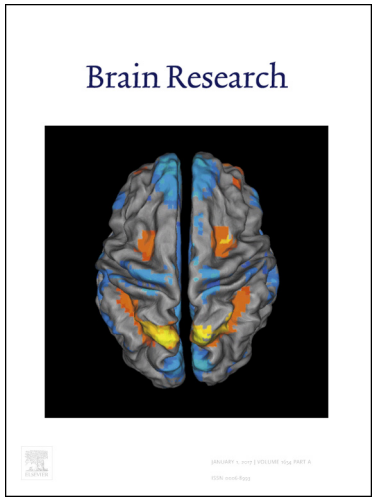

Research report

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Article

Transplantation of Mesenchymal Stem Cells that Overexpress NT-3 Produce Motor Improvements without Axonal Regeneration following Complete Spinal Cord Transections in Rats

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Abstract

Transplanting stem cells engineered to overexpress trophic factors can improve motor abilities and facilitate axon regeneration following spinal cord injury. This study compared several transplantation paradigms using mesenchymal stem cells (MSCs) that overexpress the multi-neurotrophin, NT-3/D15A (NT-3-MSCs), to determine if different grafting strategies can elicit improved axon regeneration and/or behavioral outcomes following a complete T9 spinal transection. At one week post-transection, NT-3-MSCs were transplanted above, and at several locations below, the lesion site. A rostral-to-caudal gradient of NT-3-MSCs was produced by incrementally increasing the number of transplanted cells at locations distal to the transection. Motor function was analyzed using the Basso, Beattie, and Bresnahan scale for 7-weeks post-injury. The corticospinal tract was traced using biotinylated dextran amines, while raphespinal fibers were visualized using immunohistochemistry. Cell viability was assessed using transplants of NT-3-MSCs that express tdTomato. Retrograde tracing using fluorogold, as well as spinal re-transections, were performed to discriminate between a supra-spinal or reflexive influence of regained motor functions. NT-3-MSC transplants improved motor outcomes and tissue continuity at the transection site, however retrograde tracing using fluorogold revealed no evidence of axon regeneration. A spinal re-transection also failed to eliminate the improvement in motor outcomes produced by the transplant. We conclude that transplantation of NT-3-MSCs can improve motor function and morphological outcomes following a complete spinal transection without promoting axonal regeneration.

Key Words: Axon Regeneration; Mesenchymal Stem Cell; Neurotrophin-3; Spinal Cord Injury; Re-Transection

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Abbreviations: 5-HT, 5-hydroxytryptoamine or Serotonin; **BBB**, Basso, Beattie, and Bresnahan scale for locomotor recovery; **BDA**, Biotinylated Dextran Amine conjugated to Texas Red; **BDNF**, Brain Derived Neurotrophic Factor; **CNS**, Central Nervous System; **CPG**; Central Pattern Generator; **CST**, Corticospinal Tract; **MSC**, Mesenchymal Stem Cell; **NF-70**, Neurofilament 70 kD; **NT-3**, Neurotrophin-3; **NT-3-MSCs**, Mesenchymal Stem Cells that Overexpress the Multi-Neurotrophin NT-3/D15A; **SCI**, Spinal Cord Injury; **tdTomato**, Tandem-Dimer Tomato Fluorescent Protein.