New Vistas of the Brain

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On the Brain of a Scientist: Albert Einstein

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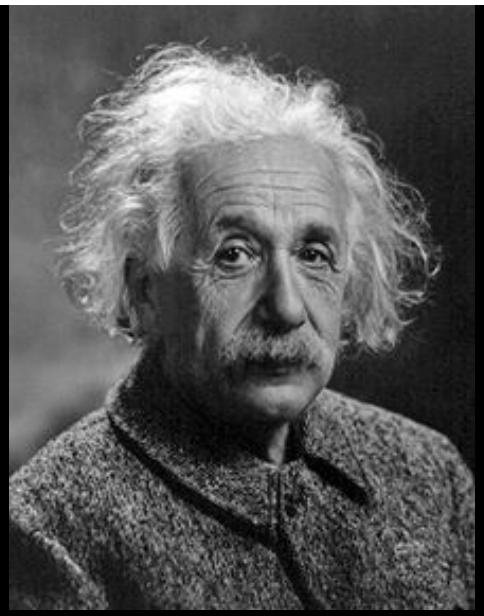


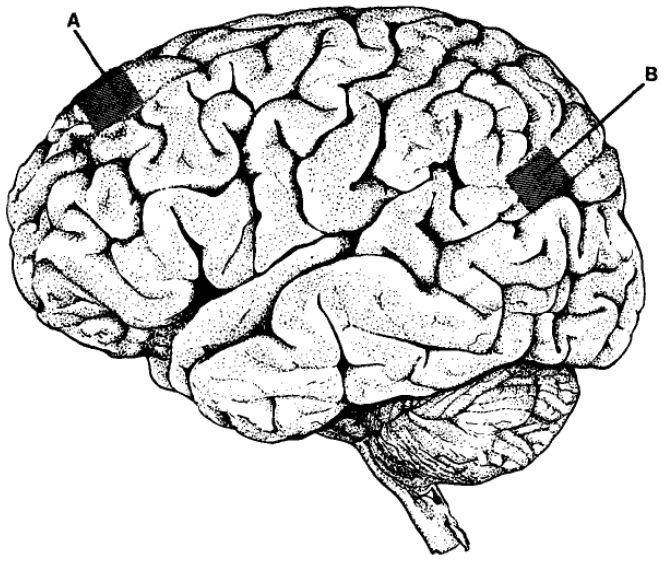
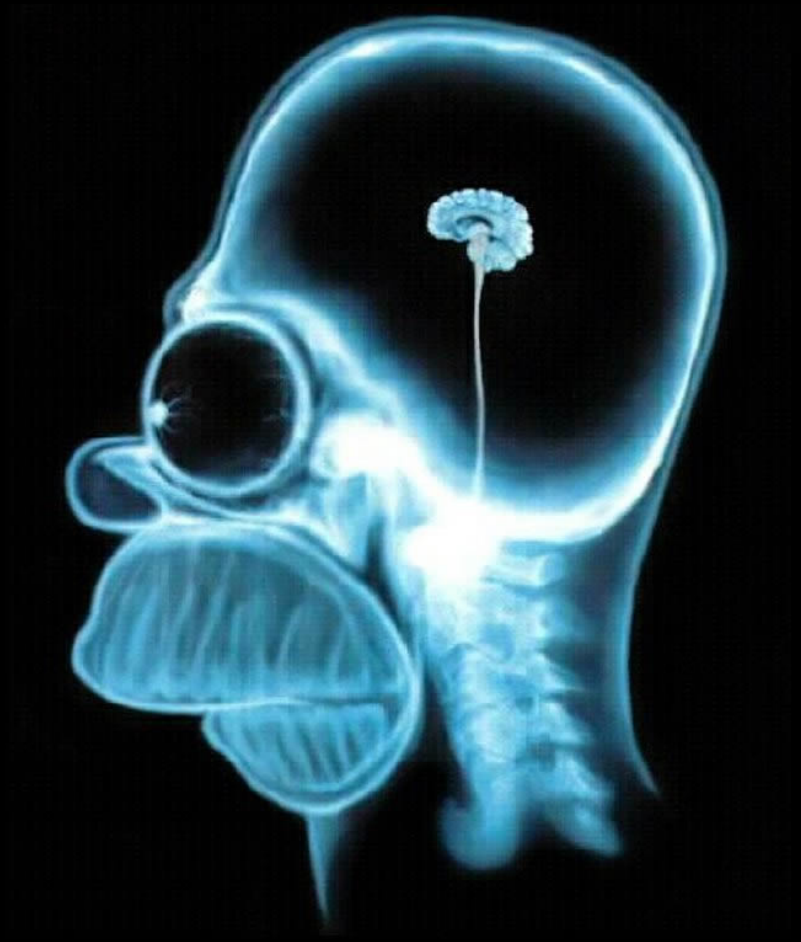


FIG. 1. A lateral view of the human brain indicating the position of the samples removed for cell counts. A represents the sample from area 9 and B, area 39.

In Einstein's brain areas involved with math had more glial cells

The brain




fotolia
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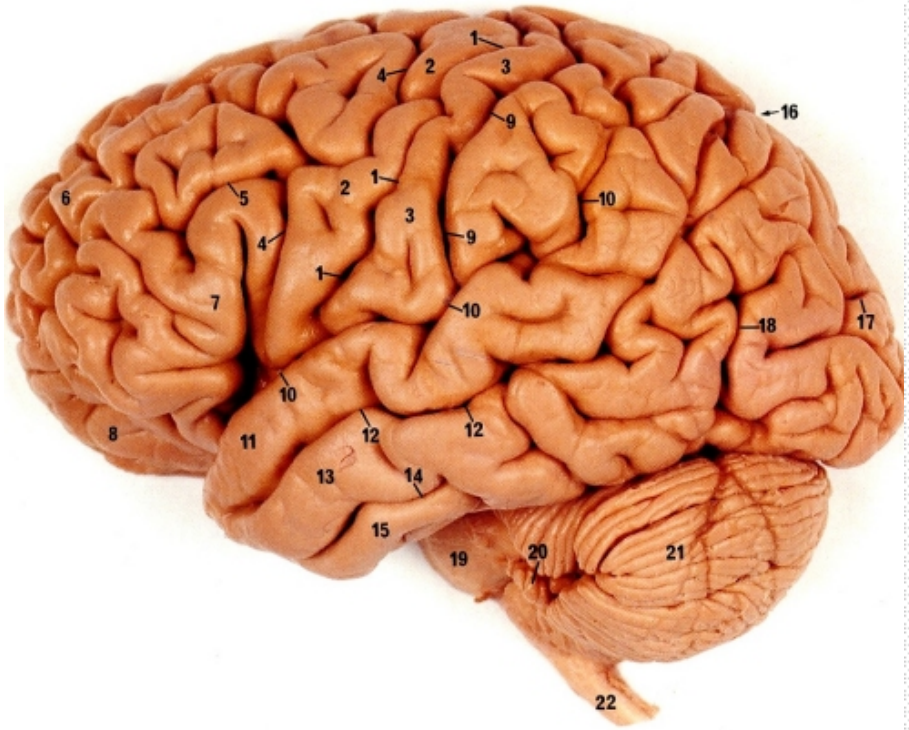
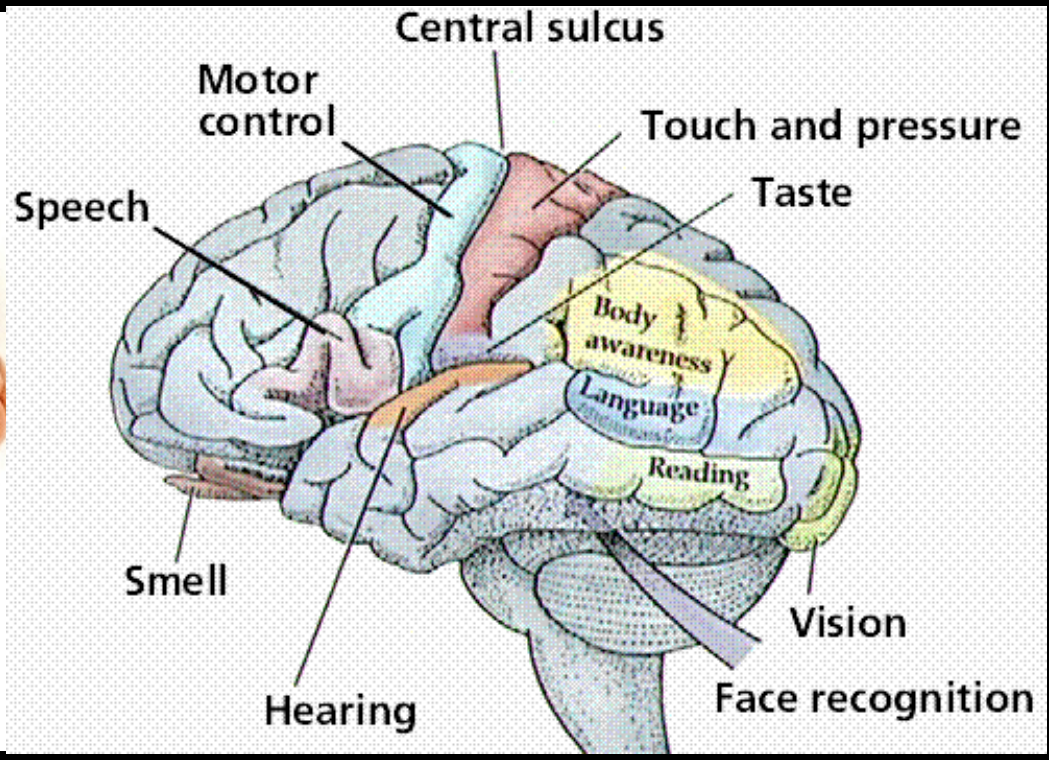
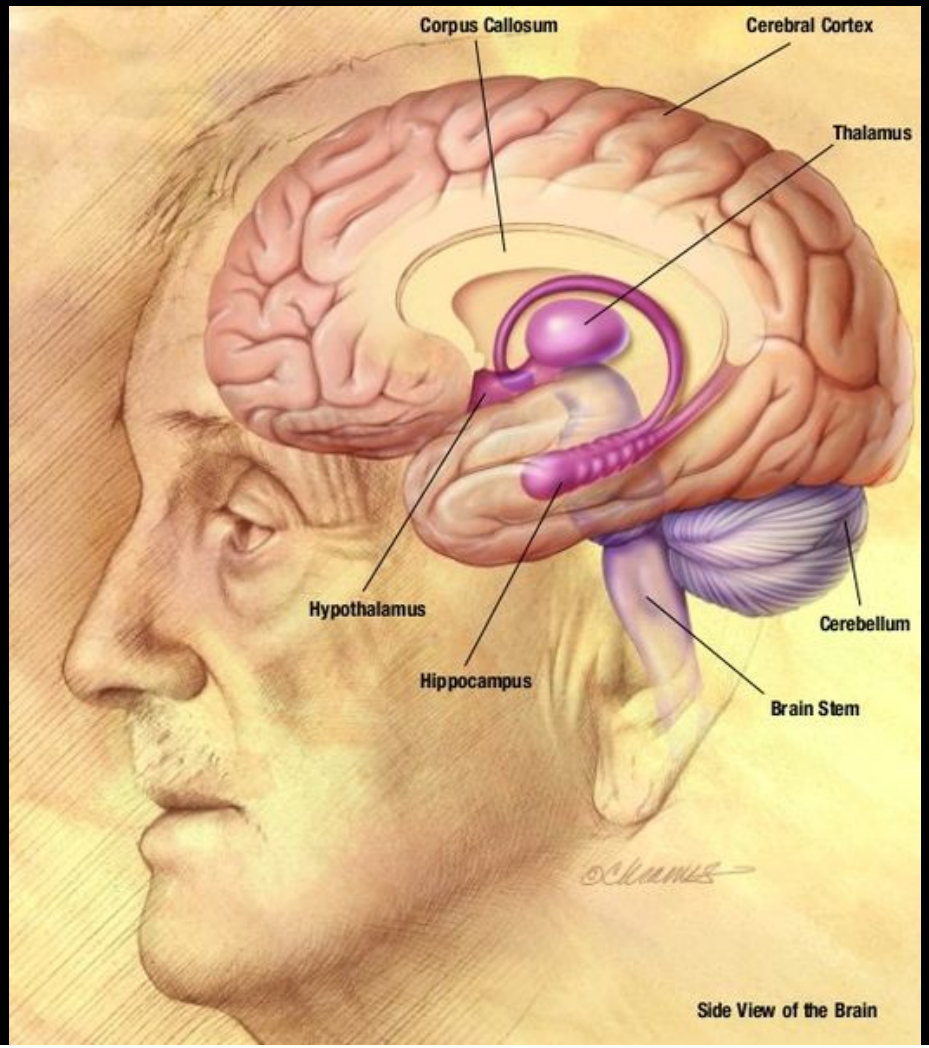
Different areas of the brain are required for different attributes, such as movement, speech or sight

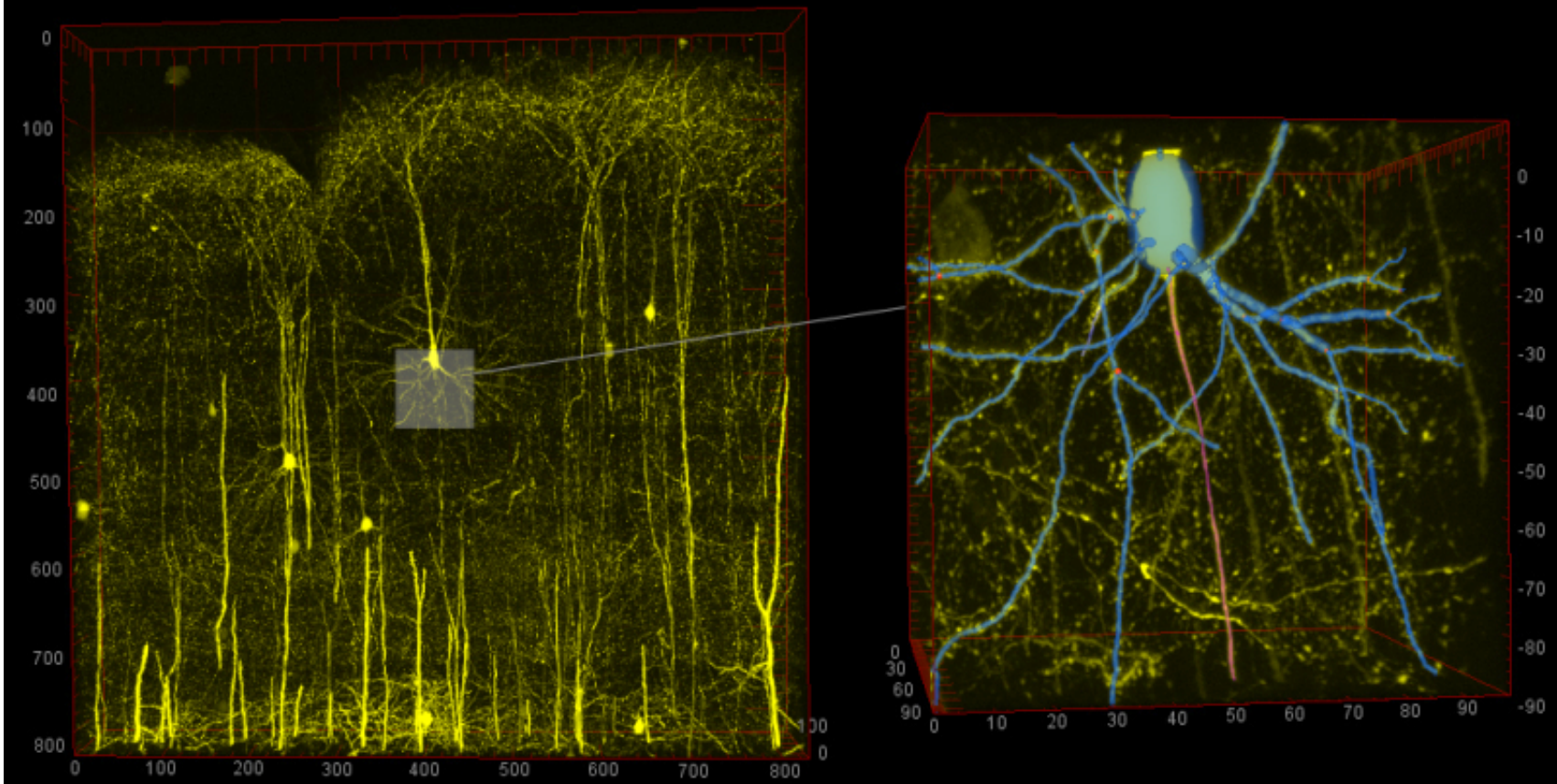




Deeper areas called the hippocampus are key for making memories and are damaged in dementia

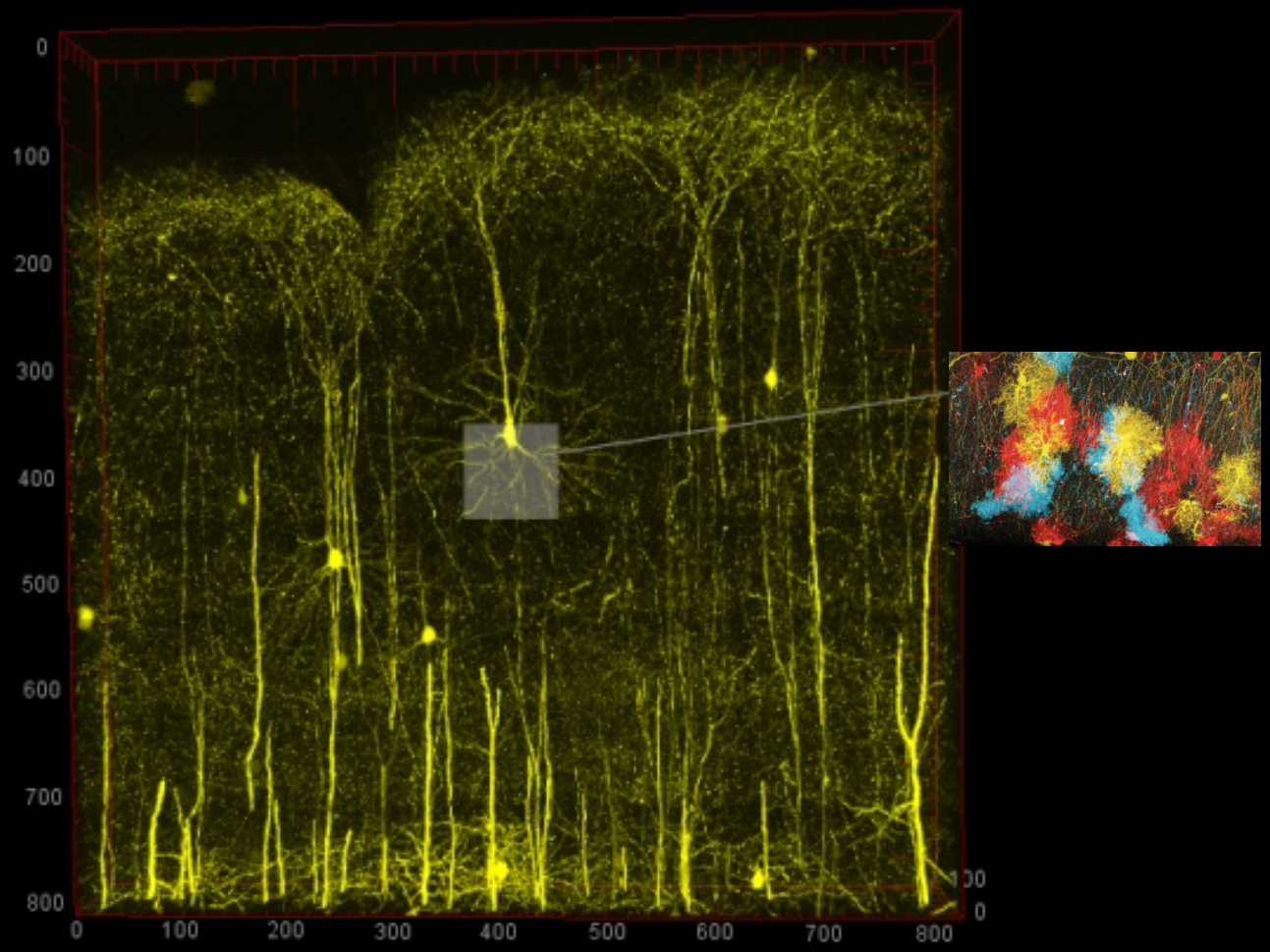


Neurons in the cortex



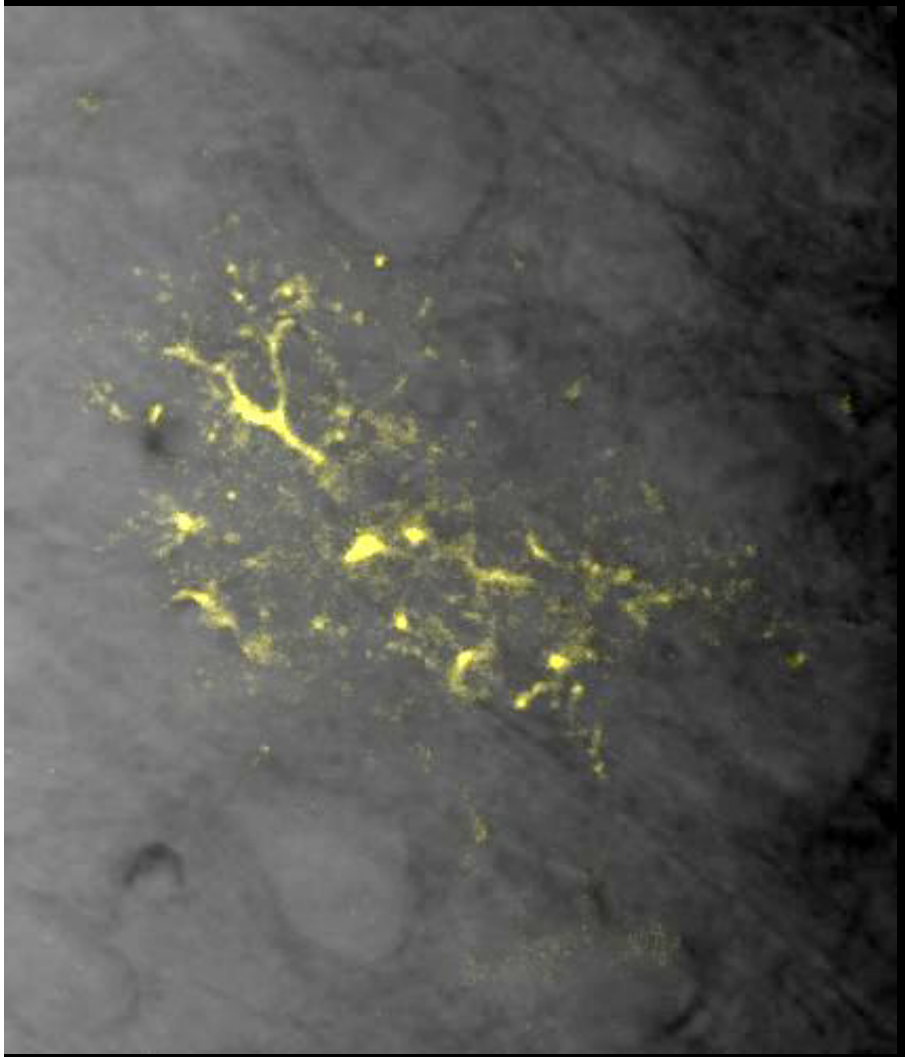
- Dendrites- where other nerve connect (or make synapses) with nerve cells
- Cell body where the nucleus is
- Spines –points on contacts of synapses on dendrites
- Axon- output of neurons where electrical activity spreads out to synapses making contacts with other neurons

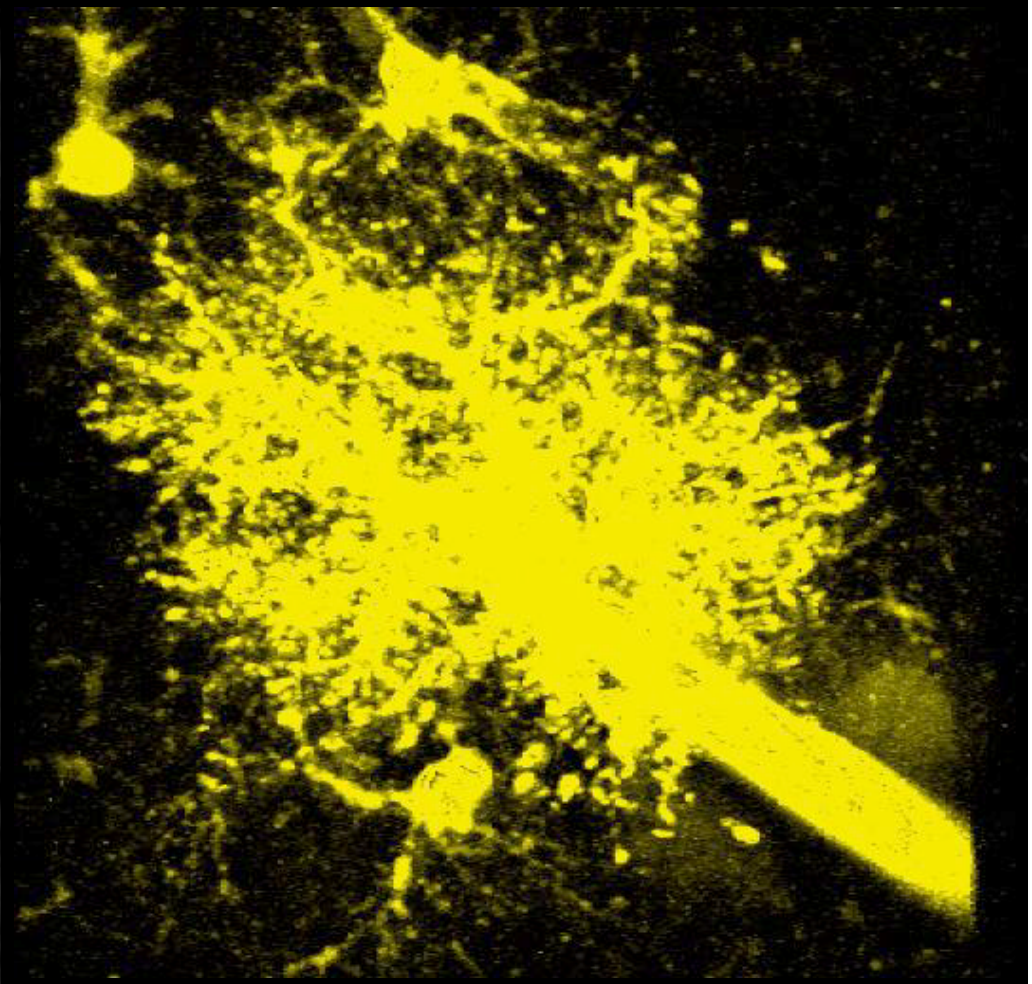
Neurons versus glia (astrocytes) in brain



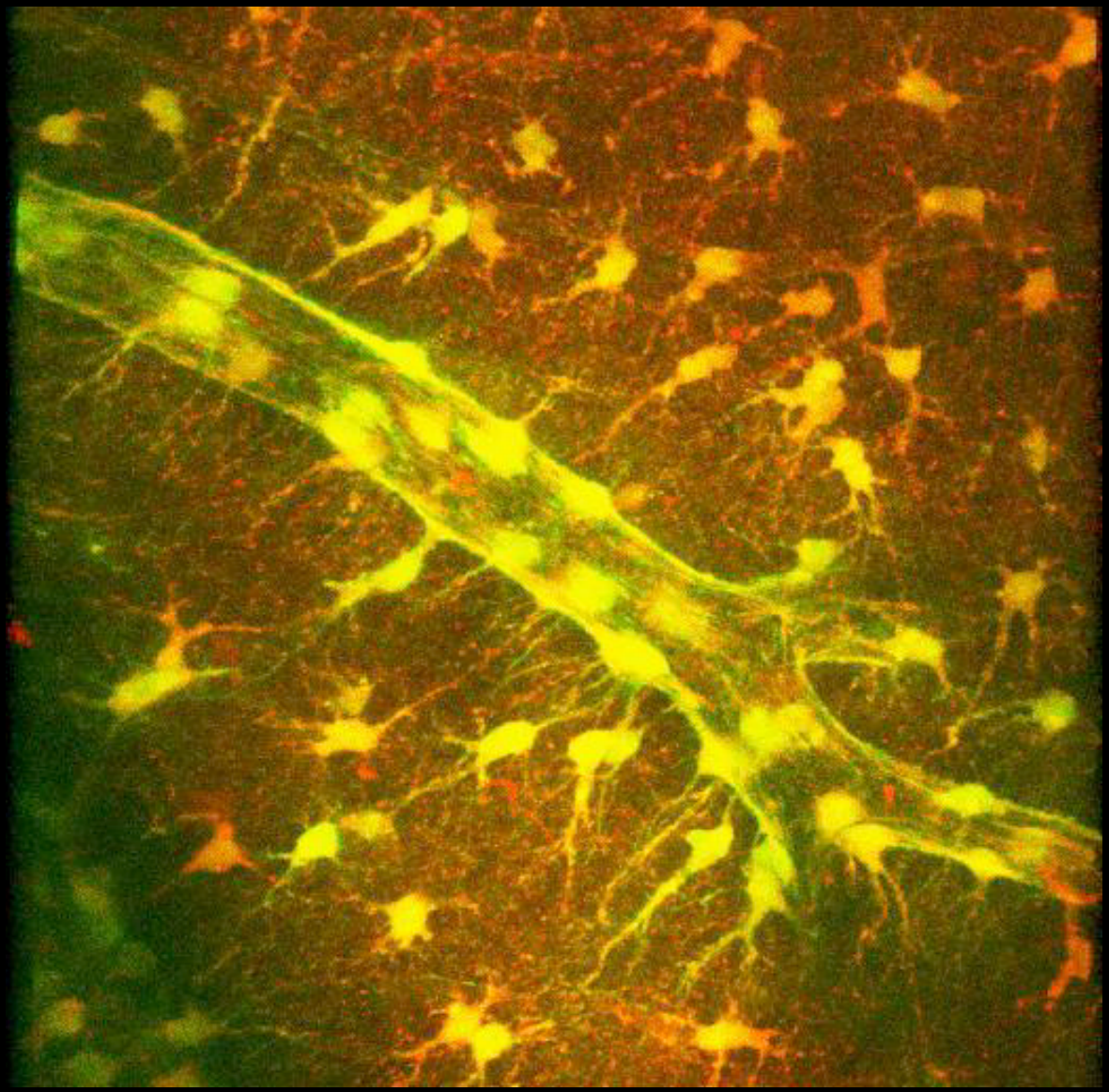
From J. Lichtman lab Harvard

Astrocytes surround neurons



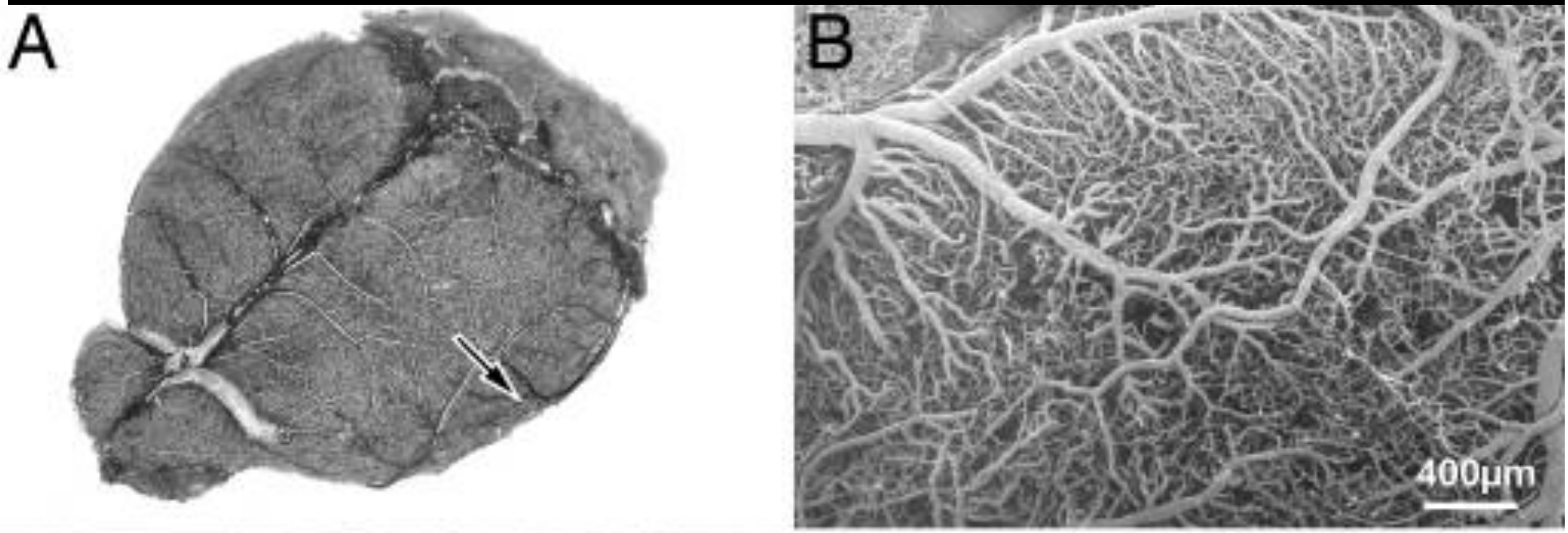


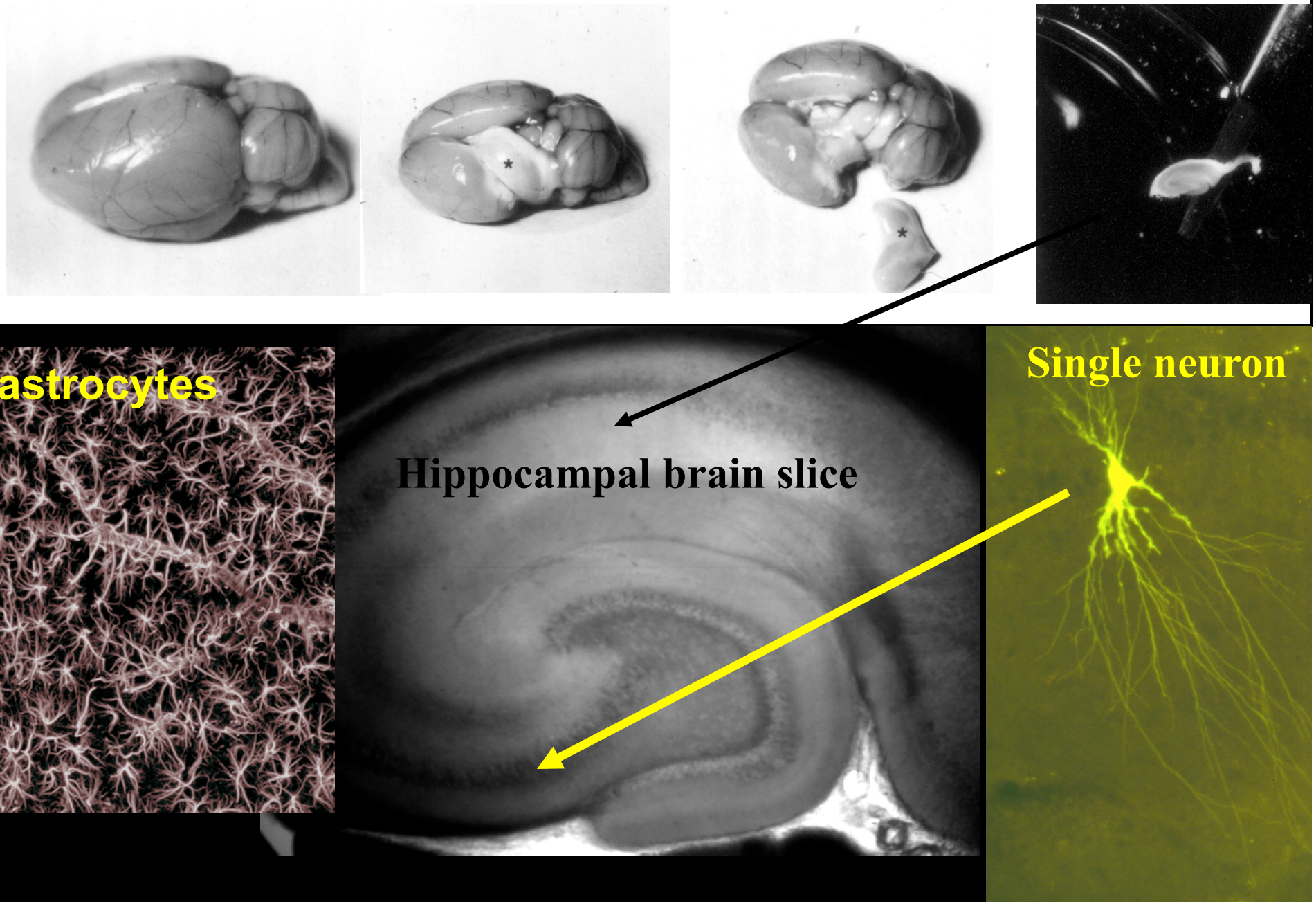
Astrocyte endfeet circumscribe arterioles



Mulligan & MacVicar (2004) Nature 431:195

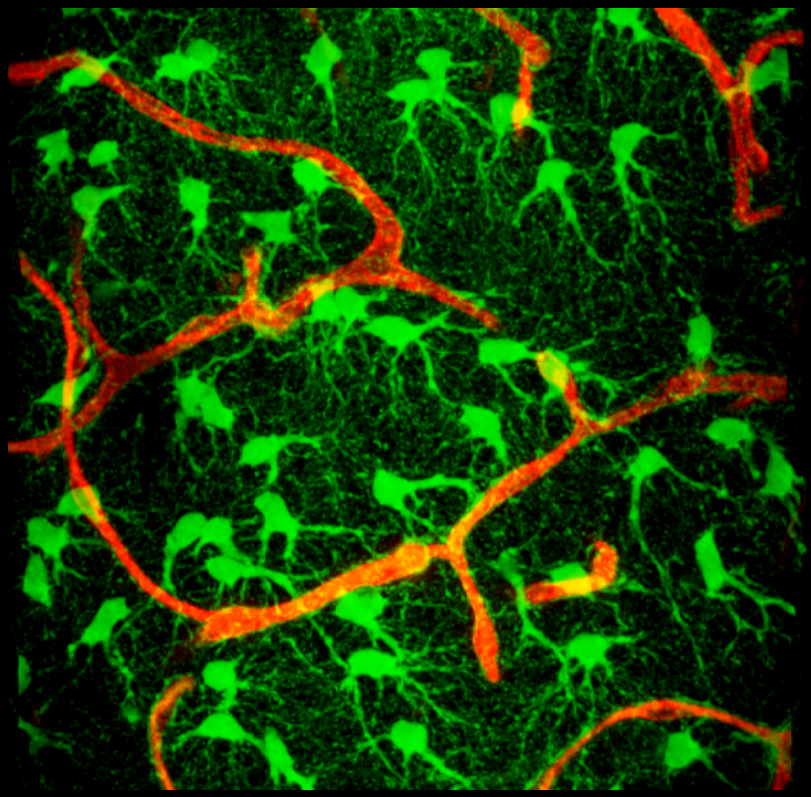
Blood vessels of the brain



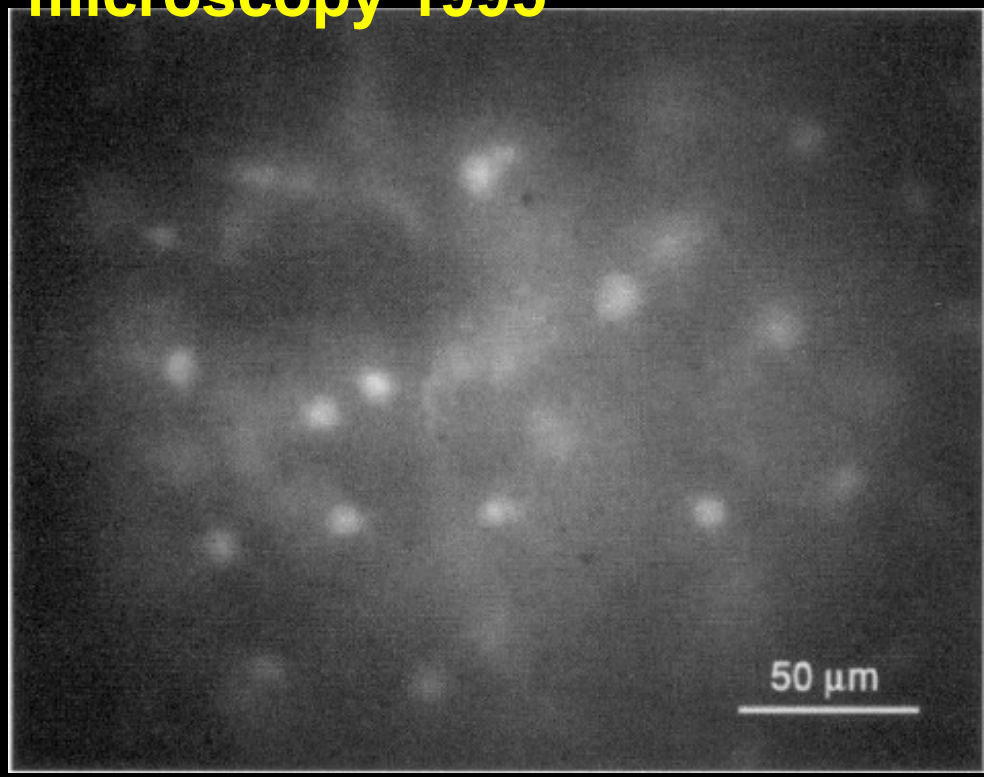

astrocytes
Hippocampal brain slice
Single neuron

Two Photon laser scanning microscopy versus CCD fluorescence microscopy in brain slices

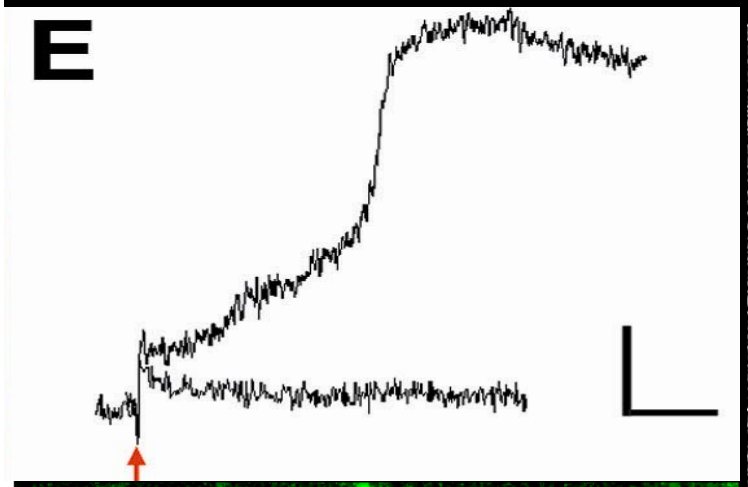
TpIsm 2003

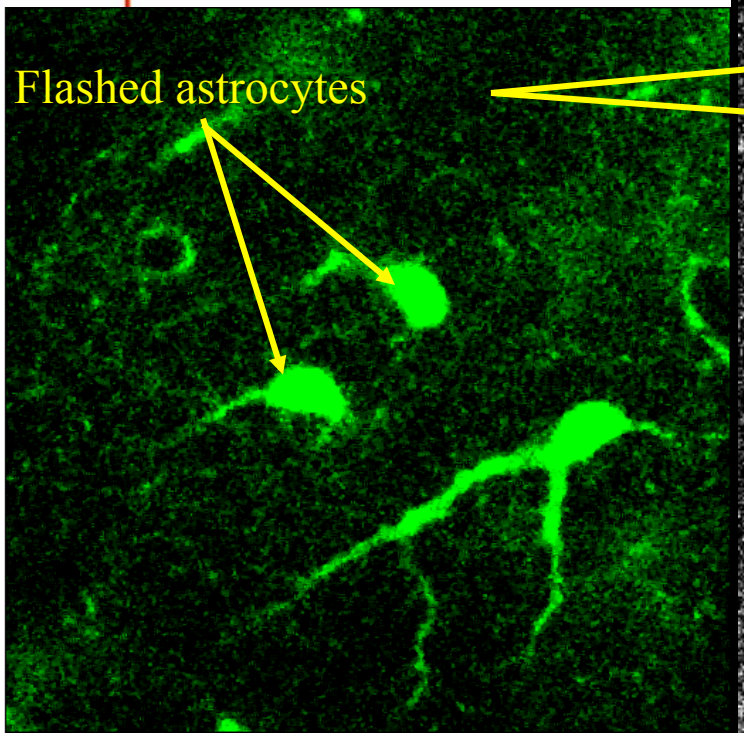


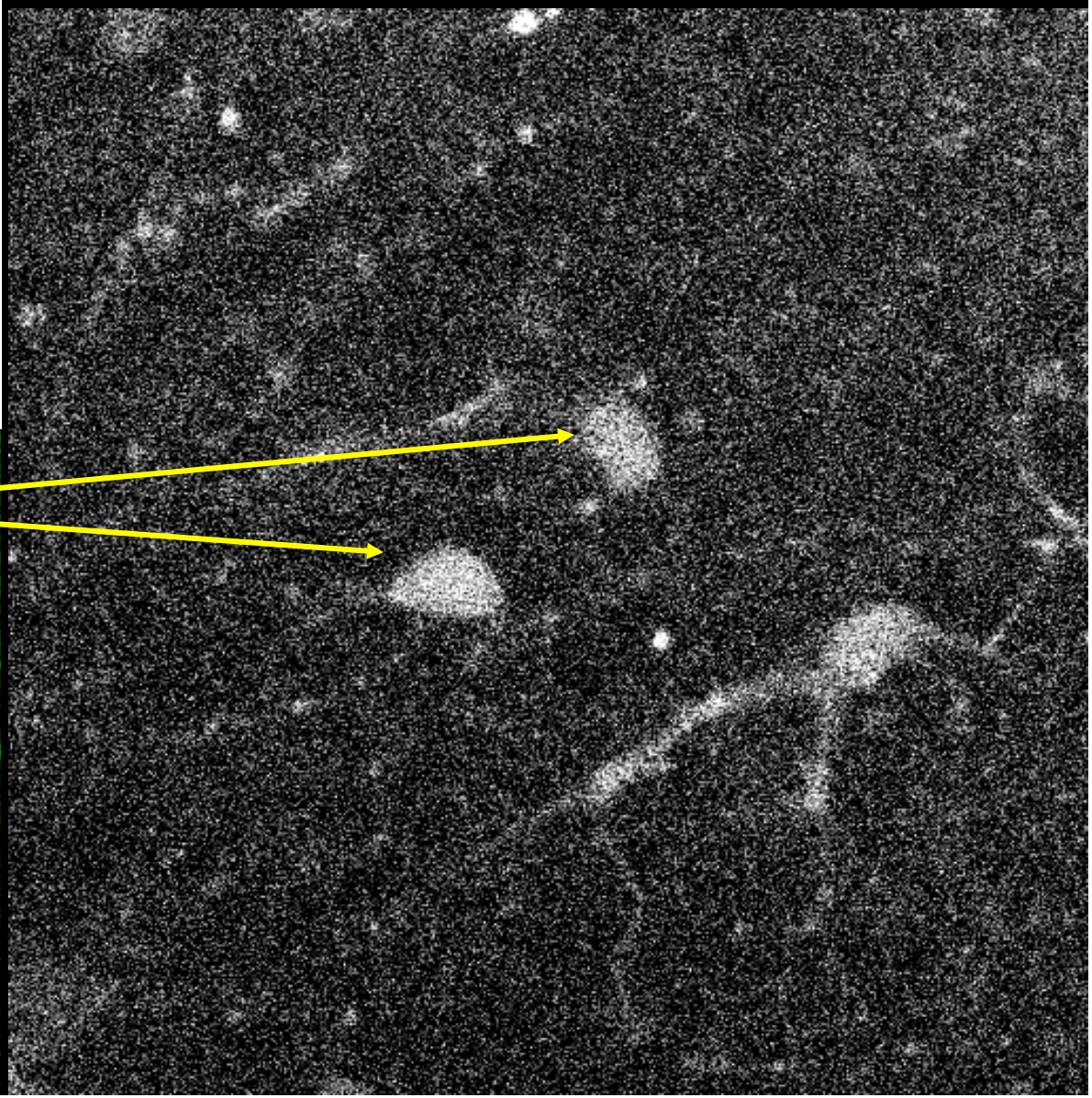
CCD fluorescence microscopy 1995



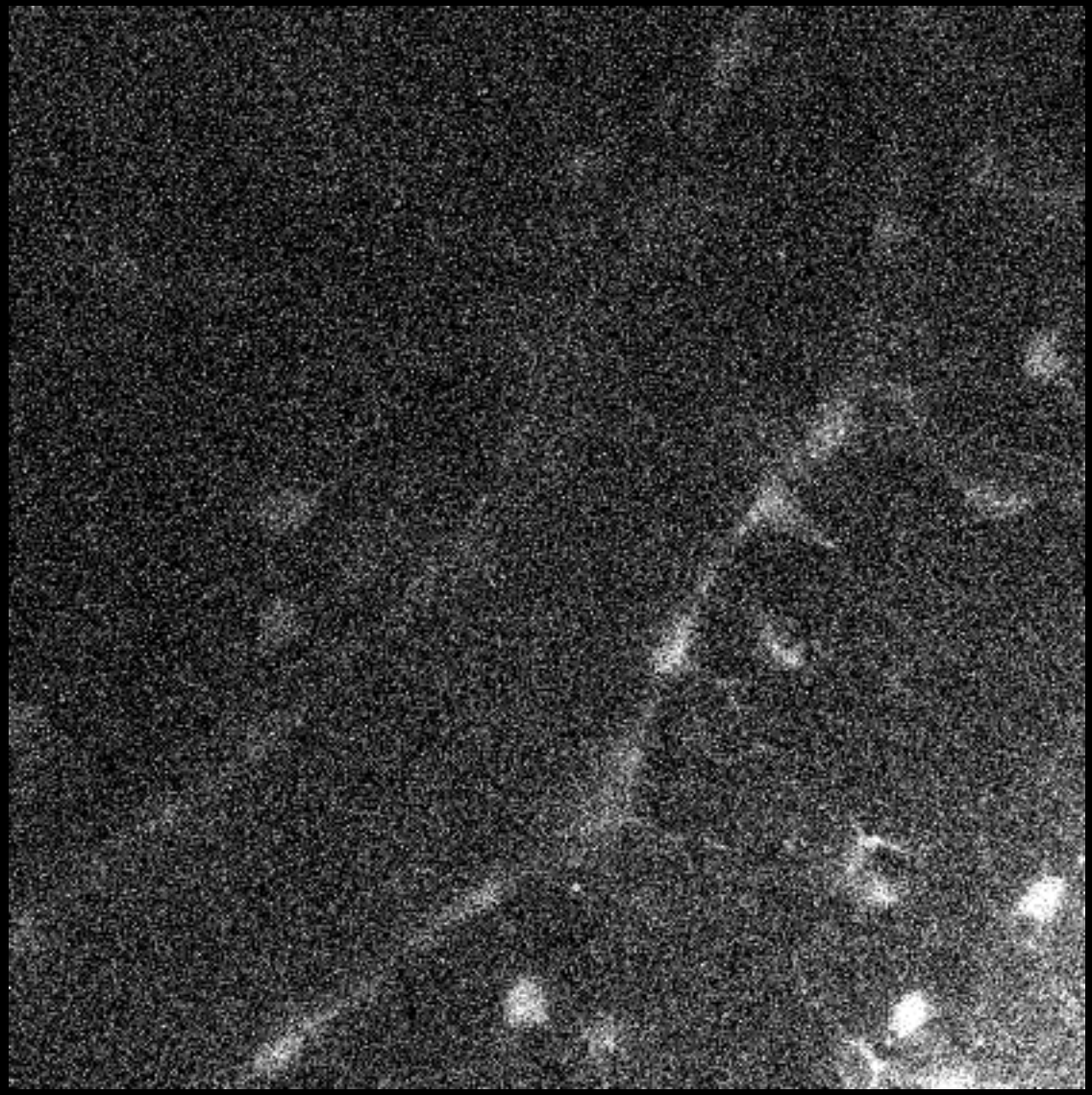
Two-photon uncaging of DM-Nitrophen at 730 nm and imaging of rhod-2







Astrocyte endfeet calcium signals control arteriole diameter



Uncage astrocyte calcium

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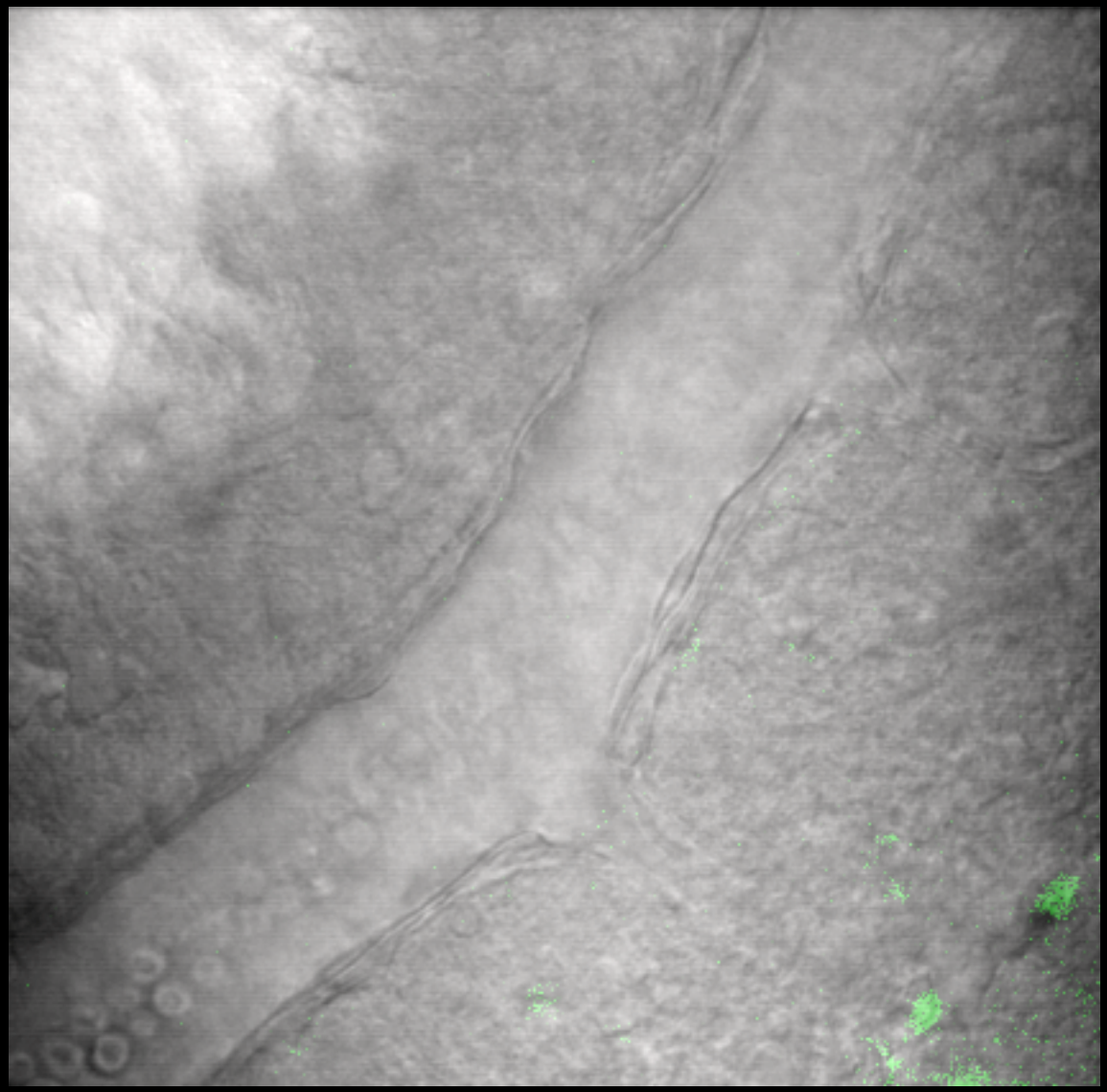

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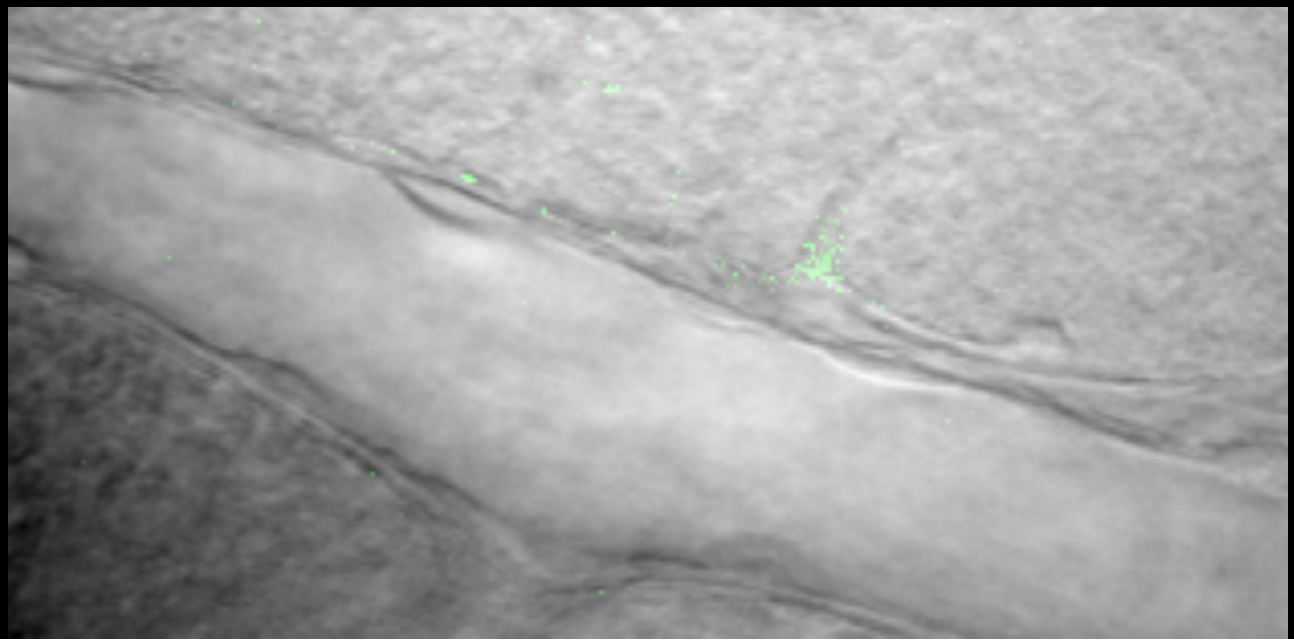
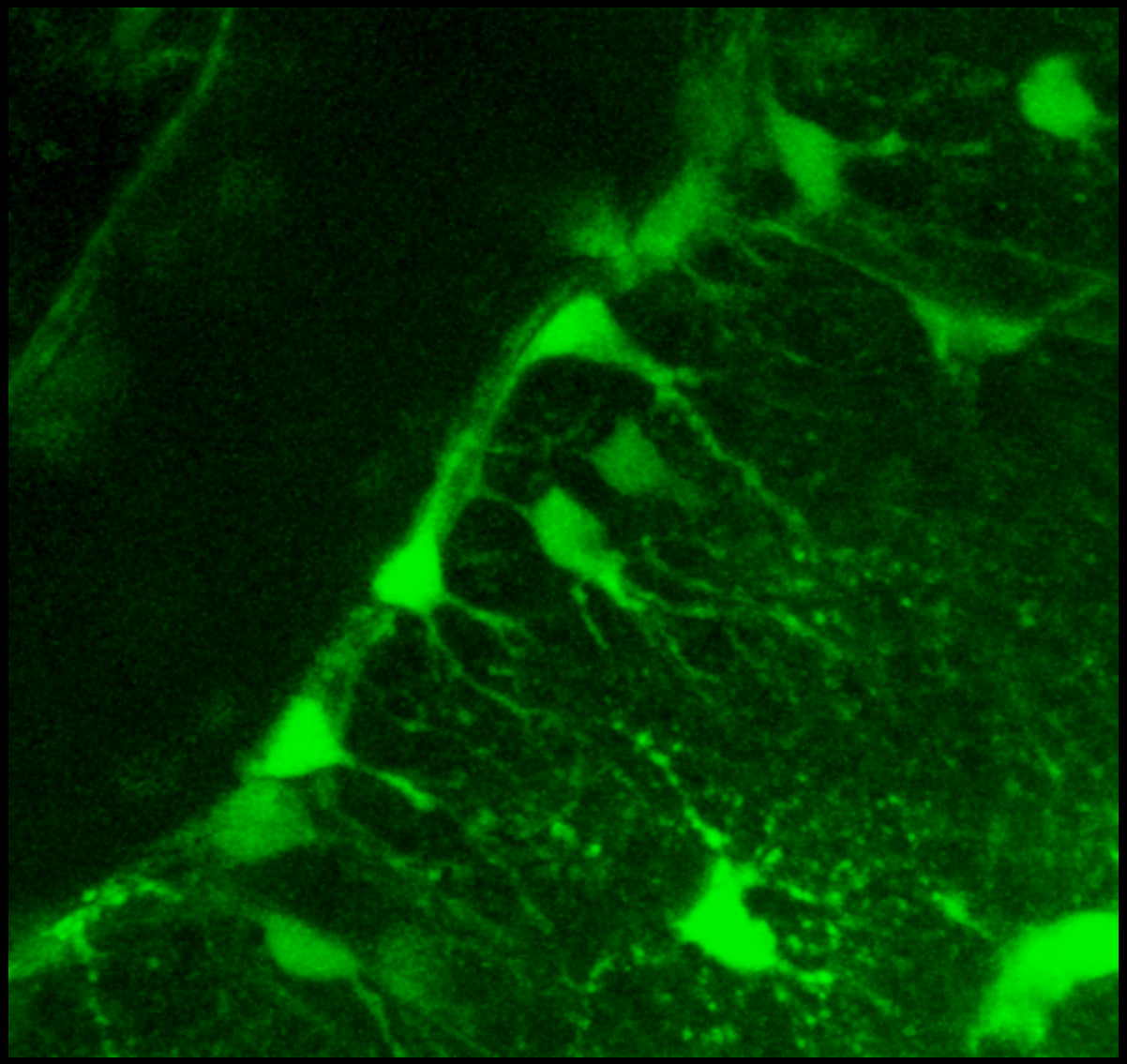
Properties of astrocyte induced arteriole constrictions

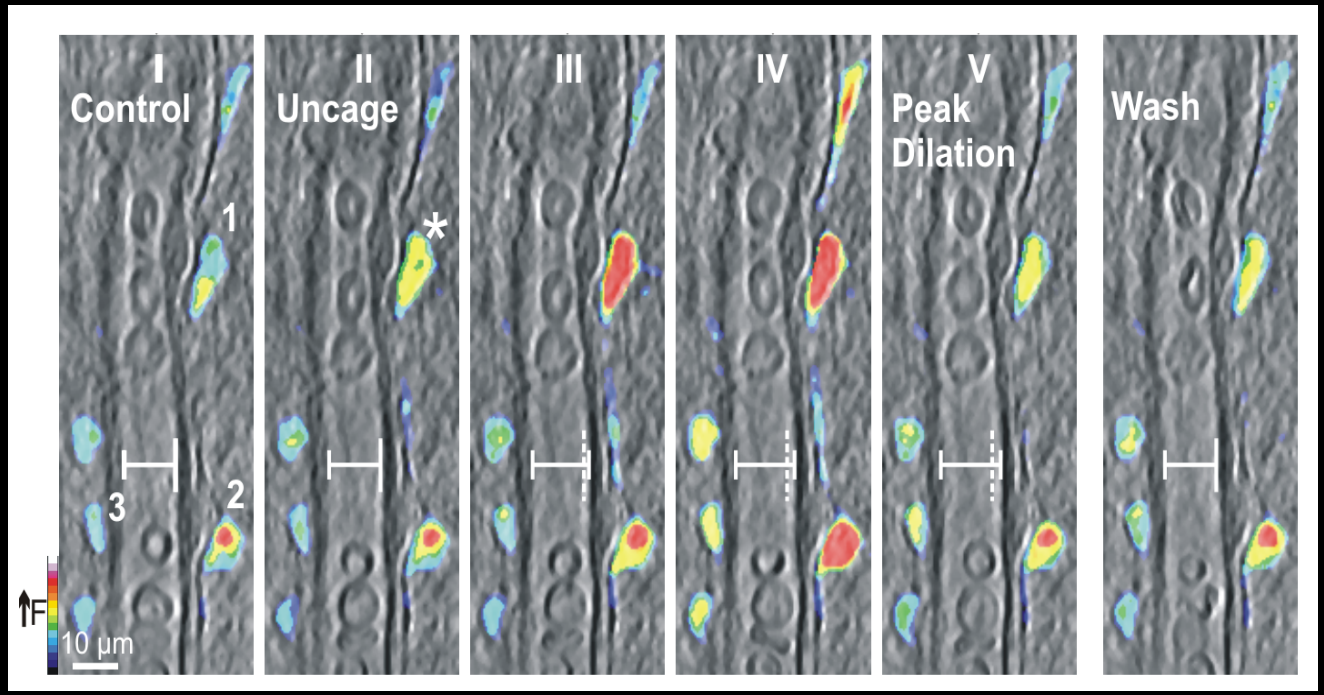
- Endfeet Ca^{2+} changes precede the onset of vessel constriction by 1.2 to 2.0 sec
- Ca^{2+} elevations in astrocyte endfeet cause robust and reproducible arteriole constrictions
- Photolysis of caged Ca^{2+} in patched astrocytes induces Ca^{2+} elevations in endfeet and arteriole constrictions
- Extent of contraction follows extent of calcium waves in endfeet

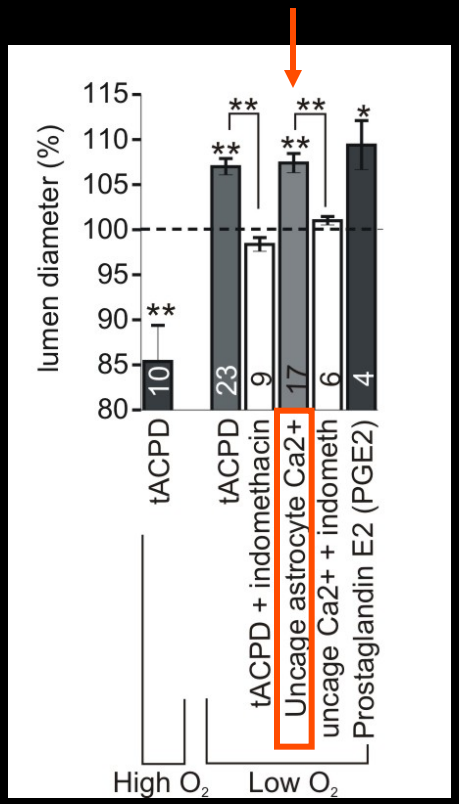


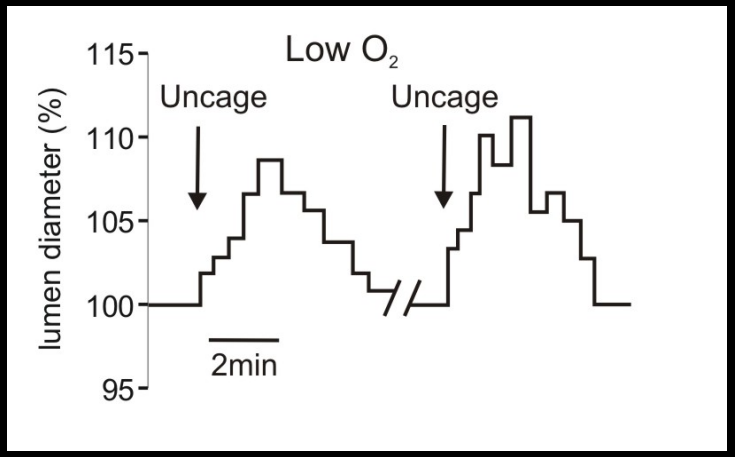
Stretching of astrocyte endfeet by vascular constrictions



Uncaging astrocyte Ca2+ causes vasodilation in low O2



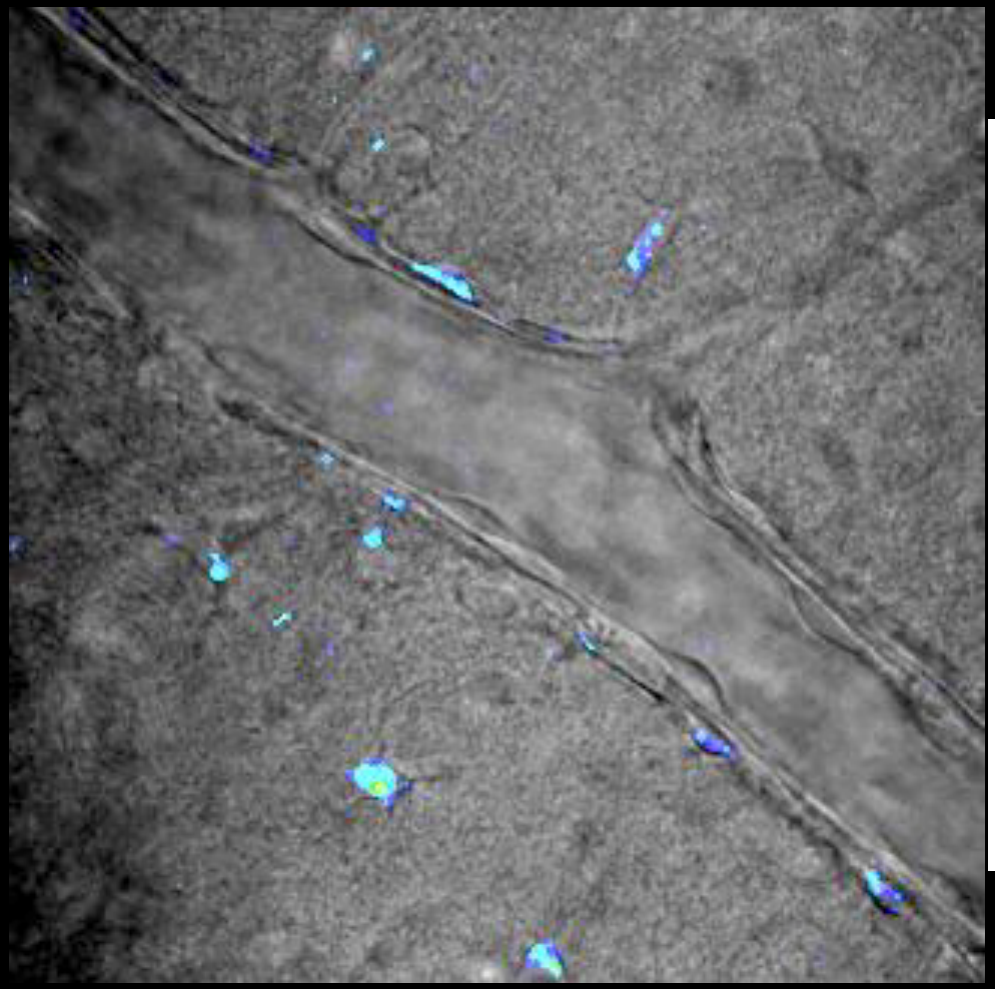


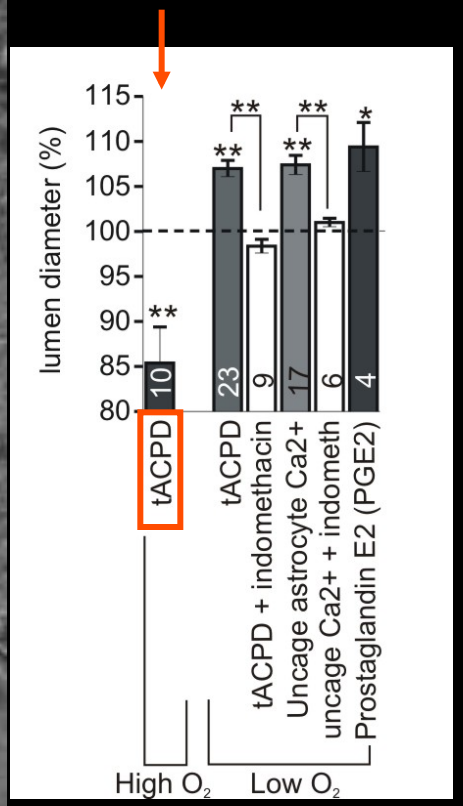


Grant R. J. Gordon, Hyun Beom Choi, Ravi Rungta, Graham C. R. Ellis-Davies, Brian A. MacVicar (2008) Brain metabolism dictates the polarity of astrocyte control over arterioles. **Nature** 456(7223):745-9.

mGluR activation in high O2 and low O2

High O2 vasoconstriction

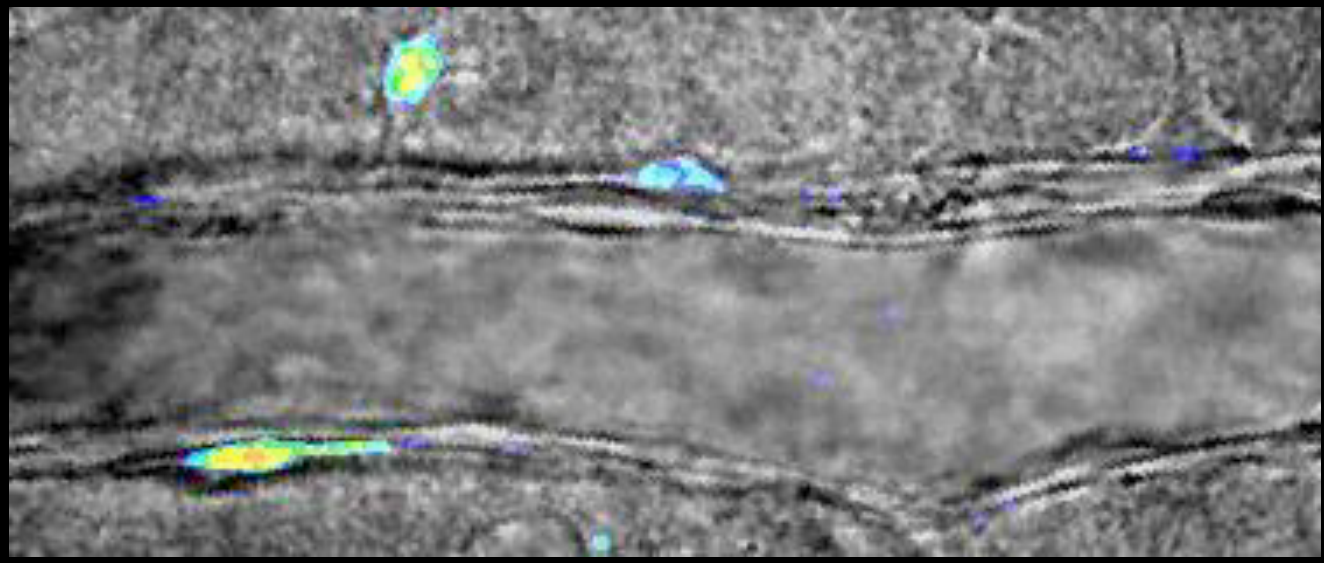




tACPD 100μM for 5 min

mGluR activation in high O2 and low O2

Low O2 vasodilation



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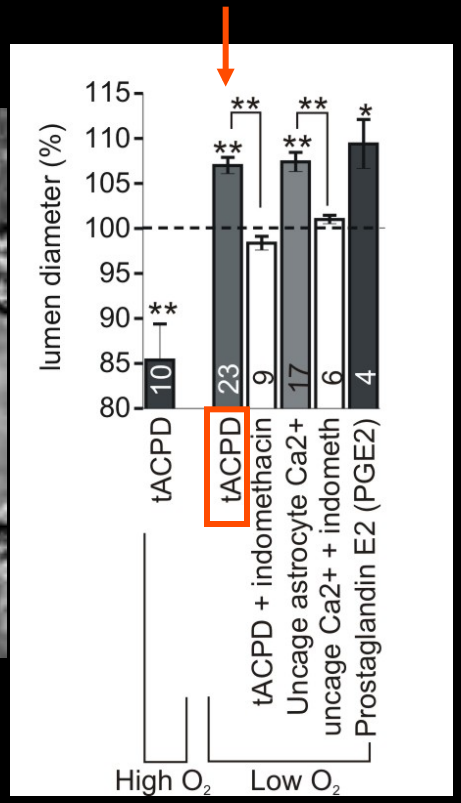
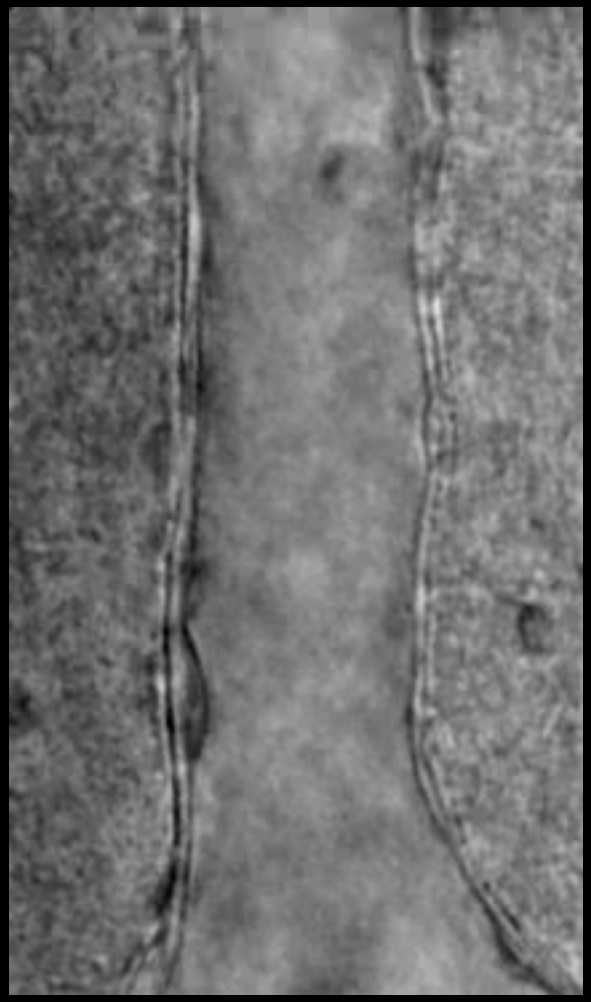
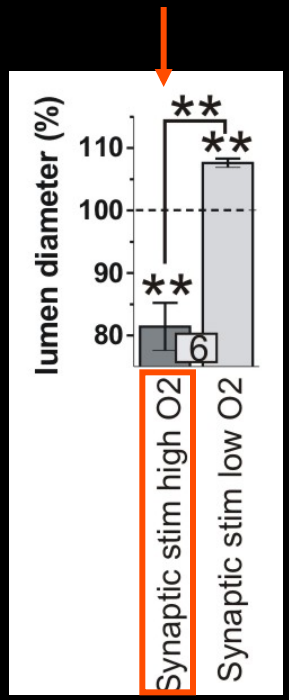


Synaptic activation in high O2 and low O2

High O2

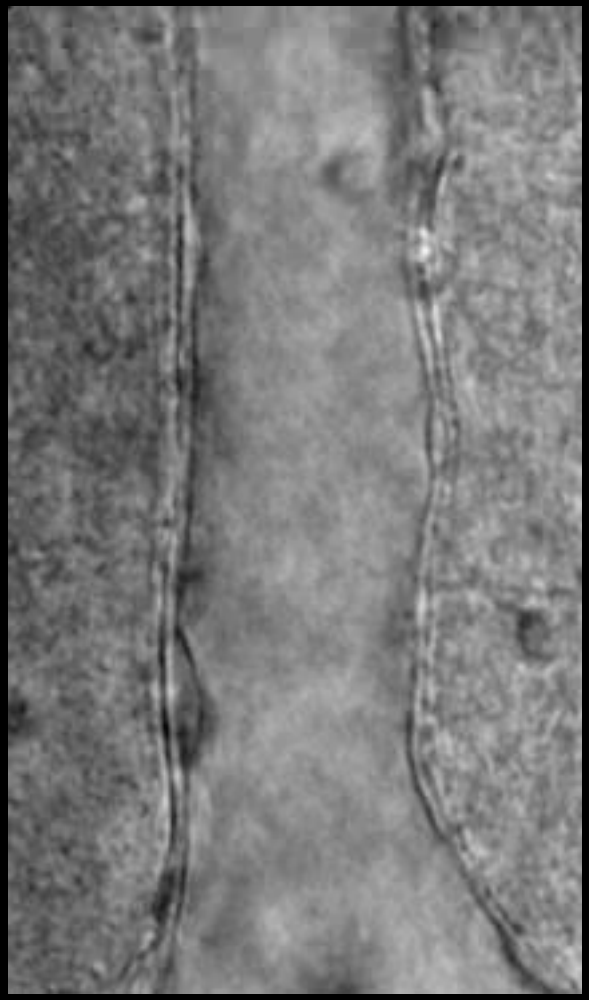


Vasoconstriction

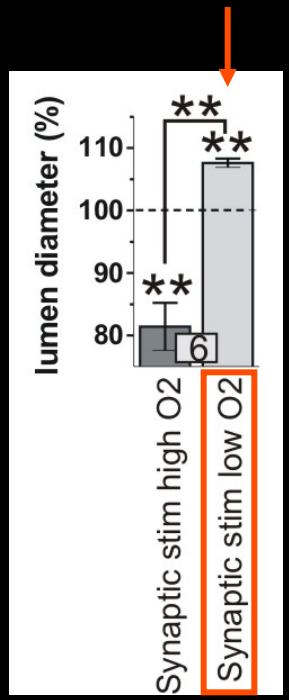


Synaptic activation in high O2 and low O2

Low O2



Vasodilation



Brain metabolic state dictates the polarity of astrocyte control over the cerebrovasculature

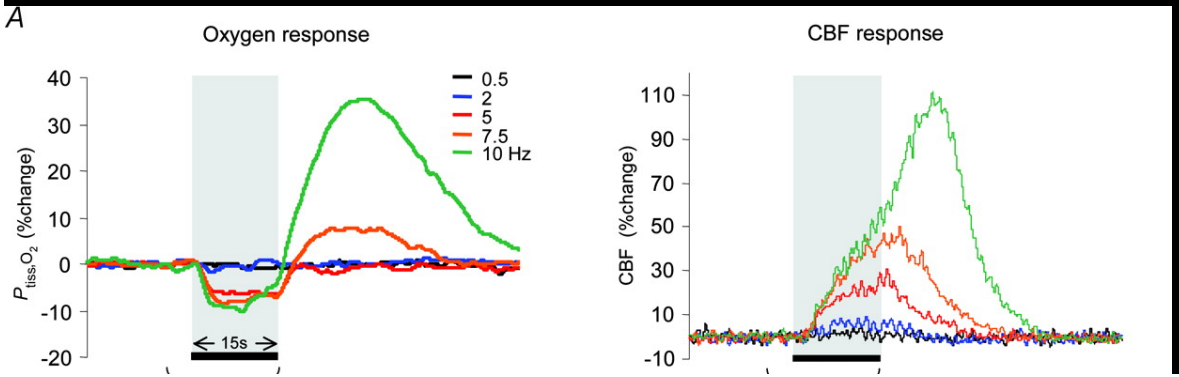
- Astrocyte regulation of cerebral blood flow will be appropriate for the metabolic state of the tissue- increased CBF when metabolic demand is high due to lactate inhibition of PGE2 uptake
- Astrocytes can constrict or dilate arterioles depending on whether the brain needs more nutrients (oxygen and glucose)
- influence on cerebral blood vessels should reach homeostatic balance leading to appropriate vascular control based on metabolic need

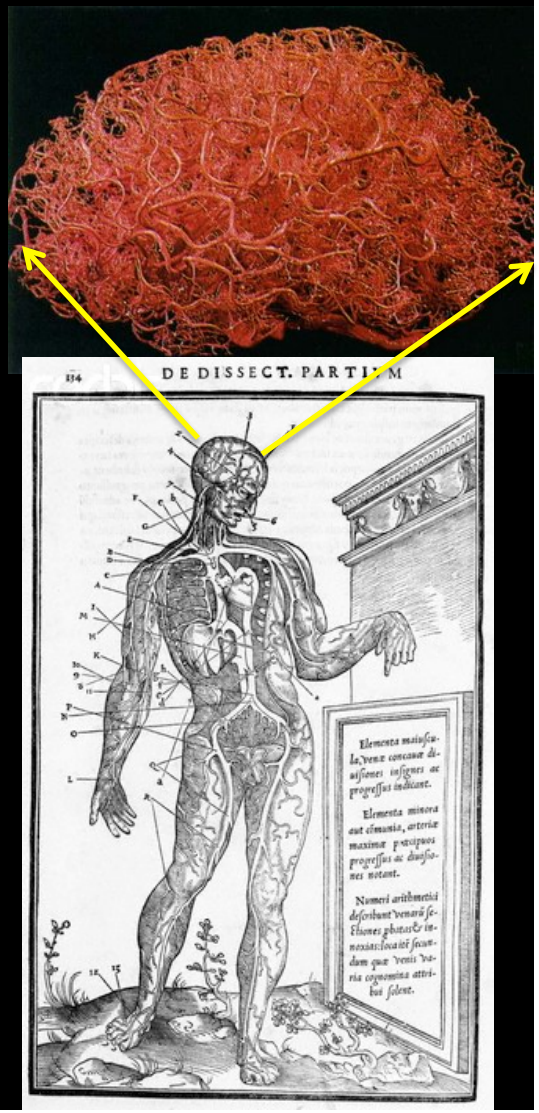
Cerebral blood flow (CBF) needs to be matched with metabolism

- Brain 2% of body weight but cerebral blood flow 15% of total body
- O2 consumption 20% and glucose consumption 50%

- Mismatch leads to impaired CNS function e.g. Vascular dementia

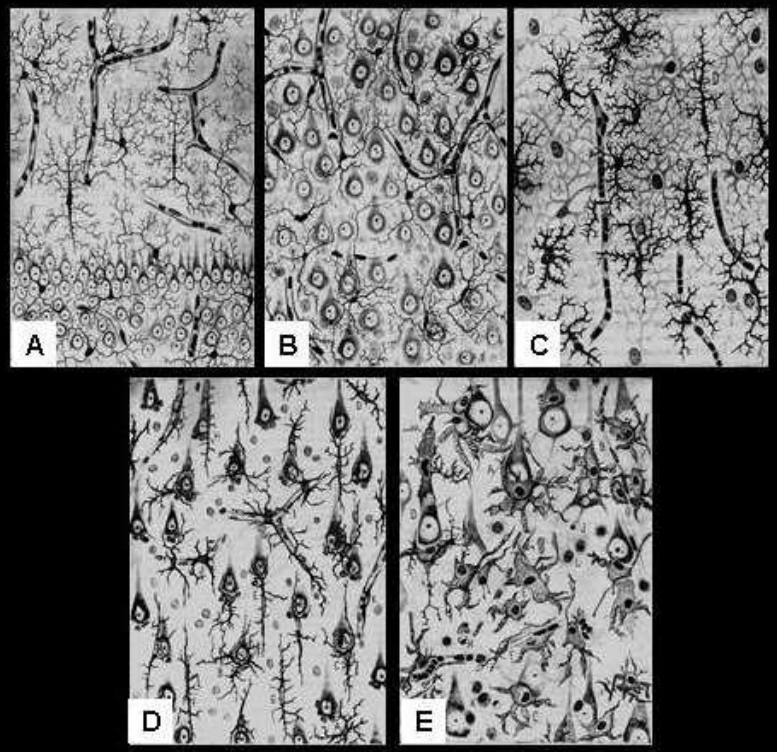
Blood flow in the brain increases when synaptic activity is evoked





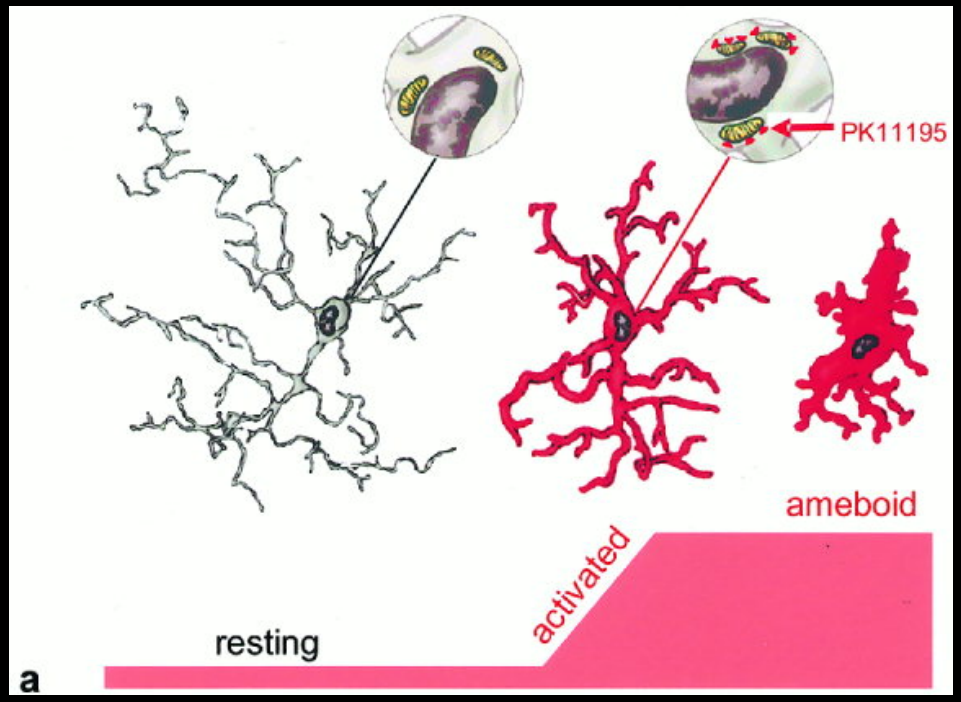
Microglia

Pío Del Río-Hortega (1882-1945)



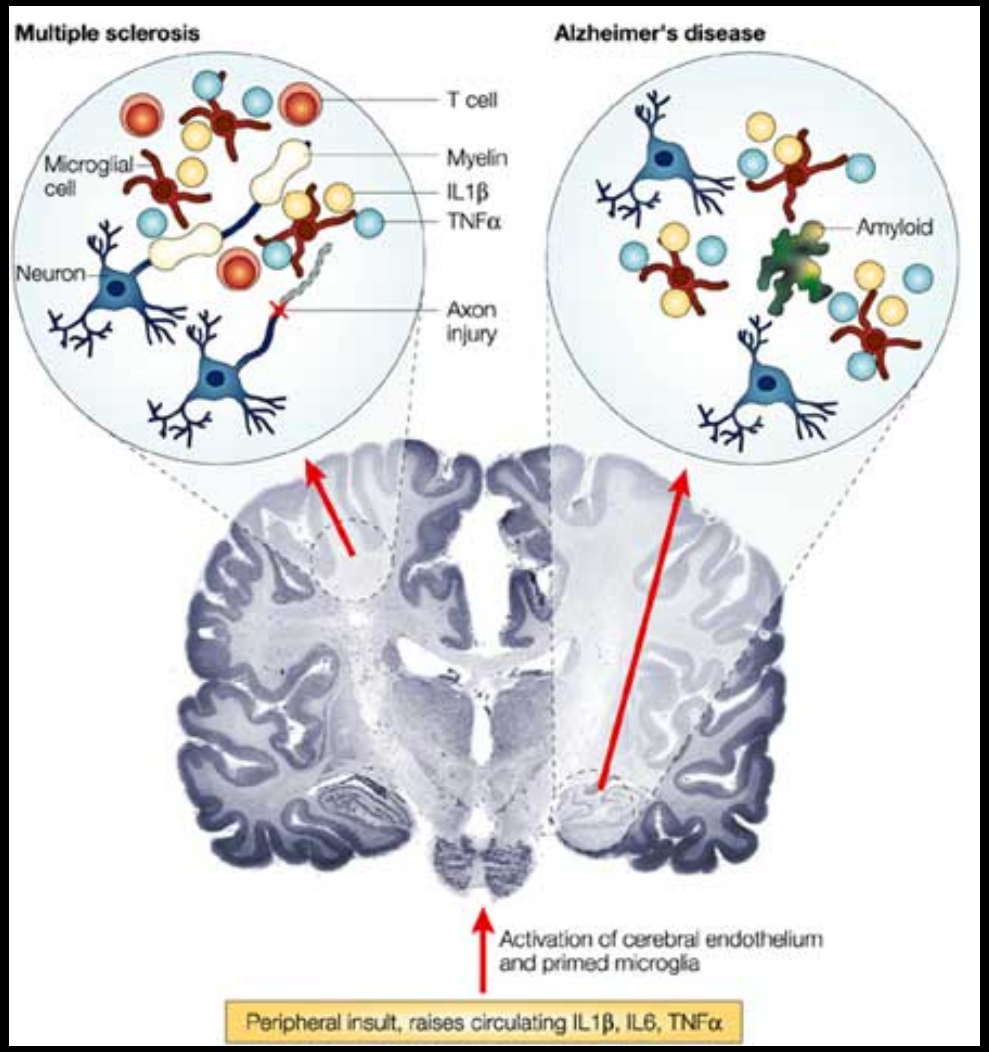
Microglia: phagocyte and glia cell

- Resident immune cell of the brain.
- Activated by brain damage or infections



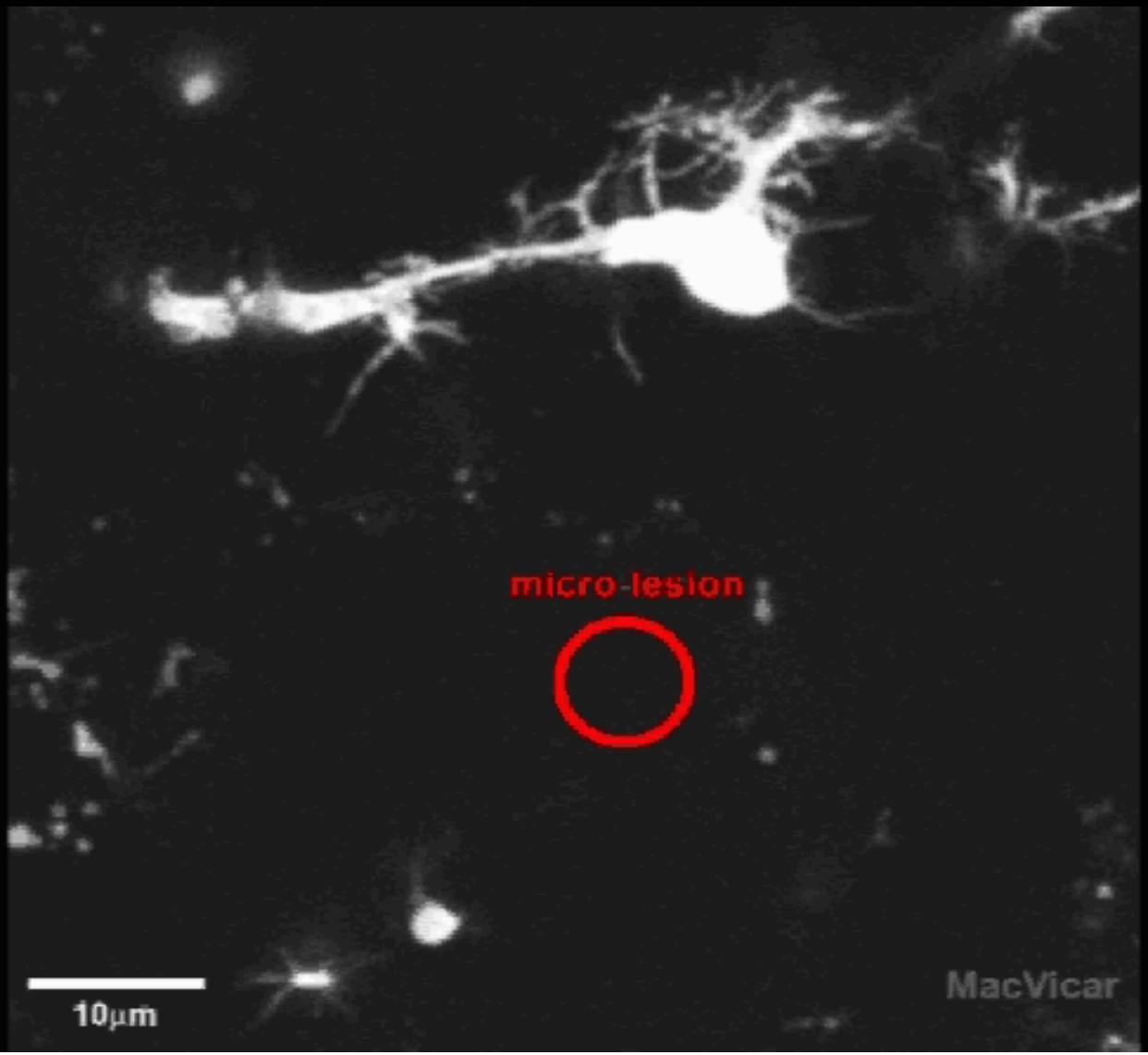
Wolfgang J. Streit*, Sharon A. Walter and Nathan A. Pennell (1999) Prog Neurobiol 57, 563-581

Central role for Microglia in Alzheimer's disease and multiple sclerosis



Perry, HV et al (2003) Nature Reviews Neuroscience **4**, 103-112

Microglia respond to lesions in brain slices



Neuroprotection Sequence initiated by damage requiring microglia

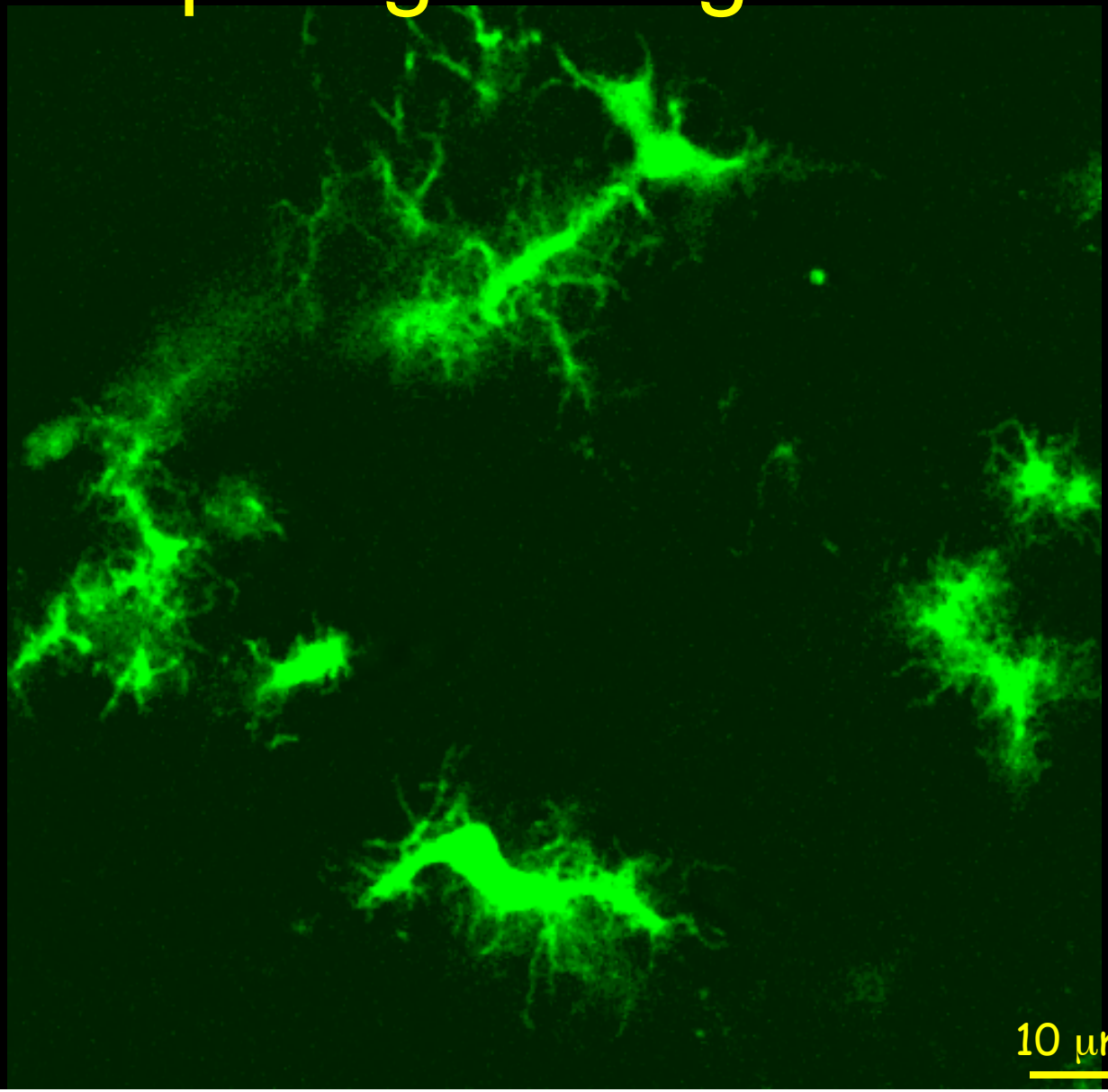
1) Surveillance

2) Detection of damage induction of polarity

3) Directed process outgrowth, frontrunners win race inhibiting late processes

4) Detection of damaged tissue and phagocytosis

6) PROTECTION!



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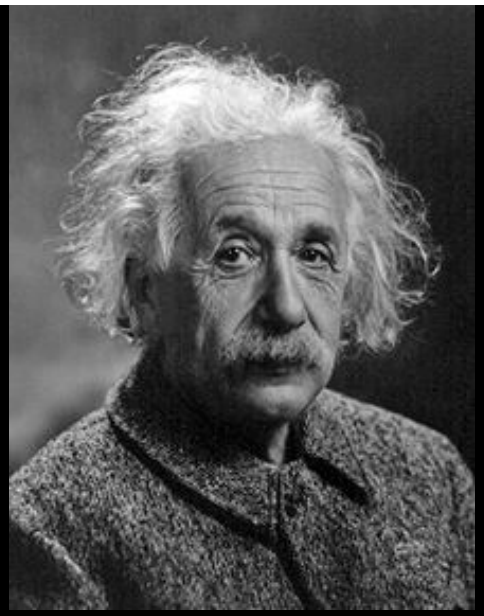

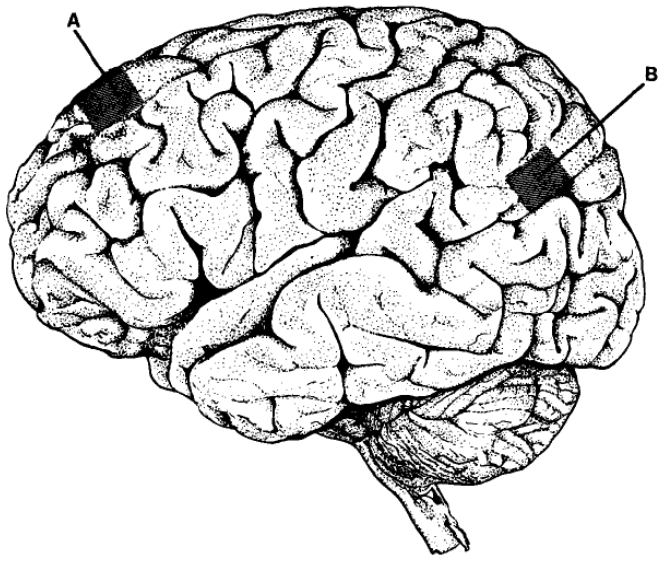

FIG. 1. A lateral view of the human brain indicating the position of the samples removed for cell counts. A represents the sample from area 9 and B, area 39.

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