The Microcirculation—Fantastic Voyage: Introduction

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The past several decades have seen remarkable advances in the understanding of the cerebral microcirculation and in the powerful effects that disruption of small cerebral blood vessels has on brain function, especially cognition. It is therefore incumbent on us to gain a deeper understanding of the function of small cerebral vessels and of the brain alterations deriving from their dysfunction. As crystallized in the concept of neurovascular unit, it is now well-recognized that the interaction among neurons, glia, and vascular cells is of critical importance for brain development and for preserving brain integrity in the normal state and in disease. Unfortunately, despite these advances, fundamental questions concerning the pathobiology of these vessels and their impact on brain function remain to be answered.

In this year’s Princeton conference, the session entitled “The Microcirculation—Fantastic Voyage” provided notable insights into novel aspects of cerebral microvasculature function with significant pathophysiological relevance. Unprecedented methodological advances have allowed investigators to probe the neurovascular unit at the molecular and cellular level, with tremendous analytic power and in the living brain. Here, we have provided a brief overview of the key findings highlighted in this section and presented in detail in the accompanying articles. Grutzendler1 provided evidence for a novel mechanism for microvascular recanalization termed “angiophagy.” This mechanism involves the engulfment of emboli by the endothelium followed by their translocation through the vessel wall into the perivascular space and leads to blood flow reestablishment within hours of the embolus extrusion process. This process is impaired during aging, and, possibly, by cerebrovascular risk factors, raising the possibility that defective microvascular recanalization could play a role in brain diseases associated with microembolization. Iliff and Nedergaard2 provided evidence that a considerable fraction of extracellular proteins and peptides, including amyloid β, are cleared by the convective fluxes of interstitial fluid facilitated by astrocytic aquaporin-4 water channels. This brain-wide clearance pathway, that they termed “glymphatic system,” may be altered after brain injury and in the long-term may contribute to the aggregation of extracellular or intracellular proteins, such as amyloid β and τ. Cenk Ayata3 presented evidence that spreading depression, a traveling wave of depolarization that occurs after brain injury, has complex cerebrovascular vasomotor effects reflecting the balance between vasodilatory and vasoconstrictory effectors. Remarkably, vasoconstriction and hypoperfusion predominate under pathological conditions, such as ischemic or hemorrhagic stroke, imposing additional stress on the tissue. Therefore, these injury-induced depolarizations and attendant hypoperfusion could be a therapeutic target in acute brain injury. Finally, Schaffer and Nishimura4 used cutting-edge laser-based approaches to occlude or induce hemorrhages in single brain microvessels. They found that ischemia caused by microvascular occlusions is more damaging to neurons than a bleed from the same vessel class. However, microhemorrhages lead to long-lasting inflammation, which may have profound and long-lasting effects on neuronal function and could underlie the cognitive deterioration associated with cerebral microhemorrhages.

This voyage through the cerebral microcirculation provides a glimpse into the extraordinarily diverse functions in which these small vessels are involved. Although regulation of cerebral perfusion remains a cardinal aspect, new roles in microvascular recanalization and lymphatic-like drainage also emerge. Hence, damage to single microvessels has profound and sustained effects on the brain’s health. As voyages often do, these discoveries not only expand our horizons, but also provide new frontiers that need to be explored and conquered. The rapid expansion of advanced technologies to probe the function of neurovascular unit in health and disease promises continued advances in this new and exciting area of research.

Disclosures

None.

References


Key Words: angiophagy • cerebral blood vessels • microcirculation
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Stroke. 2013;44:S83
doi: 10.1161/STROKEAHA.112.680215

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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