

Special Glial Journal Club Seminar

“Energy Supply
to the CNS”

Clare Howarth

Department of Physiology
University College, London

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3-159 Jackson Hall

ABSTRACT

Clare Howarth - Energy supply to the CNS

I will consider three aspects of the energetic design of the brain:

- (1) The mechanisms of switching of blood flow to active neurons. This is fundamental for the brain to maximise its information processing capacity and for the generation of functional imaging signals.
- (2) How the blood supply to particular brain regions is matched to the regions' signalling energy use.
- (3) How much energy is used on a perceptual decision in the brain.

(1) The mechanisms of switching of blood flow to active neurons

Neural activity increases local blood flow in the CNS, and this increase is the basis of both BOLD and PET functional imaging techniques. Understanding how this occurs is important for understanding both how energy supply is matched to brain function, and what is measured in fMRI and PET imaging. Blood flow is partly controlled by smooth muscle around pre-capillary arterioles, which are innervated by noradrenaline-releasing neurons. However, 65% of vascular noradrenergic innervation in the brain is of capillaries rather than arterioles (Cohen et al.; 1997), suggesting that blood flow may also be regulated at the capillary level. Capillaries lack smooth muscle but in places are surrounded by contractile cells called pericytes, which express actin and myosin. In culture or on isolated vessels pericytes have been shown to contract and dilate in response to neurotransmitters, altering the capillary diameter. I will report a role for pericytes in controlling capillary diameter in situ in whole retina and in cerebellar slices (Peppiatt, Howarth, Mobbs & Attwell, 2006). Electrical stimulation of retinal pericytes evoked a localised constriction of capillaries, which propagated at $\sim 2\mu\text{m}/\text{sec}$ to constrict distant pericytes. Superfused ATP or UTP also caused localised constriction of capillaries at points close to pericytes, suggesting a role for purinergic P2 receptors in the control of capillary diameter. In cerebellar slices, noradrenaline constricted pericytes on capillaries in the molecular layer. This constriction could be reversed by applying glutamate to mimic glutamate release by neuronal activity. These data identify pericytes as possible contributors to the vascular response to changes in neural activity. Pericytes potentially have a role in CNS vascular disease and therapy.

(2) How the blood supplies to particular brain regions are matched to the estimated energy expenditure on signalling in these regions

The relationship between energy expenditure and information processing in the brain is only understood in the broadest terms. I have analysed this relationship for the cerebellar cortex, a brain area for which the cellular properties and the computations carried out are reasonably well understood. Based on the calculations of Attwell & Laughlin (2001), and using the known neuronal and glial properties, we estimated the signalling energy expended in the rat cerebellum. Each Purkinje cell uses $\sim 1.6 \times 10^{10}$ ATP/sec, whereas the much smaller granule cell uses approximately 3×10^8 ATP/sec. However, the much larger number of granule cells results in them consuming the great majority of the cerebellar cortical energy. Thus, most energy goes on granule cells re-mapping the sensory and motor command input arriving on the mossy fibres into a sparsely coded representation used by the Purkinje cells to retrieve motor output patterns. Spatially, signalling energy use was predicted to be split between the granular, Purkinje cell soma and molecular layers in the ratio 30%: 2%: 68%. Comparing the capillary area available for O₂ and glucose supply to the different cerebellar cortical layers suggests that the blood supply to these layers is only approximately matched to the computations carried out in each layer.

(3) The brain energy used on a perceptual decision

From published electrophysiological data I will present an estimate of the energy change associated with perceptual decisions in the visual, somatosensory and auditory systems. Surprisingly, perception is associated with only a small (<6%) increase in cortical energy use.

Attwell, D. & Laughlin SB. (2001) *J. Cereb. Blood Flow Metab.* 21, 1133-45

Cohen, Z., et al; (1997) *J. Cereb. Blood Flow Metab.* 17, 894-904

Peppiatt, C., Howarth, C., Mobbs, P. & Attwell, D. (2006) *Nature* 443, 700-4