Macro problems of microvessels in ischemic stroke

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Ischemic stroke is a leading cause of mortality and disability worldwide, and is a major public health problem. Currently approved treatment methods for acute ischemic stroke patients are primarily targeted to opening the occluded cerebral vessels by tPA or endovascular thrombectomy. Thus, improving the functionality of the ischemic cerebrovasculature will foster better outcome after ischemic stroke. However, recent clinical trials consistently show that despite achieving this goal and providing recanalization in the main cerebral vessels, blood flow might not improve at the microcirculatory level, hence reperfusion of the ischemic tissue is often incomplete. The success of recanalization therapies can be improved by diminishing incomplete reperfusion caused by loss of patency of some microvessels during ischemia that persists after recanalization. Recent experimental studies demonstrated the importance of pericyte cells, which are responsible for the regulation of cerebral and retinal microcirculation by wrapping the vessels at the capillary level, in this so called 'no-reflow phenomenon'. It is shown that alpha smooth muscle actin is the critical protein which is closely related to the contractile properties of pericytes, and thereby plays an important role in cerebral and retinal ischemia/reperfusion pathophysiology. Reducing 'no-reflow' by pharmacological treatments or by in vivo alpha smooth muscle actin targeted small interfering RNA (siRNA) seems to be an important and viable target for recanalization therapies. As the importance of microcirculation is not only limited to stroke, all these findings in the cerebro-retinal microcirculation under physiological and pathological conditions would probably have implications in the field of other brain pathologies such as neurodegenerative diseases, and would provide opportunities for new therapeutic approaches in all these diseases.