Endothelial BK_{Ca}, but not TRPV4 activity is altered in focal cerebral ischemic stroke

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Large conductance calcium-activated potassium channels (BK_{Ca}) are absent in healthy intact artery endothelium, but have a stress-induced expression following chronic hypoxia and cell isolation/culture. BK_{Ca} can form complexes with transient receptor potential vanilloid type 4 channels (TRPV4) that are implicated in control of vessel tone and in some models, stroke etiology. Confocal-immunohistochemistry determined BK_{Ca}-α and -β1, and TRPV4 distribution in adult male SD rat middle cerebral artery (MCA) in acute endothelin-induced stroke and chronic hypoxia; and hypoxia following stroke, and in human cerebral pial arterioles from terminal cerebral stroke and control subjects. MCA pressure myography and BK_{Ca} and TRPV4 activators and blockers determined channel function. BK_{Ca}-α and -β1 were absent in endothelium of MCA from untreated and saline-treated control rats, but present in stroke, hypoxia and hypoxia following stroke. Smooth muscle BK_{Ca}-α and -β1 were present in control and upregulated in stroke, hypoxia and hypoxia following stroke. Endothelial TRPV4 were present in control and upregulated in stroke and hypoxia, but unchanged in hypoxia following stroke. Smooth muscle TRPV4 were present in control, and unchanged in hypoxia; with reduced expression in stroke and hypoxia following stroke. Endothelial BK_{Ca}-α was absent in control human pial arterioles, present in stroke; and upregulated in smooth muscle of stroke. In rat MCA, basal BK_{Ca} regulating myogenic tone is increased in stroke; whereas TRPV4 function is unchanged. Intact MCA endothelium can be induced to express functional BK_{Ca}, and thus targeting of BK_{Ca} and its related signaling pathways is a rational approach to correct altered cerebral perfusion.