Abstract

There is thought to be a strong relationship between sphingosine-1-phosphate (S1P) signaling and pathophysiolosy of cerebral ischemia. We examined the change of expression and distribution of S1P receptors (S1PRs) and sphingosine kinases (SphKs) after cerebral ischemia in male C57BL6/J mice using immunohistochemical analysis at 1, 5, 14, and 28 days after 30 min of transient middle cerebral artery occlusion (tMCAO). S1PR1, 3, and 5 were transiently induced in the cells, which were morphologically similar to neurons in the peri-infarct lesion with a peak seen at 1 day after tMCAO ($p < 0.01$ vs. sham control). S1PR2 appeared in the inner layer of vessels in the ischemic core ($p < 0.01$ vs. sham control) and the peri-infarct lesion ($p < 0.01$ vs. sham control) at the acute phase after tMCAO. However, SphK1 was strongly induced at 1 and 5 days after tMCAO ($p < 0.01$ vs. sham control) in the peri-infarct lesion, whereas SphK2 expression did not change. Western blot analysis at 1 and 5 days after 30 min of tMCAO revealed that the expression of S1PRs and SphK1 were transiently enhanced at the acute phase, which was consistent with the immunohistochemical results. Double immunofluorescent analysis revealed S1PR2/NG2- and S1PR2/CD31-, S1PR3/CD31-, and S1PR5/CD31-double positive cells in the peri-infarct lesion 1 day after tMCAO. The present results suggest that S1PRs and SphK1 may be important therapeutic targets for rescuing the peri-infarct lesion.