Acute brain injury

Glia cells play crucial role in enabling vascular remodelling

Glia cells and in particular astrocytes play pivotal roles in maintaining multiple forms of metabolic coupling with neurons and the brain microvasculature. However, during most common forms of brain injury, including traumatic injury and stroke, this coupling becomes severely compromised leading to a metabolic challenge that further aggravates the initial insult. Astrocytes have emerged for playing important roles in brain tissue repair, however the underlying mechanisms remain poorly understood. Scientists from the Max Planck Institute for Biology of Ageing and the Cluster of Excellence CECAD in Cologne have now shown that acute injury and blood-brain barrier disruption trigger the formation of a prominent mitochondrial-enriched compartment in astrocytic perivascular processes which enables vascular remodelling. The results are published in the journal Cell Metabolism.

Traumatic brain injury and stroke are among the leading causes of death worldwide. Patients often present with significant damage to the cerebrovasculature, which is invariably accompanied by intracerebral haemorrhage, secondary inflammation and neurodegeneration. According to Matteo Bergami “Several factors contribute to the extent of the primary tissue damage, however our understanding of the mechanisms underlying neovascularization and brain tissue recovery in the injured area, is still quite rudimentary”.

To gain insights into this important question, the scientists focused their investigation on a certain type of glial cells, the astrocyte, whose specialized perivascular processes ensure the supply of metabolites to the brain parenchyma. They found that brain injury and the ensuing vascular damage trigger a profound remodelling of two cellular organelles which are enriched in these perivascular processes, the mitochondria and the endoplasmic reticulum (ER). In particular, this remodelling led to the generation of a spatially-defined metabolic domain surrounding newly formed vessels. “We actually didn’t expect such a reorganization of these organelles around vessels, especially in a fully developed, adult brain. This would only make sense to me if astrocytes would be actively involved in vascular remodelling” explains Jana Göbel, who recently graduated and is the first author of the study. The authors went on by introducing innovative approaches to manipulate the dynamics of these two organelles in astrocytes, as well as their physical tethering, which is known from other studies to underlie specific metabolic functions in cells. They found that preventing this localized enrichment of mitochondria-ER contact sites significantly affected the complexity of the newly-formed vascular network, while boosting organelle tethering favoured the restoring of a more elaborated network following injury. “These results are truly intriguing” continues Elisa Motori, the other senior author of the study who crucially contributed by devising new imaging and metabolic assays “as they reveal an entirely new layer of complexity in the way contact sites between mitochondria and other organelles underlie brain cell
plasticity and tissue remodelling, which we hope to exploit in future translational studies”.

This collaborative study between CECAD and the Max Planck Institute for Biology of Ageing, which as the authors explain was a “tour de force” and only possible thanks to complimentary expertise offered within the SFB1218, represents a conceptually and technologically clear advance in the understanding of how brain cells integrate organelle function and dynamics in disease settings in vivo. It has key implications for a number of neurological and cerebrovascular disorders and provides the opportunity for targeted interventions to ameliorate brain recovery, for instance after traumatic injury.

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Figure legend:

Visualization of a single astrocyte expressing ER-GFP (in pseudocolors) in the mouse cerebral cortex, contacting the nearby microvasculature (in grey).