Spinal Cord (2003) 41, 59–60

www.nature.com/sc

Book Review

Spinal Cord (2003) **41,** 59–60. doi:10.1038/sj.sc.3101413

IN SEARCH OF THE LOST CORD: Solving the Mystery of Spinal Cord Regeneration

Luba Vihanski

Published by The Dana Press & The Joseph Henry Press, 500 Fifth St., NW Washington, DC 20001, USA. ISBN 0-309-07437-1 US$27.95 269 pp

Neuroscience is an unfinished project. One consequence of this is that clinicians must still utter those dread words 'you will never walk again' to many of their patients who have recently sustained a traumatic spinal cord injury (SCI). Not so very long ago, people paralyzed in this way were unlikely to live long. The advent of antibiotics, new diagnostic and surgical techniques, low-pressure cushions and mattresses, together with more enlightened rehabilitation has changed that and extended life expectancy for those with SCI to one not so very far short of the overall average.

SCI healthcare professionals must in part share the inevitable frustrations of their chronically paralyzed patients and likely grow despondent on occasion over their inability to reverse the devastating consequences of traumatic injury to the spinal cord. The sense of helplessness will not have been lessened by a steady drip drip of, frequently sensationalized, media reports on the work of this or that neuroscientist claiming a breakthrough in SCI research. Expectations of cure are easily inflamed in the newly paralyzed and those responsible for their treatment and rehabilitation must deal with the fallout once the realization that effective therapies to reverse SCI do not yet exist begins to bite with their vulnerable charges. Professionals in the field can only palliate SCI and encourage their patients to deal with the reality of their catastrophically altered state as best they can. There is no cure.

But that, of course, is not the whole story. Luba Vikhanski's book is a courageous and ambitious one. At an important level this work will not satisfy but that is not the fault of the author, rather a disappointment with a mystery unsolved. The subject is a tantalizing and heroic story, as yet unconcluded, well told by this award-winning writer. The emphasis is on regeneration, 'a compelling quest to reverse the irreversible', but not exclusively. The politics and economics of the SCI research effort are touched upon. There is an important chapter on spinal cord plasticity and the attempts to 're-educate' the cord after injury through various forms of treadmill training. The subject of neural prosthesis is also covered and there is a useful illustrated appendix. 'The Spinal Cord Before and After Injury'. But in the author's words, it is first and foremost 'the tale of the turnaround that has occurred in spinal cord research and of the people who make hope real – their failures and successes and their dedication to a scientific pursuit of a goal once considered an impossible dream.' Her treatment of this subject is verging on the passionate and her style journalistic. The attempts to popularize and make more accessible the unraveling of the arcane intricacies of this branch of neuroscience may grate for some readers, especially those with any scientific or clinical training.

In part I, 'The Science of the Impossible', the reader is treated to an exploration of the historical highlights of this realm of neuroscientific discovery. She picks out the very few, and their landmark contributions, from the few who made or have made this their life's work for, in truth, this field has been a backwater of scientific endeavor until recently. Each chapter is a story in itself as we join the likes of Albert Aguayo *et al* demonstrating the regrowth of cut spinal cord fibres of adult mammals, or the discovery by Martin Schwab's team of a molecule that opposes axonal growth and then an antibody to counter that effect. Inextricably linked with the acquisition of fresh knowledge and understanding has been the availability of new tools and techniques for investigation and this point is well made. The arrival of the electron microscope and the development of new and more sophisticated staining techniques transformed the study of the CNS. The relatively new disciplines of genomics and proteomics permit an ever more detailed understanding of fundamental mechanisms and the possibility of their manipulation for therapeutic purposes. The scientist who stands out most of all from this section is, of course, Rámon Cajal whose extraordinary percipience and sheer genius discerned so much about the CNS without the benefit of modern tools and techniques.

The second part, 'The Many Faces of Hope', is more of a hotchpotch. The emphasis is on regeneration work and the author has sought to identify and examine the main avenues of research. As such there is an important chapter on the different types of cells – stem, fetal, olfactory ensheathing – that are or have been considered as transplantation candidates (Schwann cells are covered in Part I). 'Elixir of Youth for Damaged Nerves' is a chapter dealing at the molecular level and in particular with the intriguing subject of growth factors. The chapter on axonal guidance describes work designed to unravel the mysteries of and how to manipulate biochemical recognition whereby axons can be encouraged to grow and seek out appropriate targets in the context of their intrinsic properties and the extrinsic ones of the supporting cellular environment through which they must pass. More controversially, there is a whole chapter that focuses on the work of Michal Schwartz, from the Weizmann Institute of Science where the author is based, which is concerned with making use of the manipulation of the immune system to counter the effects of SCI in both acute and chronic injuries. This is a relatively new and less broadly based approach to the problem and it is questionable whether it deserves the prominence it is given here.

Part II also covers the thorny issue of chronic injuries and what experimental work is being conducted to reverse these. It concludes, on the basis of this, that there is worthwhile hope for the long-term injured. 'The Smart Spinal Cord' is an essentially pertinent chapter for clinicians and rehabilitation specialists as the research work that is described can be seen to have the possibility of tangible benefit soon and also how this might marry up with future therapeutic interven-

tions. The full potential of the 'plastic' human spinal cord 'retrained' is still to be established which is exciting.

Whilst commendably broad in scope, Vikhanski's book perhaps fails to consider more fully the many and varied hurdles that promising experimental approaches will have to negotiate if they are to be successfully translated to the clinical setting. Most of the work to date has been conducted in rodent models and it is not yet clear just how relevant (for example many scientists now largely discount improvements in hind leg function after SCI) or safe these approaches might be in humans. There is the whole issue of larger animal models and what would be required to establish safety and efficacy before clinical trials. And yet clinical trials have begun (including a growing number since the book was published), many would say prematurely. There is an urgent requirement to establish reliable clinical assessment protocols in order to measure with much more accuracy than is currently possible any change in the state of a SCI. Without these, it is likely that these early trials will be of strictly limited value. There is another important aspect that is only touched upon and that is the whole issue of combinatorial approaches. The idea that a winning therapy would combine, say, an enzyme to help digest the scar, growth factor(s) to encourage strong axonal growth, an inhibitory molecule antibody and some sort of bridging material seeded with, perhaps olfactory ensheathing cells to help draw out and encourage axonal growth. This approach is clearly more complex and time consuming to translate successfully but may well be what is required.

The compelling and comprehensible format of '*In Search of the Lost Cord*' is accessible for a lay readership and as such, many with SCI and their families will eagerly devour its contents. Authorship of a book such as this though should carry with it an implicit responsibility towards this particular group for whom its contents have an especially poignant relevance. The journalist in Luba Vikhanski is clearly keen to be able to write about a successful conclusion to this epic tale when none yet exists. The book's epilogue belies this state of mind and goes, for my taste, rather too far in suggesting the imminence (despite all the 'health' warnings) of an effective treatment when that cannot yet be safely done.

Christopher Reeve's injury and his subsequent campaigning have undoubtedly raised awareness of SCI and the severe affliction that it represents. This and the rapid expansion of neuroscience as a whole, together with the idea that SCI repair has relevance to the more extensive challenge of brain repair, augurs well for continued and accelerated progress. In a few years time a clinical trial of a reparative treatment may be coming to a spinal unit near you. If you happen to work in one then this book may offer you a valuable insight into the basic scientific discoveries and trends that underpin a hope that is more realistically based than ever before – the hope that function can at least partially be restored to those with SCI in the foreseeable future through some sort of therapeutic intervention. Furthermore, it should act as a spur to the development of rehabilitation practice to ensure that the paralyzed are kept fit enough and suitably trained to an optimum state whereby they can usefully benefit from any future therapy. Treadmill training, for example, may in the future become a vital part of regeneration approaches and one of its pioneers, Reggie Edgerton, has suggested that, without it, 'you may have 100% regeneration and not be able to walk.'

John Hick
(John Hick is a trustee of the International Spinal Research Trust)