Title: Regeneration of neural progenitors after spinal cord injury

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Abstract

Purpose of Study

Near 300,000 people in the U.S. suffer from spinal cord injury (SCI) with an average age of 43, and the lifetime cost of SCI is $1.2-5.0 million per person. Patients with SCI often experience chronically impaired motor deficits, which leads to a tremendously reduced quality of life. Motor neurons (MNs) and oligodendrocytes (OLs) are two important cell populations in the spinal cord. MNs control locomotion, and OLs myelinate neuronal axons to ensure their normal functions. During development, these cells are both differentiated from pMN progenitors, which originate from neural progenitors. In this study, we investigated the responses of pMN and neural progenitors after SCI. A better understanding of the regeneration process will help develop new treatments to promote spinal cord repair and improve the quality of life for patients with SCI.

Methods Used

We used zebrafish as the model organism because they have powerful regeneration ability and their nervous system shares great similarities with humans. Transgenic lines and immunohistochemistry were used to label Sox2 and Olig2, which are genetic markers for neural progenitors and pMN progenitors, respectively. A complete spinal cord transection was performed in zebrafish at 5 days post-fertilization by making a dorsal-to-ventral incision perpendicular to the spinal cord up to the dorsal margin of the notochord. The injured fish were imaged immediately after injury (0 DPI), one day after injury (1 DPI), and two days after injury (2 DPI) using both static and timelapse confocal microscopy.

Summary of Results

Soon after SCI, static imaging revealed a dramatic decrease in both Sox2 and Olig2 signals at the injury site, suggesting cell death of neural progenitors and pMN progenitors caused by the injury. Furthermore, timelapse imaging showed a 55.6% loss of Sox2+ neural progenitors happening progressively during 3-8 hours after the injury. At 2 DPI, increased Sox2 and Olig2 signals were observed at the injury site, which indicated a regeneration of these two progenitor populations, and this increased number of progenitors remained stable during 48-50 hours post-injury.

Conclusions

Spinal cord injury initially resulted in progressive cell death of neural progenitors and pMN progenitors after the injury. Such cell loss was then followed by a repopulation of these cells at the injury site, and the number of the replenished progenitors reached a steady point by two days after injury. Together, these findings indicate a potential post-injury repair mechanism driven by the regeneration of neural progenitors and pMN progenitors that can differentiate into motor neurons and oligodendrocytes to promote SCI recovery.