BOOK REVIEW

In Search of the Lost Cord: Solving the Mystery of Spinal Cord Regeneration

by Luba Vikhanski

2001 Dana Press and John Henry Press 269 pages

Reviewed by Hadley Wilson Horch

Biology Department and Neuroscience Program, Bowdoin College, Brunswick, ME 04011.

Nearly 100 years ago, Ramon y Cajal used the phrase "abortive regeneration" to describe the attempted regrowth of injured central nervous system neurons. As Luba Vikhanski describes in her book, *In Search of the Lost Cord: Solving the Mystery of Spinal Cord Regeneration* this phrase embodies much of the confusion and potentially misleading dogma at the heart of this field. While the enigma of spinal cord regeneration has decidedly not been solved, Vikhanski tells the fascinating story of the historical paradigm shifts and the courageous researchers that have paved the way for today's hope-inspiring therapeutic approaches.

The history begins with Ramon y Cajal's work on neuronal regeneration. Vikhanski takes the opportunity to discuss historical issues such as the neuron doctrine and the related tussle between Cajal and Camillo Golgi, a proponent of the competing reticular theory. As always, the genius of Cajal is striking, and the CNS regeneration experiments performed by Cajal and his student Francisco Tello are remarkable for their prescience. More recent contributions include William Windel's early piromen work and Albert Aguayo's grafting experiments. Vikhanski also describes Richard and Mary Bunge's work on Schwann cells, Martin Schwab's work on IN-1 and nogo, and the surgical approaches in Lars Olson's lab that, for the first time, allowed spinally damaged rats to walk. These chapters also seamlessly include appropriate sections on the use of animals in research as well as the science behind many methods described throughout the book.

The second half of the book, entitled "The Many Faces of Hope" details various therapeutic options and the science behind them. It reads like a compelling mystery: which therapy will finish first? Among the covered topics are stem cells, neurotrophins, macrophages, central pattern generators, and neural prostheses. The background science is simplified, but not overly so. The book includes fairly complete endnotes citing original papers and popular press articles. Aside from occasional errors, these citations are excellent sources for supplemental class readings.

Spinal cord injury experts generally like this book, though they are critical of the emphasis placed on some of the topics, and complain that others are shortchanged (Hick, 2003; Goldberg, 2001). It seems obvious that any cure will rely on a combination of many of the therapies covered in this book, a possibility that Vikhanski barely touches upon (Hick, 2003). In fact, Vikhanski's exuberant account gives the impression that not only is a cure imminent, but that people are already beginning to reap the benefits of this clinical work. However, according to a recent review of spinal cord injury research, "no patient has yet benefited from a regeneration therapy" (Fawcett, 2002), a crucial fact that should balance any reading of this book.

I used this book as part of a mid-level Molecular Neuroscience course. I could also envision using this book at an introductory level, as it would give students practical examples of basic neurobiological concepts. My class focused on neuronal regeneration in weekly discussion sections, and *In Search of the Lost Cord* provided an excellent framework. I felt it was important to understand that the countless molecules and signaling pathways we were covering in lecture could have personal ramifications. Typically, I combined a chapter or two each week with supplemental material such as a primary journal article or a "news and views" type summary. Some chapters were combined quite effectively with primary journal articles. For example, chapter 14 introduces students to axon guidance, covering the contributions of Santiago Ramon y Cajal, Roger Sperry, Mu-ming Poo, and Marc Tessier-Lavigne. In conjunction, my students read the original paper from Tessier-Lavigne's lab describing how netrins act as diffusible chemotropic factors in the embryonic spinal cord (Kennedy et al., 1994). I found this to be an excellent exercise; the book provided appropriate background for the paper, which supplied a greater level of detail.

On the other hand, I found that Vikhanski had done such a good job summarizing some of the historical experiments, there was not much to discuss after reading the original articles. Albert Aguayo and colleagues performed imaginative experiments showing that regenerating CNS axons can grow long distances if presented with peripheral nerve tissue (David and Aguayo, 1981). These experiments are of obvious importance, but instead of finding fundamental concepts to debate, we kept coming back to the details of surgical techniques—questions that were outside the scope of the class.

The students overwhelmingly liked the book and enjoyed reading it, as it provided a distinct change of pace from typical neuroscience textbook reading. Several students commented on the helpful appendix describing the spinal cord before and after injury. They became somewhat annoyed at the "fluffy" details Vikhanski depends on to describe the personalities of the scientists. For example, Aguayo has a "bushy mustache, warm brown eyes, and a love for opera and tango" (p. 66). However, I do think they began to appreciate the human side of these scientists, something they rarely encounter in other

classes. A few complained about the dramatic tension Vikhanski manufactures at times. Related to this, I think a fundamentally interesting issue is the inevitable oversimplification that occurs when scientific journalists write for the layperson. While Vikhanski does an excellent job accurately describing complex research, the popular press sometimes does not. Several popular press references are included throughout, and reading these along with the related primary journal articles could bring home to students the importance of being an informed scientific consumer.

An inherent problem of this fast-paced field is that any literary snapshot soon becomes outdated. However, this very fact provides a wonderful opportunity for students to research the status of the science by monitoring the outcomes of clinical trials and "google-ing" biotechnology company web sites. Veteran spinal cord researcher Wise Young contributes heavily to an excellent website (www.sciwire.com) that keeps patients and their families up-to-date on clinical trials, medical quackery, and patient care issues. I have occasionally asked students to prepare for discussion by using the web to find more current information, and have discovered that they independently do PubMed or other searches to satisfy their curiosity at the end of a chapter.

In short, tackling this subject matter is enjoyable with *In Search of the Lost Cord* as a guide. It is an excellent book about a fascinating topic, and it works well in a classroom setting. We can hope that Vikhanski continues to add chapters until the mystery of spinal cord regeneration is ultimately solved.

REFERENCES

David S, Aguayo AJ (1981) Axonal elongation into peripheral nervous system "bridges" after central nervous system injury in adult rats. Science 214:931-933.

Fawcett J (2002) Repair of spinal cord injuries: where are we, where are we going? Spinal Cord 40:615-623.

Goldberg JL (2001) Review: In search of the lost cord: solving the mystery of spinal cord regeneration. Nature Medicine 7:1275.

Hick J (2003) Book Review: In search of the lost cord: solving the mystery of spinal cord regeneration. Spinal Cord 41:59-60.

Kennedy TE, Serafini T, de la Torre JR, Tessier-Lavigne M (1994) Netrins are diffusible chemotropic factors for commissural axons in the embryonic spinal cord. Cell 78: 425-435.