



Effective GDNF brain delivery using microspheres-A promising strategy for Parkinson's disease

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Glial cell line-derived neurotrophic factor (GDNF) has shown promise in the treatment of neurodegenerative disorders of basal ganglia origin such as Parkinson's disease (PD). In this study, we investigated the neurorestorative effect of controlled GDNF delivery using biodegradable microspheres in an animal model with partial dopaminergic lesion. Microspheres were loaded with N-glycosylated recombinant GDNF and prepared using the Total Recirculation One-Machine System (TROMS). GDNF-loaded microparticles were unilaterally injected into the rat striatum by stereotaxic surgery two weeks after a unilateral partial 6-OHDA nigrostriatal lesion. Animals were tested for amphetamine-induced rotational asymmetry at different times and were sacrificed two months after microsphere implantation for immunohistochemical analysis. The putative presence of serum IgG antibodies against rat glycosylated GDNF was analyzed for addressing safety issues. The results demonstrated that GDNF-loaded microspheres, improved the rotational behavior induced by amphetamine of the GDNF-treated animals together with an increase in the density of TH positive fibers at the striatal level. The developed GDNF-loaded microparticles proved to be suitable to release biologically active GDNF over up to 5 weeks in vivo. Furthermore, none of the animals developed antibodies against GDNF demonstrating the safety of glycosylated GDNF use.

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