

Combining Schwann Cell Bridges and Olfactory-Ensheathing Glia Grafts with Chondroitinase Promotes Locomotor Recovery after Complete Transection of the Spinal Cord

Abstract

Numerous obstacles to successful regeneration of injured axons in the adult mammalian spinal cord exist. Consequently, a treatment strategy inducing axonal regeneration and significant functional recovery after spinal cord injury has to overcome these obstacles. The current study attempted to address multiple impediments to regeneration by using a combinatory strategy after complete spinal cord transection in adult rats: (1) to reduce inhibitory cues in the glial scar (chondroitinase ABC), (2) to provide a growth-supportive substrate for axonal regeneration [Schwann cells (SCs)], and (3) to enable regenerated axons to exit the bridge to re-enter the spinal cord (olfactory ensheathing glia). The combination of SC bridge, olfactory ensheathing glia, and chondroitinase ABC provided significant benefit compared with grafts only or the untreated group. Significant improvements were observed in the Basso, Beattie, and Bresnahan score and in forelimb/hindlimb coupling. This recovery was accompanied by increased numbers of both myelinated axons in the SC bridge and serotonergic fibers that grew through the bridge and into the caudal spinal cord. Although prominent descending tracts such as the corticospinal and reticulospinal tracts did not successfully regenerate through the bridge, it appeared that other populations of regenerated fibers were the driving force for the observed recovery; there was a significant correlation between numbers of myelinated fibers in the bridge and improved coupling of forelimb and hindlimb as well as open-field locomotion. Our study tests how proven experimental treatments interact in a well-established animal model, thus providing needed direction for the development of future combinatory treatment regimens.