

Implantation of encapsulated glial cell line-derived neurotrophic factor-secreting cells prevents long-lasting learning impairment following neonatal hypoxic-ischemic brain insult in rats

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**Title:** Implantation of encapsulated glial cell line-derived neurotrophic factor-secreting cells prevents long-lasting learning impairment following hypoxic-ischemic brain insult in neonatal rats

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**Abstract**

**Objective:** Implantation of encapsulated glial cell line-derived neurotrophic factor (GDNF)-secreting cells into brain parenchyma reduces histological brain damage following hypoxic-ischemic (H/I) stress in neonatal rats. We examined the effect of GDNF on long-term learning and memory impairment and morphological changes up to 18 weeks after HI stress in neonatal rats.

**Study Design:** Baby hamster kidney (BHK) cells were transfected with expression vector either did (GDNF-HI group; n=10) or did not (Control-HI group; n=8) include human GDNF cDNA, and encapsulated in semi-permeable hollow fibers, and implanted into the left brain parenchyma of 7-day-old Wistar rats. Two days after implantation the rats received H/I stress, and their behavior was then examined in several learning tasks: the 8-arm radial maze, choice reaction time, and water maze tasks, which examine short-term working memory, attention process, and long-term reference memory, respectively. The rats were sacrificed 18 weeks after the H/I insult for evaluation of brain damage. Two additional control groups were used: the Control group (n=15), which underwent no treatment, and the GDNF group (n=6), which underwent implantation of the GDNF capsule, but did not undergo H/I stress.

**Results:** The decrease in the size of the cerebral hemisphere was significantly

less in the GDNF-HI group, compared with the Control-HI group, and improved performance was observed in all three tasks for the GDNF-HI group: for the Control-HI group vs. the GDNF-HI group, respectively, in the 8-arm radial maze test, average number of correct choices:  $6.2 \pm 0.1$  vs.  $6.9 \pm 0.1$  ( $p < 0.01$ ); in the choice reaction time test, average reaction time for a correct response:  $2.35 \pm 0.1$  s vs.  $1.97 \pm 0.09$  s ( $p < 0.01$ ); in the water maze test, average swimming length:  $1120.0 \pm 95.2$  cm vs.  $841.6 \pm 92.1$  cm ( $p < 0.01$ ). All results for the GDNF group were similar to those for the Control group.

**Conclusion:** GDNF treatment is effective not only in reducing brain damage but also in inhibiting learning and memory impairment, following H/I insult in neonatal rats. No adverse effects in learning and memory tests were observed in the GDNF group.