Long-term effects of hypothermia on neuronal cell death and the concentration of apoptotic proteins after incomplete cerebral ischemia and reperfusion in rats.

Abstract:
BACKGROUND: The present study investigates the long-term effects of postischemic hypothermia on neuronal cell damage and concentration changes of apoptotic proteins after cerebral ischemia. METHODS: Sixty-four Sprague-Dawley rats were anesthetized, intubated and ventilated with 2.0 Vol% isoflurane and 70% N2O/O2. After preparation the animals were randomly assigned to the following groups: group 1 (n = 32, fentanyl-N2O/normothermia 37.5 degrees C), and group 2 (n = 32, fentanyl-N2O/hypothermia 34.0 degrees C. Ischemia (45 min) was induced by common carotid artery occlusion plus hemorrhagic hypotension (MAP = 40 mmHg). Arterial blood gases and pH were maintained constant. After 1, 3, 7, or 28 days (each n = 8) the brains were removed, frozen and cut. Neuronal damage was assessed by analyzing Bax, Bcl-2, p53, and Mdm-2 proteins, activated caspases-3-positive and eosinophilic cells. A third group (n = 8) of untreated animals served as naive controls. RESULTS: In hypothermic animals, Bax concentration was decreased by 50-70% over time compared to normothermia. On days 1 and 3, Bcl-2 was increased by 50% with hypothermia. The amount of activated caspase-3-positive cells in the ischemic hemisphere was 0.5% in the hypothermic and 1-2% in the
normothermic animals. Of the hippocampal cells, 10-25% were eosinophilic in both groups over time. CONCLUSION: The present data show that hypothermia prevents an ischemia-induced increase of the pro-apoptotic protein Bax for as long as 28 days and increases the concentration of the antiapoptotic protein Bcl-2 up to 3 days compared to normothermic animals. Therefore, after cerebral ischemia, hypothermia has the sustained neuroprotective potential to shift apoptosis-related proteins towards neuronal cell survival.