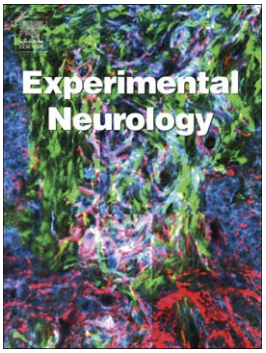

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Does the preclinical evidence for functional remyelination following engraftment into the injured spinal cord support progression to clinical trials?

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ABSTRACT

This article reviews all historical literature in which rodent-derived myelinating cells have been engrafted into the contused adult rodent spinal cord. From 2,500 initial PubMed citations identified, human cells grafts, bone mesenchymal stem cells, olfactory ensheathing cells, non-myelinating cell grafts, and rodent grafts into hemisection or transection models were excluded, resulting in the 67 studies encompassed in this review. Forty five of those involved central nervous system (CNS)-derived cells, including neural stem progenitor cells (NSPCs), neural restricted precursor cells (NRPs) or oligodendrocyte precursor cells (OPCs), and 22 studies involved Schwann cells (SC). Of the NSPC/NPC/OPC grafts, there was no consistency with respect to the types of cells grafted and/or the additional growth factors or cells co-grafted. Enhanced functional recovery was reported in 31/45 studies, but only 20 of those had appropriate controls making conclusive interpretation of the remaining studies impossible. Of those 20, 19 were properly powered and utilized appropriate statistical analyses. Ten of those 19 studies reported the presence of graft-derived myelin, 3 reported evidence of endogenous remyelination or myelin sparing, and 2 reported both. For the SC grafts, 16/21 reported functional improvement, with 11 having appropriate cellular controls and 9/11 using proper statistical analyses. Of those 9, increased myelin was reported in 6 studies. The lack of consistency and replication among these preclinical studies are discussed with respect to the progression of myelinating cell transplantation therapies into the clinic.

Key words: Remyelination; Spinal Cord Injury; Transplantation; Oligodendrocytes; Neural Precursor Cells; Neural Stem Progenitor Cells; Schwann Cells