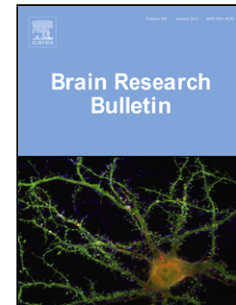


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Evaluation of direct and cell-mediated triple-gene therapy in spinal cord injury in rats

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HIGHLIGHTS

- Gene therapy is an innovative approach to treat spinal cord injury (SCI)
- Cell-mediated gene therapy in SCI seems to be more effective than direct gene delivery
- Umbilical cord blood cells (UCBCs) are effective carriers of therapeutic genes
- Triple-gene therapy with intra-thecal delivery has been found to be effective in SCI
- Genetic modification of UCBCs with therapeutic genes promotes healing processes in SCI

ABSTRACT

Current treatment options for spinal cord injury (SCI) are scarce. One of the most promising innovative approaches include gene-therapy, however no single gene has so far been shown to be of clinical relevance. This study investigates the efficacy of various combinations of vascular endothelial growth factor (VEGF), glial cell-derived neurotrophic factor (GDNF), angiogenin (ANG) and neuronal cell adhesion molecule (NCAM) in rats. Multiple therapeutic genes were administered intrathecally either via adenoviral vectors or by using genetically modified human umbilical cord blood mononuclear cells (hUCBMCs). Following the induction of SCI, serial assessment of cord regeneration was performed, including morphometric analysis of gray and white matters, electrophysiology and behavioral test. The therapeutic gene combinations VEGF+GDNF+NCAM and VEGF+ANG+NCAM had positive outcomes on spinal cord regeneration, with enhanced recovery seen by the cell-based approach when compared to direct gene therapy. The efficacy of the genes and the delivery methods are discussed in this paper, recommending their potential use in SCI.

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