The neuroprotective effect of glial cell line-derived neurotrophic factor in fibrin glue against chronic focal cerebral ischemia in conscious rats.

Authors: Cheng H., Huang S.S., Lin S.M., Lin M.J., Chu Y.C., Chih C.L., Tsai M.J., Lin H.C., Huang W.C., Tsai S.K.

Publication Date: 2005

Abstract:

Glial cell line-derived neurotrophic factor (GDNF) is a transforming growth factor-beta which has shown beneficial effects in rats after acute focal cerebral ischemia (FCI). To study the effects of GDNF on chronic FCI injury in conscious rats, we used fibrin glue (GDNF-fibrin glue) and fibrin glue free (GDNF-only)-GDNF topically applied to the ischemic brain after right middle cerebral artery (MCA) ligation. Infarct brain volume and functional motor deficits were measured before and after FCI injury. After FCI injury induced by right MCA ligation, rats were randomly assigned to one of four treatment groups: (a) sham, (b) control, (c) topically applied GDNF (1 mug)-only, and (d) topically applied GDNF (1 mug)-fibrin glue. The degree of ischemic brain injury was estimated by infarct volume of right MCA territory at 4 weeks after occlusion. The functional motor deficits were quantified with rotarod test and grasping power test once a week. Topically applied GDNF-fibrin glue at infarct brain tissue after 4 weeks FCI injury significantly reduced the total infarct volume by 44.3% and 36%, respectively, compared to that of control group and GDNF-only group. The mean latencies for rats to stay on the rotarod were 55.0%, 50.3%, and 92.2% ($P < 0.05$ vs. control group and GDNF-only group) of baseline, respectively, in the control, GDNF-only, and GDNF-fibrin glue groups at the end of the 1st week after FCI injury but 75.3%, 67.3%, and 106.6% ($P < 0.05$ vs. control group and GDNF-only group) of baseline at the end of the 4th week after FCI injury. The mean values of grasping power were 78.7%, 71.7%, and 101.2% ($P < 0.05$ vs. control group and GDNF-only group)

of baseline, respectively, in the control, GDNF-only, and GDNF-fibrin glue groups at the end of 1st week after FCI injury but 89.6%, 97.6%, and 120.7% ($P < 0.05$ vs. control group) of baseline at the end of 4th week after FCI injury. These results indicate that GDNF-fibrin glue not only reduced the total infarct volume after FCI injury but can also improve motor deficits after FCI injury. We concluded GDNF-fibrin glue could facilitate delivery of GDNF to the damaged brain tissue with subsequent reduction of ischemic brain injury accompanied by enhancing functional recovery in rats with chronic FCI injury.