Lactacidosis-induced glial cell swelling depends on extracellular Ca2+.

Abstract: Cerebral tissue acidosis following ischemia or traumatic brain injury contributes to cytotoxic brain edema formation. In vitro lactacidosis induces swelling of glial cells by intracellular Na+ and Cl− accumulation by the Na+/H+-antiporter, Cl−/HCO3−-antiporters and the Na+/K+/2Cl−-cotransport. The present study aimed to elucidate whether mechanisms of lactacidosis-induced glial swelling are dependent on intracellular or extracellular Ca2+ ions. Therefore, C6 glioma cells were exposed to a lactacidosis of pH 6.2 in standard or calcium-free medium and following intracellular calcium chelation. Cell volume and intracellular pH were assessed by flow cytometry. Lactacidosis of pH 6.2 induced a prompt and sustained swelling of suspended C6 glioma cells reaching a maximum of 128% within 60 min. Omission of Ca2+ from the suspension medium strongly attenuated cell swelling while chelation of intracellular Ca2+ had no effects. Intracellular acidosis was not affected by either treatment. The present data show a strong dependency of lactacidosis-induced glial swelling upon extracellular Ca2+ while intracellular acidosis is not affected by omission of [Ca2+]e. Therefore, our data suggest that the Na+/K+/2Cl−-cotransporter, the only so far known transporter involved in cell volume regulation but not in pH regulation during lactacidosis, is activated in a [Ca2+]e-dependent manner.

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