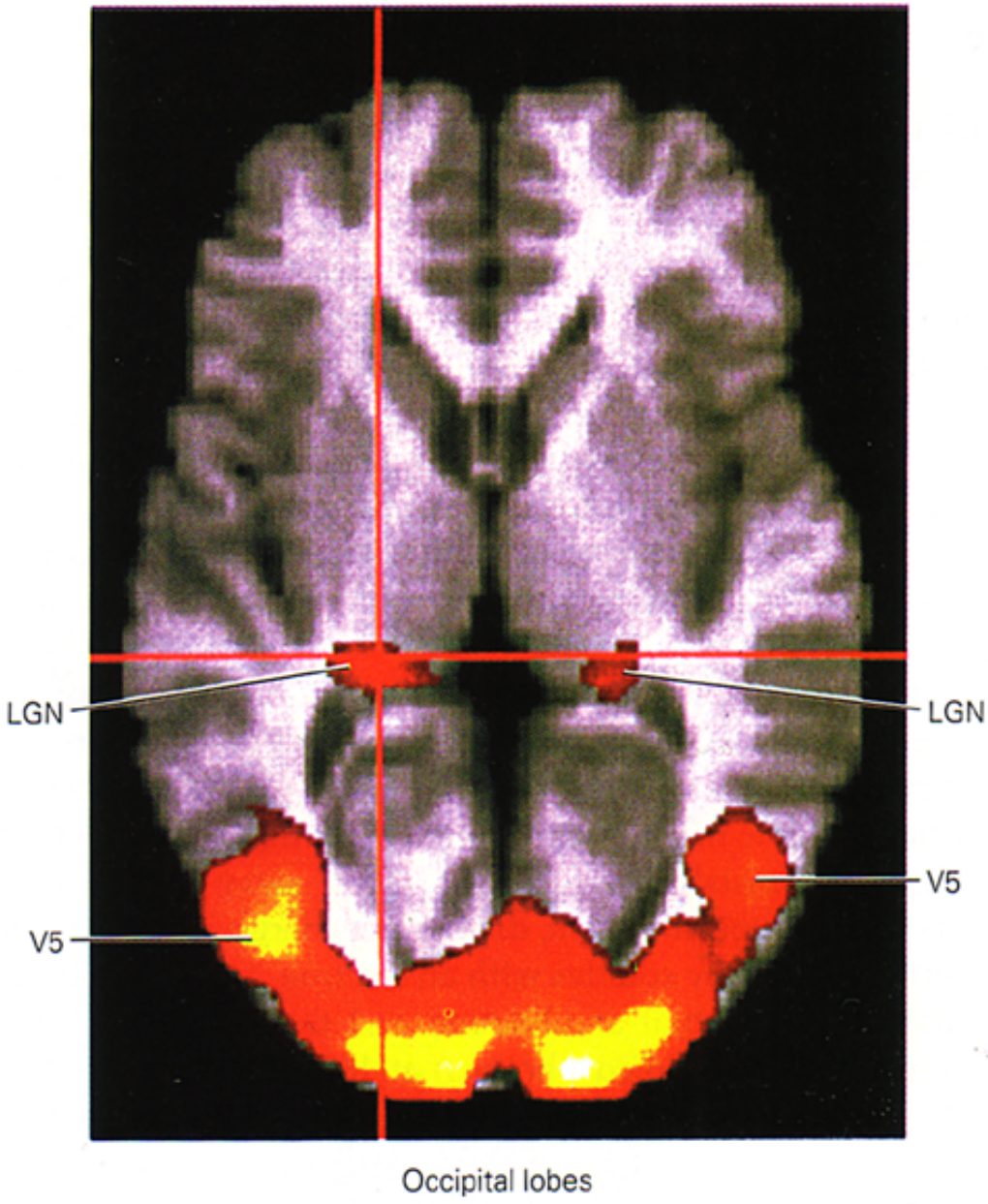
Fluid spaces, gray matter looks bright

Increased blood oxygenation level detection (BOLD) by MRI

oxygenated hemoglobin can be detected by MRI.

so increased oxyhemoglobin reflects increased blood flow which reflects increased brain activity.





Response to light

Science

REPORTS

Cite as: Andics *et al.*, *Science* 10.1126/science.aaf3777 (2016).

Neural mechanisms for lexical processing in dogs

A. Andics,[1,2,3]* A. Gábor,[2] M. Gácsi,[1] T. Faragó,[1] D. Szabó,[1,2] Á. Miklósi[1,2]

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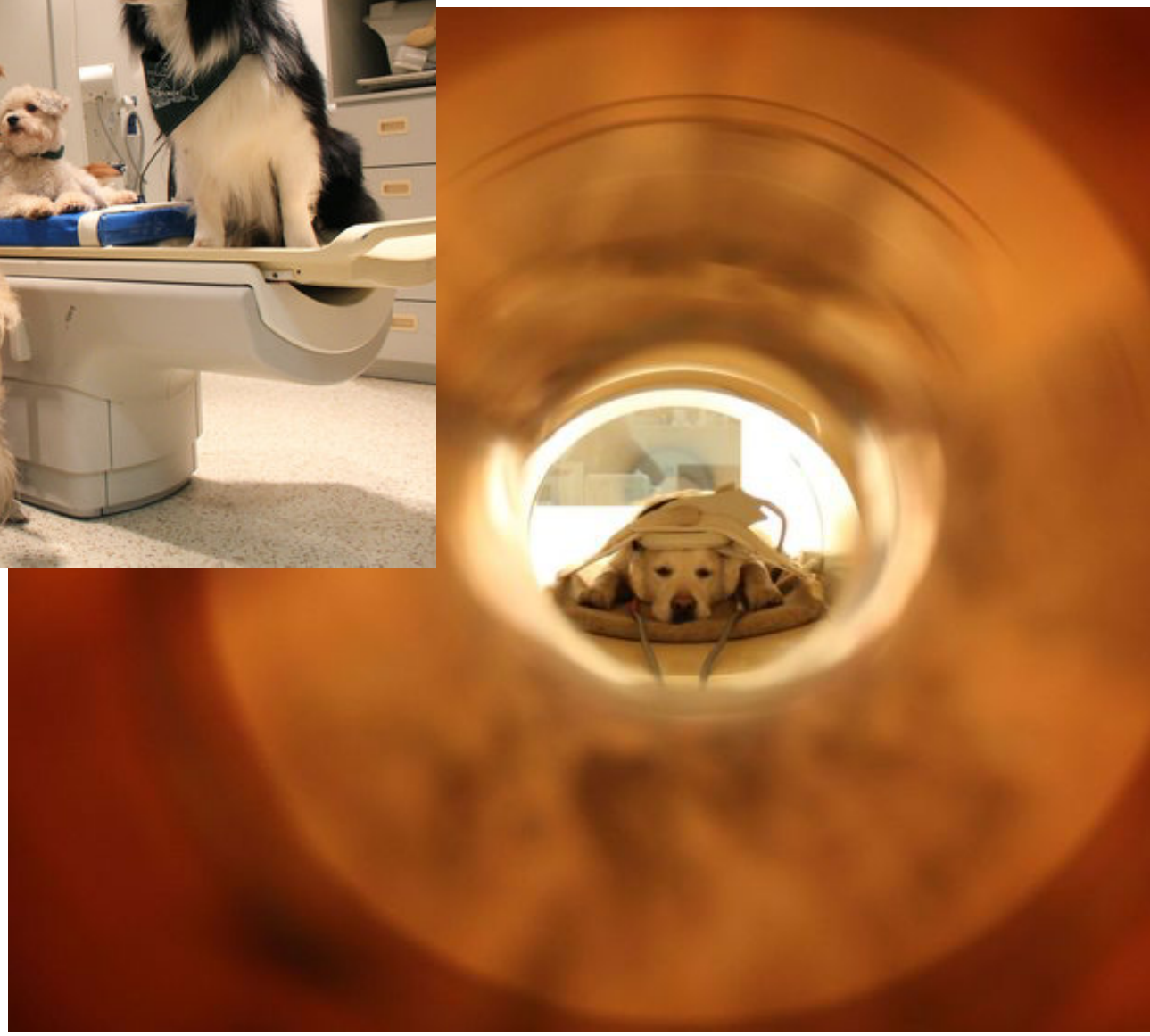
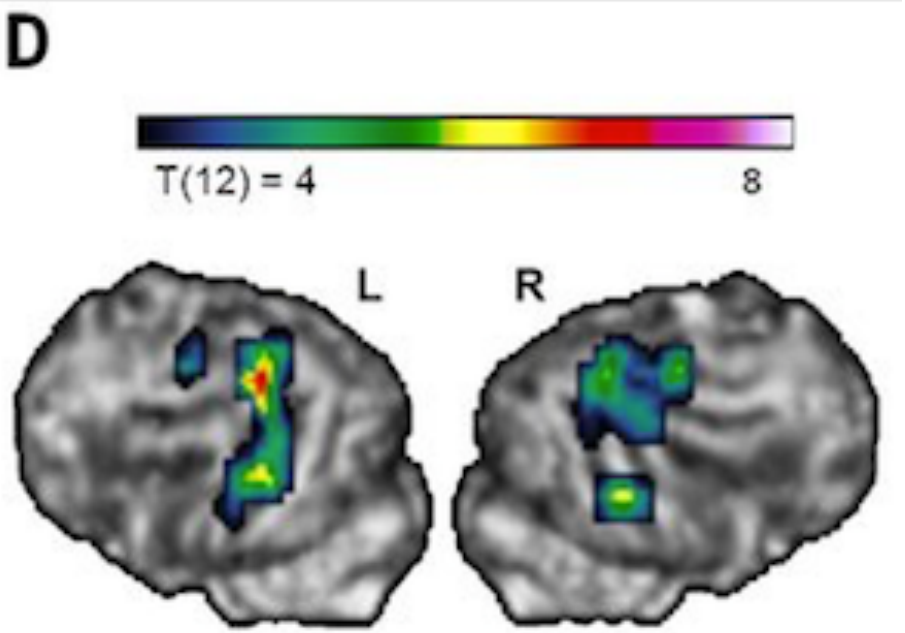
During speech processing, human listeners can separately analyze lexical and intonational cues to arrive at a unified representation of communicative content. The evolution of this capacity can be best investigated by comparative studies. Using functional magnetic resonance imaging, we explored whether and how dog brains segregate and integrate lexical and intonational information. We found a left-hemisphere bias for processing meaningful words, independently of intonation; a right auditory brain region for distinguishing intonationally marked and unmarked words; and increased activity in primary reward regions only when both lexical and intonational information were consistent with praise. Neural mechanisms to separately analyze and integrate word meaning and intonation in dogs suggest that this capacity can evolve in the absence of language.

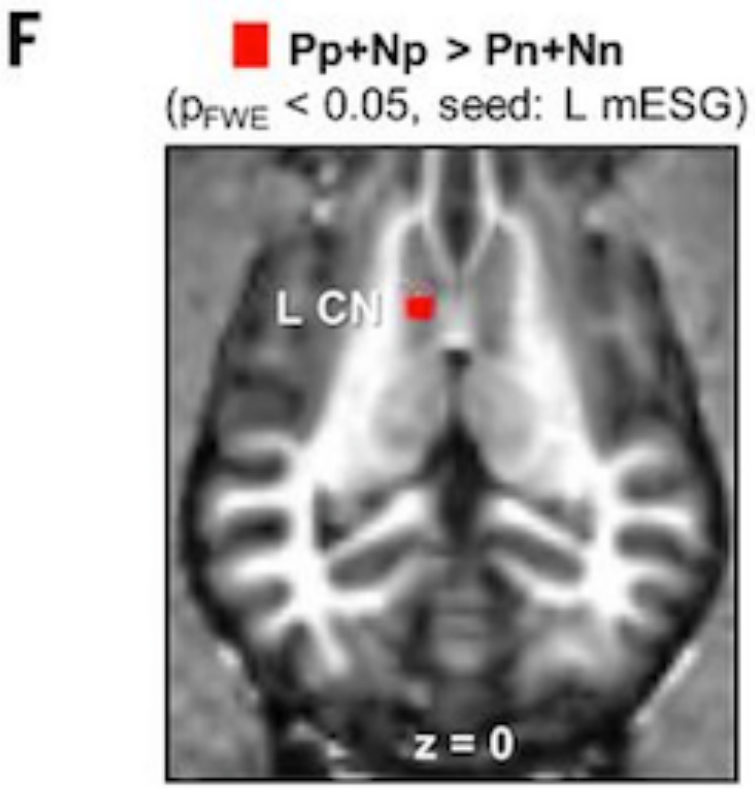


http://science.sciencemag.org/content/353/6303/1030.full

https://www.youtube.com/watch?time_continue=131&v=N9QQxa6eLPc

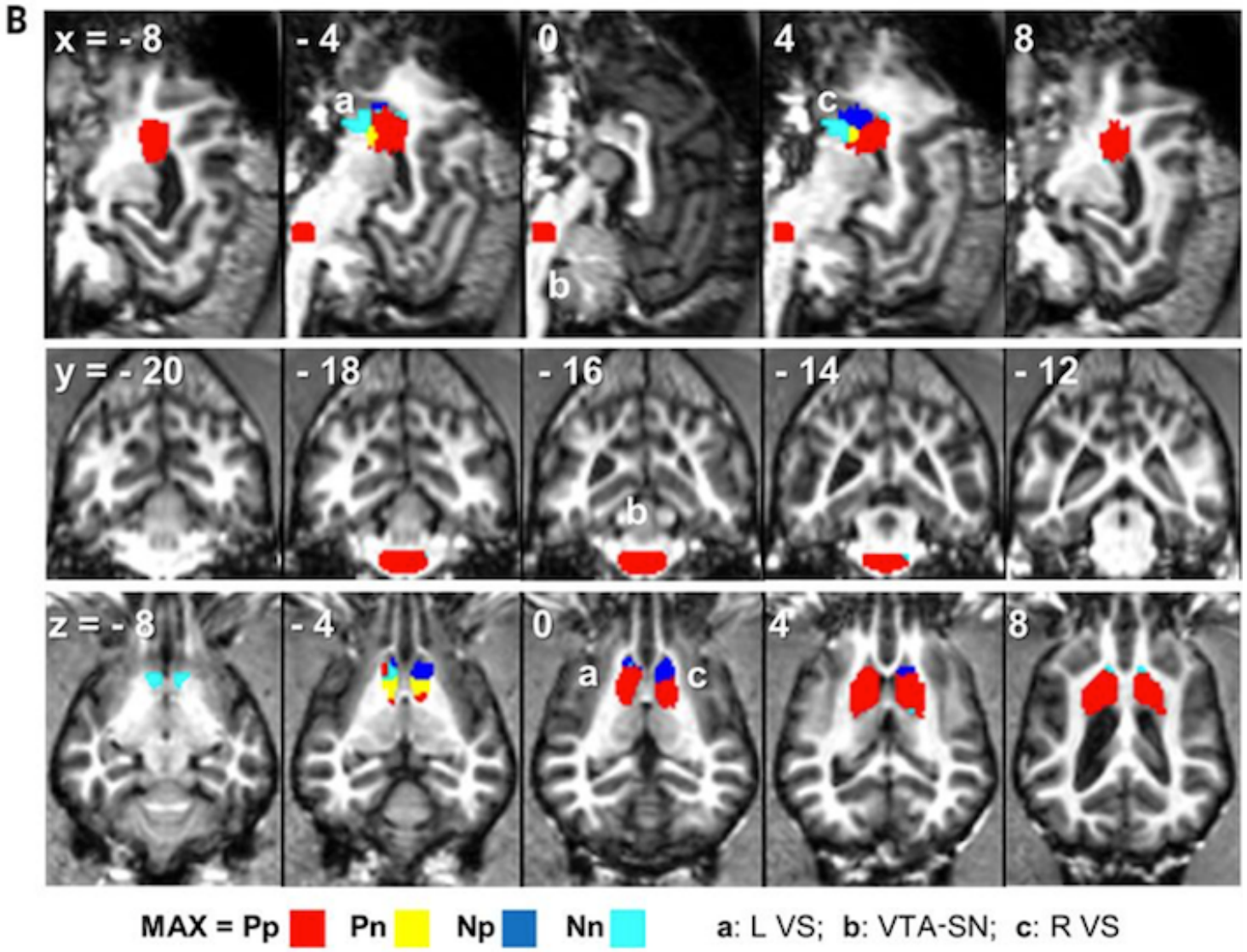
https://www.youtube.com/watch?v=N9QQxa6eLPc



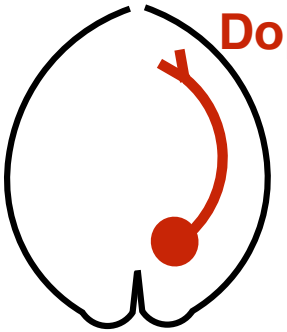


D) Dog auditory regions responsive to speech (table S2). The color bar shows the range for one-sample t-test scores (12 degrees of freedom) for the speech (Pp + Pn + Np + Nn) > silence contrast.

Praise Words - Positive Intonation
Praise Words - Neutral Intonation
Neutral Words - Positive Intonation
Neurtal Words - Neutral Intonation



Reward Pathway



ERRATUM

Erratum for the Report “Neural mechanisms for lexical processing in dogs” by A. Andics, A. Gábor, M. Gácsi, T. Faragó, D. Szabó, Á. Miklósi

In the Report “Neural mechanisms for lexical processing in dogs,” the directions left and right were inadvertently switched in reporting the results from dogs’ brains. This was caused by an error in interpreting the coordinates of MRI images, specifically in the process of accounting for the different body positions of humans and dogs in the MRI scanner. This error does not affect the main conclusions of the paper. The HTML and PDF versions have been corrected.