In the present study, we investigated the potential beneficial effects of methanolic extract of onion (Allium cepa) on brain ischemia-induced edema and blood-brain barrier (BBB) dysfunction. The possible underlying mechanisms are investigated especially those linked to the antioxidant effects of the onion extract. Brain ischemia was induced by middle cerebral artery occlusion (MCAO) for 2 h followed by reperfusion in mice. Brain water content in the ischemic hemisphere was significantly reduced by treatment with onion extract. Onion extract also had a significant effect both on decrease of Evans blue extravasation and on inhibition of zonula occludens-1 (ZO-1) and occludin disruption caused by brain ischemia. In addition, onion extract significantly prevented brain ischemia-induced reduction in CAT and GPx activities and elevation of MDA level in the brain tissue. The results from this study demonstrate that onion extract prevents brain edema, BBB hyperpermeability and TJs disruption, possibly through its antioxidant effects in the mouse MCAO model. This study suggests that onion extract may be a beneficial nutrient for the prevention of BBB function during brain ischemia.