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Titel des Beitrags: A role of the sodium pump in spreading ischemia in rats.

Abstract: In rats, spreading depolarization induces vasodilation/hyperemia in naïve tissue but the inverse response when artificial cerebrospinal fluid is topically applied to the brain containing (a) a nitric oxide-lowering agent and (b) elevated K(+). The inverse response is characterized by severe vasoconstriction/ischemia. The perfusion deficit runs together with the depolarization in the tissue (=spreading ischemia). Here, we found in male Wistar rats that pre-treatment with artificial cerebrospinal fluid containing elevated K(+) in vivo led to a selective decline in ?2/?3 Na(+)/K(+)−ATPase activity, determined spectrophotometrically ex vivo. Moreover, spreading ischemia, recorded with laser-Doppler flowmetry and electrocorticography, resulted from artificial cerebrospinal fluid containing a nitric oxide-lowering agent in combination with the Na(+)/K(+)-ATPase inhibitor ouabain at a concentration selectively inhibiting ?2/?3 activity. Decline in ?2/?3 activity results in increased Ca(2+) uptake by internal stores of astrocytes, vascular myocytes, and pericytes since Ca(2+) outflux via plasmalemmal Na(+)/Ca(2+)-exchanger declines. Augmented Ca(2+) mobilization from internal stores during spreading depolarization might enhance vasoconstriction, thus, contributing to spreading ischemia. Accordingly, spreading ischemia was significantly shortened when intracellular Ca(2+) stores were emptied by pre-treatment.
with thapsigargin, an inhibitor of the sarco(endo)plasmic reticulum Ca(2+)-ATPase (SERCA). These findings might have relevance for clinical conditions, in which spreading ischemia occurs such as delayed cerebral ischemia after subarachnoid hemorrhage.