New Vistas of the Brain

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In Einstein’s brain areas involved with math had more glial cells.
The brain
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

Blood vessels of the brain
Neurons and epilepsy mechanisms are studied in Brain slices from Rats

Hippocampal brain slice

astrocytes

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

Tplsm 2003

CCD fluorescence microscopy 1995
Two-photon uncaging of DM-Nitrophen at 730 nm and imaging of rhod-2

Flashed astrocytes
Astrocyte endfeet calcium signals control arteriole diameter

Uncage astrocyte calcium

Astrocyte endfeet calcium signals control arteriole diameter

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

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

tACPD 100µM for 5 min
Synaptic activation in high O2 and low O2

High O2

Vasoconstriction
Synaptic activation in high O2 and low O2

Low O2

Vasodilation
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
Central role for Microglia in Alzheimer’s disease and multiple sclerosis

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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