



ARTICLE OF THE MONTH

The Role of Brain Vasculature in Neurodegenerative Disorders

Sweeney MD, Kisler K, Montagne A, Toga AW, Zlokovic BV.
Nature Neuroscience. 2018 Oct; 21(10):1318-1331.

Happy New Year! Welcome to the January 2019 SNACC Article of the Month! This month's article discusses the basic science of the neurovascular unit in regards to cerebral autoregulation and was chosen by Dr. Mads Rasmussen from Aarhus University, Denmark.

Our audience might remember Dr. Rasmussen as a speaker at the 2018 SNACC conference ("Goliath enjoying a SIESTA"). He is the head of the neuroanesthesia research division at Aarhus University Hospital. His research interests include anesthetic and blood pressure management during endovascular procedures for acute ischemic stroke, influence of vasopressors on microvascular disturbances in patients with cerebral pathology, and transfusion and coagulation in pediatric craniostomosis surgery.

As always, we encourage our readers to give us their feedback on the SNACC [Twitter](#) feed or on [Facebook](#).

~ Nina Schloemerkerper, MD; Oana Maties, MD; Adrian Pichurko, MD

Commentary

Mads Rasmussen, MD, PhD

Under normal circumstances, the cerebral circulation is tightly regulated to meet the brain's metabolic demands. The mechanism, which ensures adequate cerebral blood flow in response to increased neuronal activity, is termed functional hyperaemia or neurovascular coupling. The cerebrovascular physiology and regulatory mechanisms involved in neurovascular coupling are not completely understood. However, in recent years, research has discovered that a group of functionally integrated cells composed of vascular cells, endothelial cells and glia (termed the neurovascular unit) contribute to functional hyperaemia and blood brain barrier (BBB) integrity and function. In this excellent review, Sweeney MD and colleagues provide new intriguing insights into the integrated role of the brain vasculature and BBB in the regulation of cerebral blood flow under normal circumstances and in the development of neurodegenerative disease.¹ Knowledge of altered cerebrovascular regulatory mechanisms in patients with neurodegenerative disorders may have important clinical implications in the neuroanesthesia and neurocritical care of this group of patients.

First, they describe the newly discovered concept of “vascular zonation” in the cerebral vasculature which refers to the molecular and phenotypic changes of endothelial and mural cells (smooth muscle cells vs. pericytes) along the cerebral vascular tree. This identifies the genetic and probably the functional heterogeneity of these cells, which is in contrast to my own understanding of the BBB as a more uniform functional unit. This finding may be extremely important for future studies investigating different cell types in vascular physiology and treatments which targets specific cells and segments of the brain vasculature.

They then discuss the key cellular and molecular pathways involved in the regulation of cerebral blood flow (CBF). Interestingly, the pericytes encircling the capillaries have both contractile and vasodilative properties and appear to be involved in active regulation of cerebral blood flow through pathways which are not completely understood. Thus, regulation of cerebral blood flow is not only at the arteriolar level, but also appears to involve cerebral capillaries. Further, it has previously been shown that cerebral capillaries can dilate ahead of arterioles suggesting close regulatory communication between different vascular segments.²

Finally, the authors review neurovascular dysfunction, impaired CO₂ reactivity and increased BBB permeability as important pathogenetic factors in the development of neurodegenerative disease. In this context, it has previously been suggested that pericytes may play an important role in the development of neurovascular and capillary dysfunction.³ Pericyte dysfunction may increase capillary transit time heterogeneity (CTH) with functional shunting of oxygenated blood through the capillary bed, potentially causing critical reduction in cerebral oxygen availability.⁴ If capillary dysfunction is present, elevation of mean arterial blood pressure may paradoxically result in a further increase in CTH followed by reduced oxygen extraction and consequently reduced cerebral oxygen supply.⁴ This may have implications for the use and choice of vasopressor drugs which are widely used to augment cerebral perfusion pressure in patients with acute cerebral pathology. However, whether vasopressor drugs amplify existing capillary flow disturbances has not been demonstrated and needs further exploration.

References:

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