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Feature Article Commentary

Glial laminar cortical architecture matches metabolic demand

Nadia A Scott[1,2] and Timothy H Murphy[1,2,3]

[1]*Department of Psychiatry, Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, British Columbia, Canada;* [2]*Brain Research Centre, University of British Columbia, Vancouver, British Columbia, Canada;* [3]*Department of Cellular and Physiological Sciences, University of British Columbia, Vancouver, British Columbia, Canada*

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The link between increased neural activity and cerebral blood flow is well established (Roy and Sherrington, 1890); yet, the mechanism by which blood flow is matched to neuronal activity both spatially and temporally is unclear. Based on their morphology, gray matter (protoplasmic) astrocytes are ideally situated to translate regional synaptic activity to hyperemia (increased flow) as they extend processes that envelop both synapses and vasculature (reviewed in Iadecola and Nedergaard, 2007). Indeed, evidence from *in vitro* and *in vivo* two-photon imaging has suggested that stimulus-induced elevations in astrocyte intracellular calcium are positioned to modulate vascular tone (Zonta *et al*, 2003; Takano *et al*, 2006; Mulligan and MacVicar, 2004; Winship *et al*, 2007). These local interactions are purported to occur at the astrocytic endfoot–blood vessel interface (reviewed in Iadecola and Nedergaard, 2007). Regionally, the spatial organization of astrocytes and vasculature should also have implications for matching blood flow to activity. While previous works have examined the interrelationships between astrocytes and microvasculature across cortical lamina, these studies have been conducted using histology and thus may not always faithfully represent the living tissue (White *et al*, 1981; Tsai *et al*, 2009). The present work of McCaslin *et al* (2011) has taken an important step to extend these findings in the live murine brain.

Using *in vivo* two-photon imaging, the authors found that the density of astrocytes showed distinct peaks at 40 to 60 and 440 to 500 μm below the cortical surface, corroborating an earlier report (Tsai *et al*, 2009). Likewise, the density of capillaries mirrored that of astrocytes, reaching similar peaks at 30 to 40 μm and again at 500 μm; moreover, the average distance between astrocytes and capillaries decreased with increasing cortical depth. This, together with evidence from Tsai *et al* (2009), who found that neuronal density peaks at 600 μm below the cortical surface, suggests that this columnar depth carries the highest metabolic load. Indeed, it has been recently reported that the fastest changes in dilation occur in diving arterioles and capillaries that are located at this cortical depth (Tian *et al*, 2010). Both experimental data (Tian *et al*, 2010) and models (Faraci and Heistad, 1990) have suggested that dilation of local arterioles is accompanied by temporally delayed dilation in upstream arteries. Gap junction-mediated communication between astrocytes has been implicated in the upward propagation of vasodilating signals from active neurons in the parenchyma to pial arteries (Xu *et al*, 2008). In support of a functional role for an astrocytic network in conducting hemodynamic signals, McCaslin *et al* (2011) confirm that a syncytium of astrocytes is in contact with all blood vessels below the glia limitans.

The laminar variations in astrocyte–vasculature interactions revealed by McCaslin *et al* (2011) may have important implications for the spatial and temporal matching of blood flow to activity within specific cortical layers. However, delineation of the relative contribution of distinct neuronal populations (reviewed in Cauli and Hamel, 2010) versus astrocytes to hemodynamic responses will require further exploration, perhaps with new optical tools to selectively regulate neuronal and astrocytic activity (Gradinaru *et al*, 2010).

Disclosure/conflict of interest

The author declares no conflict of interest.

Correspondence: Dr TH Murphy, Department of Psychiatry, University of British Columbia, 4N1-2255 Wesbrook Mall, Vancouver, BC, Canada V6T 1Z3.
E-mail: thmurphy@interchange.ubc.ca
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