RESTOR 00150

Book Review

O. Lindvall, A. Bjorklund and H. Widner (Editors), Intracerebral Transplantation in Movement Disorders: Experimental Basis and Clinical Experiences, Restorative Neurology, Vol. 4, Elsevier, Amsterdam, 1991, 353 pp., ISBN 0-444-81364-0, Dfl. 360.00.

The book is a collection of chapters which were presented at the Eric K. Fernstrom Foundation Symposium held at Orenas Castle, Sweden, on June 20–22, 1990. As stated in the Preface, the purpose of this symposium was to foster discussion between basic scientists and clinical researchers who are attempting to understand and apply transplantation into the central nervous system (CNS) for the amelioration of movement dysfunction resulting from damage to the CNS. Therefore, in addition to the papers, transcripts of the discussions related to each paper, or related to general topics, were selected by the Editors for inclusion. Contributors from around the world who are involved either in research using animal models of Parkinson's or Huntington's disease, or in experimental intervention in human subjects with Parkinson's disease, presented detailed descriptions of their methodologies and results, and discussed many of the remaining dilemmas which must be studied further in order to progress to welldefined therapies. Therefore, this book is an excellent reference on neural transplantation as of 1990.

The book is divided into four sections. In 'Part I. Experimental Basis' two primary areas of interest are discussed: the use of chromaffin tissue derived from the adrenal medulla as an alternative to fetal dopamine cells for transplantation into the damaged striatum, and the results of adrenal medullary tissue or fetal substantia nigra transplants in the primate model of Parkinson's disease. Several issues related to these animal models were discussed. First, what are the actual mechanisms of behavioral recovery following these transplantations? Some research suggests that the damage which occurs during the transplantation may be enough to stimulate sprouting and/or an increase in neurotrophic substances in the host brain. In the case of fetal grafts, the grafts themselves may produce neuritepromoting factors. Or, the grafts may release neurotransmitters which are deficient in the damaged host. Finally, actual reinnervation of the host may produce the recovery observed. Despite the basic research to

date, the underlying mechanisms are still not well understood. Methodological issues discussed included the optimal age of the donor tissue, and how to measure behavioral recovery. Clearly, the methods to record recovery in the animal models are still quite limited. In fact, quantifying qualitative aspects of movement continue to present a challenge in the clinical arena as well. However, until such valid and reliable methods are developed, discriminating between various methods of intervention will be impossible.

In the second section of the book, the results from several of the leading clinical sites utilizing various experimental approaches were discussed. Comparisons of results using adrenal medullary tissue versus fetal ventral mesencephalic tissue for transplantation were made. Again, variations in methods were discussed, such as whether or not immunosuppression is needed, where are the optimal placements for transplants, which surgical techniques are best (stereotactic versus open), what is the optimal age of the fetal donor tissue, and what is the most reliable way to obtain that tissue. Methods of recording functional status of the patients were also discussed. It was generally agreed that all of the clinical results thus far are not very impressive, but work needs to continue with both basic and clinical research since the animal studies are so promising.

In 'Part III. General Aspects of Intracerebral Transplantations in Movement Disorders' some of these methodological issues are explored in greater detail. Of special note are chapters discussing the immunological concerns, and alternative methods of producing immunosuppression, as well as selection criteria for this type of intervention. Additionally, the need for better assessment techniques to determine survival and functional capacity of the transplants is discussed, with the sharing of some methods which are currently being used. In order to address the recognized need for common means of patient diagnosis and evaluation, a committee was formed to develop a 'Core Assessment Program for Intracerebral Transplantation (CAPIT)'. The committee developed recommendations, which were then presented and discussed at the final session, and were either accepted, or referred back to the committee for further refinement. The results of these efforts are included in Chapter 22, and are of great value to those involved in clinical research in this area.

In the last part, papers on miscellaneous issues related to this research are presented. These included a report on the development of an animal model for Huntington's Disease, and the results of attempted interventions in this model; reports on genetically engineered cells for transplantation to enhance behavioral recovery in Parkinson's disease; reports discussing the possible interaction of fetal dopaminergic cell transplants and pharmacological treatment with L-dopa; and others.

There appears to be a general consensus among the participants of this conference that much more carefully designed basic research is needed prior to the initiation of any formal clinical trials. However, ongoing clinical research will continue to add new information and direction to the basic research. Everyone must remember, as David Marsden says on page 223, 'this is an experimental surgery, it is not treatment for a disease'.

While this book thoroughly addresses most of the critical issues within this area of research, one area which is barely mentioned is the role of neurotrophic factors in the survival and function of the grafts, and the recovery of function on the behavioral level. Additionally, while the book's title refers to 'Movement Disorders', its focus is primarily the movement disorders seen in Parkinson's disease. Nonetheless, this book will serve as a valuable reference for several years to come.

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