RESECTION OF GLIAL SCAR FOLLOWING SPINAL CORD INJURY

*Bhatia, N; *Rasouli, A; *Dinh, PT; *Suryadevara, S; *Cahill, K; +*Gupta, R
+*University of California, Irvine
ranjang@uci.edu

INTRODUCTION

Spinal cord injury (SCI) remains a devastating problem with limited therapeutic options. There are currently numerous basic science and clinical trials being performed to help improve the functional outcome following SCI. While many of these studies focus on modulating the immune response and enhancing axonal regeneration, there is limited work being performed on evaluating the role of glial scar in SCI (1,2). As such, we sought to evaluate and compare the effects of surgically resecting the glial scar in a contusion model and a dorsal hemisection model of spinal cord injury.

METHODS

Animal models for SCI were created using adult Sprague-Dawley rats (n=40). A laminectomy was performed at the T10 for all animals. A dorsal hemisection model was created for two groups with a Feather MicroScalpel Feather 15° (EMS, Hatfield, PA). For two additional groups, the PSI Infinite Horizon Impactor (IH; Precision Systems & Instrumentation, Lexington, KY) was used to create a contusion injury by uniformly delivering 175 kdyn to the exposed spinal cord. At one week postinjury, all of the spinal cords were reexposed in all four groups. For one group from each injury model, 2mm of friable glial scar was excised. Functional outcome was measured using the Basso, Beattie, Bresnahan (BBB; 3) Locomotor Rating Scale at weekly intervals including preoperatively, one week post-injury, and weekly thereafter for six additional weeks. Stereotactic injections of biotinylated dextran amine- BDA (Molecular Probes, Eugene, Oregon) were performed via a craniotomy over the rat motor cortex to verify axonal regeneration in the descending tracts in a few animals. Ascending spinal periferal sympathetic nerves in the L4 dorsal root ganglion. After tract tracing, the animals were allowed to survive for two additional weeks, following which they were perfused with 4% paraformaldehyde (PFA). Intact spinal cords were harvested and post-fixed in 4% PFA, rinsed in Na2HPO4, equilibrated in 30% sucrose buffer, and embedded in TissueTek® (VWR International, West Chester, PA). The frozen tissue blocks were then sectioned to produce longitudinal sections of the lesion site, and cross-sections of the rostral and caudal segments. Visualizing the BDA-labeled axons was possible through histochemical means using avidin and biotinylated horseradish peroxidase (Vectastain ABC Kit, Vector Labs, Burlingame, CA) followed by diaminobenzidine (DAB) staining, allowing for dark staining of axons along with light staining of the gray matter (4).

RESULTS

Within the dorsal hemisection model, there was no significant difference in recovery for animals which underwent glial scar excision versus animals which did not have scar excision. Animals subjected to the contusion model, however, demonstrated lower BBB scores in the non-resected group during the earlier postoperative periods (<4 weeks; p<0.05; Table 1).

After confirmation of BDA-labeled axons within the descending spinal cord tracts (Fig. 1), histological analysis of the lesion area revealed little to no axons within the glial resection contusion model, and a moderate axon growth within the non-resected contusion group (Fig. 2 and 3).

DISCUSSION

The glial scar which forms after spinal cord injury likely plays a critical role in stabilizing spinal cord integrity and function after SCI injury. While this glial scar may serve to stabilize the preserved axonal tracts and thereby permit modest recovery in a contusion model of SCI, it may be of less importance with a dorsal hemisection model. These experiments highlight that the basic biological processes following SCI vary tremendously based on the injury model that is studied. Furthermore, the role of glial scar in spinal cord regeneration must be elucidated before therapeutic applications can be realized. Further work is necessary to characterize the cellular and molecular changes within this zone of injury in different SCI models.

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References

Table 1: Average BBB scores showing a significant difference in improvement between the contusion model groups that underwent glial resection and the non-resected group.