Cerebral ischemia and neurogenesis: a two-time comparison.

BACKGROUND: This study compares the effect of mild and severe cerebral ischemia on neuronal damage and neurogenesis. METHODS: Sixteen Sprague-Dawley rats, anesthetized with 0.8 vol% halothane in O(2)/air, were subjected to forebrain ischemia by bilateral common carotid artery occlusion plus hemorrhagic hypotension (mean arterial blood pressure = 40 mmHg) for 8 (mild) or 13 (severe) min. Four non-ischemic animals were investigated as naïve controls. Bromodeoxyuridine (50 mg/kg), a marker of new cells, was administrated for seven consecutive postischemic days. After 28 days, animals were perfused with 4% paraformaldehyde and the brains were sliced. Histopathological damage of the hippocampus and the volume of the dentate gyrus were assessed by HE-staining. With immunohistochemistry BrdU-positive cells were detected in the dentate gyrus. The amount of new generated neurons was identified by double-immunofluorescence-staining of BrdU and neuronal marker (NeuN). RESULTS: In the CA-1 region of the hippocampus, mild ischemia induced damage up to 10% (HE-index 0.8 +/- 1.2) and severe ischemia up to 50% (HE-index 2.1 +/- 1.4). There was no histopathological damage in naïve control animals. The amount of new neurons was increased by 250% after mild insult and by 160% after severe insult compared to the naïve control animals. CONCLUSIONS: These data indicate that histopathological damage
depends on the severity of the ischemic insult and that forebrain ischemia activates generation of new neurons. A mild ischemic challenge appears to be a more potent neurogenic stimulus than severe ischemia. The new neurons survive at least 28 days. This may relate to delayed histopathological and functional recovery after cerebral ischemia.