Chapter 1

Neural Transplantation in Spinal Cord under Different Conditions of Lesions and Their Functional Significance

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Introduction

Research on the problems of trauma and regeneration in the spinal cord has a long history. The importance of this research lies in the fact that trauma to this structure deprives the individual of voluntary control over the basic motor functions, such as movement of limbs involved in locomotion. The severity of trauma and the level of spinal cord where it is inflicted determine the nature and magnitude of loss of motor functions. Understanding the complexity of pathological events ensuing from the trauma, the nature and permanency of the functional loss, and the difficulties inherent in the restitution of the lost functions has been a concern for investigators in many fields. Pathologists, neurobiologists, neuroembryologists, and neurosurgeons, among others, have contributed to a considerable extent within their respective domains towards explaining why, following a serious trauma, there is no functional recovery, and have speculated variously on how to achieve it. At different periods, various investigators claimed recovery of lost locomotor functions following surgical or pharmacological treatments. But those claims could not be supported by other investigators working independently. Thus, despite the great progress made towards an understanding of the pathological events and the problems of limited or no regeneration of damaged fiber systems, the goal of achieving recovery of the lost motor functions has remained beyond our reach.

During the past decade or so, neural transplantation in the mammalian brain has emerged as an important field in neuroscience. Many basic issues related to survival, growth, differentiation, and integration of neural transplants have yet to be investigated systematically. But this field has generated some hope for the recovery of functions lost because of trauma to supraspinal structures. And, in the same vein, neural transplantation is seen to offer some promise for the conditions of spinal cord trauma.

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The use of the spinal cord as a neural structure for the study of experimental trauma and neural transplantation poses many problems, among them: How to define a trauma that consistently yields paraplegic syndrome in a high percentage of preparations? What are the characteristics of paraplegic syndrome in experimental animals? What is the relationship between sparing of selected fiber tracts and spontaneous recovery from paraplegic syndrome within a few days following the trauma? What are the problems of survival and growth of neural transplants in a pathological milieu of a damaged spinal cord? Does neural transplantation aid in the recovery of the lost motor functions? If so, how much? And what precisely is the role of a neural transplant in such a recovery? Research in our laboratory over the last several years provides some information on these questions, which is presented in this chapter. It is essential to point out that these findings are based upon the use of the most common experimental animal, the rat, and that any extrapolation of these findings to human conditions must be done with great caution.

Models of Experimental Trauma to the Spinal Cord—Historical Background

A review of literature on the experimentally induced trauma to the spinal cord indicates that, broadly speaking, two types of traumas have been investigated extensively: impact injuries and severance injuries. The former involves injuries resulting from a violent blow to the vertebral column or the spinal cord that does not directly tear through the meningeal membranes or the spinal cord parenchyma. The latter, in contrast, involves direct tearing and damage to the meningeal membranes and the spinal cord parenchyma with a sharp and penetrating instrument. This classification is helpful not only in understanding different patterns of histopathological changes following the trauma but also in differentiating the conceptual basis for therapeutic procedures suggested by various investigators. Further, under both these conditions the trauma may vary in severity, leading to conditions whereby subthreshold trauma may not produce any symptoms at all and suprathreshold trauma may affect the very survival of the animal. Over the decades, these two models of experimental trauma have been modified and improved upon to satisfy the following requirements: Operationally, they should be as close to human conditions as possible; technically, the trauma should be highly reproducible; the syndrome produced by a trauma should be clearly observable and permanent; and the course of histopathological events should correspond to that in humans. These and other issues on the experimental production of spinal cord trauma have been discussed by Dohrmann (1972), Tator (1972), Osterholm (1974), Jellinger (1976), Collins and Kauer (1979), Windle (1980), and Bohlmann et al. (1982).

Windle (1980) has distinguished closed impact injuries from open impact injuries. The former include only those injuries that involve an impact by a blunt blow or a speeding missile on the vertebrae. As a result of this, the spinal cord suffers from concussion-type trauma. In a strict sense this may be consid-