Alzheimer's disease (AD) is a multifactorial neurodegenerative disease in which vascular pathology plays an important role. Decrease in cerebral blood perfusion featuring in most Alzheimer's disease (AD) cases has documented as a critical risk for AD. Because loss of cerebral vascular function is critical for development of AD pathologies under chronic cerebral hypoperfusion (CCH) conditions, we examined if S-nitroso-glutathione (GSNO) is able to improve damaged learning-memory function and Aβ accumulation in the brains of rats with bilateral common carotid artery occlusion (BCCAO), an animal model for human CCH. GSNO is a most abundant low molecular weight S-nitrosothiol and has been regarded as an important endogenous NO source exerting anti-inflammatory and vasoprotective activities. We here report that hypoperfusion in BCCAO rats resulted in increased expression of vascular inflammatory markers, increased levels of Aβ, and learning and memory dysfunction. Administration of GSNO (50µg/kg/day for 4 months) improved learning and memory functions of BCCAO treated rats with reducing brain Aβ levels. GSNO inhibited proinflammatory signaling in bEnd3 brain endothelial cells and thus reduced gene expression related to endothelial inflammation (i.e. ICAM-1, VCAM, and MMP-9). In addition, GSNO increased uptake of Aβ by cultured bEnd3 cell with increasing S-nitrosylation of dynamin-2 protein, a protein regulating cellular endocytosis activity. Taken together, these data first time document a potential therapeutic activity of GSNO on neurovascular pathologies involved in CCH and AD.