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Ischemic Stroke and the Fate of Cerebral Microvessels

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Cerebral microvessels and their recipient neurons, as well as other components of the “neurovascular unit,” suffer a sequence of consistent and complex changes following focal cerebral ischemia. The neurovascular unit is a structural and conceptual framework that recognizes functional interactions among the cells and their environment, during normal conditions and following injury. Molecular interactions among the cell components of the neurovascular unit, and within the microvasculature *per se*, demonstrate that changes occur in receptors and their ligands that are important for structural, as well as signaling, functions. While there is substantial evidence that neuron stimulation alters flow through the adjacent microvascular bed, evidence that the microvessel endothelium-matrix-astrocyte complex communicates with neurons is sparse. Current studies may lead the way to understanding this communication.

A series of observations over the last three decades provide a basis for understanding microvessel-neuron interactions from the vascular biology perspective: i) recanalization of an occluded brain-supply artery affects the downstream microvasculature; ii) the region of injury characterized as the “penumbra” develops over time as “mini-penumbra” that coalesce; iii) during focal ischemia and with reperfusion of the brain-supplying artery occlusion of the microvasculature occurs. Contributors to this focal “no-reflow” include activated PMN leukocytes, fibrin, and platelets variably; iv) these

events occur within minutes to hours following the onset of ischemia. The endothelial cell response is as rapid as the neuronal response; v) matrix responses of the basal lamina within the microvasculature also occur rapidly (e.g., perlecan). Matrix metalloproteinases, cysteine proteases, serine proteases, and heparanase are rapidly generated. Adhesion receptors are also found to decrease in expression; vi) both the basal lamina matrix and inter-endothelial tight junction (TJ) proteins contribute to the barrier properties of the brain microvasculature. To this should be added the matrix adhesion receptors of both the endothelium and astrocytes at the basal lamina; vii) during focal ischemia, endothelial cell $\beta 1$ integrin expression significantly decreases. The expression of $\beta 1$ integrins is tied to TJ expression; viii) Similarly, astrocytes adhere to the basal lamina. They may contribute to the barrier, as well as to $\beta 1$ integrin expression; ix) the microvasculature undoubtedly responds to cells outside of its immediacy, including microglia, oligodendroglia, and other cells.

Both ultrastructural and adhesion receptor responses to ischemia suggest that the microvessel cell and matrix responses are coordinated and timed with neuron injury. How this may be, and other issues, will be explored during this presentation.

※The authors declare there is no conflict of interest relevant to this article.