The 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) have been associated with stroke prevention. The aim of our study was to investigate the effect of simvastatin on c-fos gene activity and its relation to delayed neuronal death in CA1 region of hippocampus following transient forebrain ischemia in the adult rat hippocampus. 17 male Wistar albino rats were used in this study. The animals were divided into three groups: sham-operated; ischemised without statin pre-treatment and ischemised rats with statin pre-treatment. We used simvastatin in dose 20mg/kg during 14 days prior to ischemic attack. 15 minutes long transient forebrain ischemia was induced by the four-vessel occlusion. 2.5 hours reperfusion was used for c-Fos activity detection using immunostaining and 72 hours reperfusion was used for the determination of neurons surviving using hematoxylin/eosin staining. The average neuronal density in the CA1 region of hippocampus in the sham-operated rats, in ischemised without and with statin pre-treatment was 47.03 ± 3.09/0.025mm², 9.05 ± 2.46/0.025mm² and 16.45 ± 2.78/0.025mm², respectively. Significant neuroprotective effect was observed in the pre-treated ischemic group (P< 0.001) in comparison to ischemic group without pre-treatment. Significant difference (P < 0.001) was found between sham-operated group and both ischemic groups in c-Fos positivity. No significant difference in c-Fos positivity was observed between untreated ischemic and pre-treated ischemic groups (P>0.05). These findings indicate that simvastatin provides protection against CA1 hypoxic neuronal injury, which is independent of c-fos activation. This work was supported by project “Center of excellence for research on personalized therapy” co-financed from EU sources and European Regional Development Fund.