Bridging nigrostriatal pathway with fibroblast growth factor primed peripheral nerves and fetal ventral mesencephalon transplant recuperates from deficits in Parkinsonian rats

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摘要

Abstract

Previous studies have indicated that the nigrostriatal dopaminergic (DA) pathway can be reconstructed in hemiparkinsonian rats with a bridge transplantation technique involving fetal ventral mesencephalic transplants and glial cell line-derived neurotrophic factor. In this study, we examined if the nigrostriatal pathway can be restored by combining peripheral nervous tissue with the fetal ventral mesencephalon transplants. Adult rats were injected with 6-hydroxydopamine into left median forebrain bundle. Those with marked rotational behavior, which has been previously shown to indicate complete DA dennervtion, were used for transplant treatments. One month after the lesion, fetal ventral mesencephalic cells were transplanted into the nigral region followed by nigral-striatal grafting of peripheral nerves as a bridge. The bridging nerves (sciatic or intercostals) were pretreated with basic fibrous growth factor (nerve+bFGF+) or Hank's saline (nerve+bFGF-). We found that (a) animals receiving transplantsof VM and bFGF+ nerve had a reduction in rotational behavior; (b) animals receiving bFGF-- nerve bridge only had a partial improvement in rotation. Reinnervation of tyrosine hydroxylase (TH)-immunoreactive (ir) fibers into the striatum was found in both of the above groups with more innervation in the former than in the latter. No TH-ir fibers in lesioned striatum or reduction in rotational behavior were found in animals receiving VM only, or VM plus bFGF. Taken together, our data indicate that peripheral nerve, with the aid of bFGF, greatly facilitates the reconstitution of the TH pathway from nigra to striatum and improves motor function in hemiparkinsonian rats.