Brain ischemia is well known for its ability to change the function of the blood-brain barrier (BBB). We assessed BBB integrity by examining the leakage of horseradish peroxidase (HRP) and amyloid precursor protein (APP) from the vascular network into ischemic hippocampus. Using Wistar rats (n=10) BBB and APP changes were studied by light microscope following 10 min brain ischemia with 6 months survival. As controls sham-operated animals (n=6) were sacrificed in due time. Rats were perfusion fixed for these investigations. HRP introduced i.v. and circulated for 30 min was used as an indicator of BBB changes. Five brains were cut at 50-80 μm slices in the coronal plane by a vibratome for HRP staining. Paraffin sections from other 5 brains were selected for APP immunohistochemistry and structural observations. Control brains went through the same procedures as ischemic. The areas of BBB leakage were associated with increased expression of HRP and C-terminal of APP/α-amyloid peptide in perivascular space suggesting, respectively, an additional response to ischemia and neuronal death. These results suggest that the events associated with delayed neuronal death in hippocampus compromise BBB function. Additionally these data suggest that the leakage of cytotoxic APP parts in the CA1 and other sectors of hippocampus may play a role in the development of continuous delayed neuronal death after the ischemia. These findings also suggest that the BBB vessels along the hippocampal fissure especially in the medial part of the hippocampus are more vulnerable to ischemic episodes than those in other hippocampal areas.