NEURAL TRANSPLANTATION: AN INTRODUCTION.
By William J. Freed.

NEURAL REPAIR, TRANSPLANTATION AND REHABILITATION.
By Roger A. Barker and Stephen B. Dunnett.

These two books introduce the reader to the exciting and fascinating field of brain repair—a field which has substantially influenced both basic science and clinical research of the nervous system over the past 20 years. Unlike the peripheral nervous system, the brain and spinal cord have only very limited self-renewing capacity following acute or chronic disease processes. Degeneration of neurones in the central nervous system due to acute or chronic illnesses, e.g. trauma, stroke or neurodegenerative diseases, e.g. Parkinson’s or Huntington’s disease, leads to a loss of function that is currently not amenable to successful restoration by intrinsic brain repair mechanisms and/or therapeutic interventions such as medication and brain surgery. In this respect, neural transplantation holds great potential to promote structural repair and functional recovery within the central nervous system. The basic concept is the replacement of degenerated cells by the implantation of new cells that repopulate damaged brain areas to restore local neuronal circuitries and neurotransmission, and thereby, brain function.

Freed has extensive personal experience in the field as one of the pioneering scientists in the ‘modern era’ of neural transplantation starting in the late 1970s. In Neural Transplantation: An Introduction, he wants to be ‘interesting, amusing, or at least irritating’ (Preface) mainly to scientists and students from other areas of biology and medicine, who are attracted to the ideas and concepts on brain repair mechanisms and treatment strategies.

The book is subdivided into seven main sections starting off with a general overview of brain anatomy and development,
history of neural transplantation and principles of current neural transplantation strategies and protocols. Throughout this and the following sections Freed ‘considers both the reality and the fantasy of brain repair’, and, in many places, he does not provide a clear distinction between them, which impedes the extraction of scientific facts in favour of a more speculative and personal interpretation of the history of discoveries in the field of brain repair.

A substantial chapter is dedicated to the research on neural transplantation in Parkinson’s disease, reflecting the pivotal role of this chronic disease in the development of this novel technology. The first parts of this section provide a comprehensive overview of the basic principles and experimental strategies including the animal models of Parkinson’s disease used in neural transplantation. The text is well written, informative and illustrated with some of the key experimental data accumulated since 1979, when the first functional graft effects were demonstrated in a rat Parkinson’s disease model. The second part of this section, however, loses some of this scientifically oriented approach and represents a rather unbalanced description of the research reports, categorized not by topics, but by the individual scientists or research groups involved in neural transplantation studies in subhuman primates and humans, which holds some interest for the expert in the field.

Section IV highlights further applications of neural transplants to influence localized brain functions in pain, the hypothalamic–pituitary axis and in the cerebral cortex. The effects of adrenal medulla transplants have been examined both in experimental models and clinical studies of chronic pain. Freed concludes that pain is an ‘attractive application of neural transplantation’ as well because graft-derived effects on pain mediated via opioid and enkephalin release do not depend on a specific and complicated establishment of reciprocal graft–host neuronal connections. Similarly, a restitution of hormonal deficiencies can be achieved by hormone-releasing cells into the hypothalamus and recalibrate important physiological parameters. Other more speculative scenarios are intermingled, such as the treatment of violent sex offenders by hypothalamic transplants. This section is closed by remarks on how transplantation of cerebral cortex has been studied in animal experiments of stroke and the potentials and risks of a clinical application.

This is followed by a discussion on reconstruction of neuronal circuitries via neural transplants in Huntington’s disease, in the spinal cord and visual system. In most of this section Freed elaborates on more complex issues of reciprocal and specific neuronal interconnections between graft and host neurones in the different systems that may ultimately lead to an organotypic reconstruction of the host’s damaged neuronal circuitries.

The emerging fields of gene therapy and stem cells are introduced in the next section, which currently represent very important platform technologies for the further development of successful brain repair strategies. These chapters provide basic information on genetic engineering and stem cell technology with useful protocols and illustrations.

Finally, Freed guides the reader through his personal speculations on future dimensions and limitations of brain repair, which represent a chimera of science fiction and neurobiology, being amusing, provocative and, sometimes, irritating on topics such as brain cloning and replacing the human brain by artificial intelligence.

A 20-page glossary, a 43-page updated reference list and a detailed subject index are helpful additions that allow a quick orientation for the student and a further in-depth review of special topics for the more interested reader.

Overall, the book by Freed highlights the important advancements in the field of brain repair and neural transplantation along with a more speculative interpretation of its perspectives and limits. This combination provides a certain level of information entertained by personal remarks from the author that seems more appropriate for knowledgeable scientists than undergraduate students.

Neural Repair, Transplantation and Rehabilitation appears as the first modular handbook in the new series: Neuropsychological Rehabilitation, edited by Barbara A. Wilson and Ian H. Robertson. The authors, Dunnett and Barker, are two well-known experts in the field of brain repair, with a long-standing history in experimental neural transplantation and regeneration. Their main aim with this book is to ‘draw together the latest progress in our knowledge of the principles that underlie development and cell death in the nervous system as the basis for a new science of neural protection, transplantation, and repair’ (Preface), for both scientists and clinicians seeking a comprehensive, interesting and instructive resource of information.

In the first three out of 10 chapters, the evolution of the field of brain repair is described starting with Cajal’s famous dogma at the beginning of the 20th century that ‘in adult centres, the nerve paths are something fixed and immutable; everything may die, nothing may be regenerated’. It had long been believed that the central nervous system lacked any regenerative capacity, although the authors indicate that clinical observations of spontaneous recovery (e.g. after a stroke) seem to contradict this assumption. But it was not until the past two to three decades that further experimental evidence validated the ‘proof of principle’ of an exciting restorative plasticity in the adult CNS, which is still becoming increasingly recognized. Two main strategies for brain repair have derived from these insights: (i) the protection of cell death by neurotrophic molecules; and (ii) cell replacement by the implantation of immature neuronal or glial cells.

The authors then proceed to the development and application of neural transplantation techniques in specific disease models, such as Parkinson’s, Huntington’s and Alzheimer’s diseases and spinal cord injury. These chapters are well structured and provide an excellent overview of the underlying concepts, the different approaches and results in experimental studies, the state-of-the-art in clinical neural transplantation studies in Parkinson’s and Huntington’s
diseases and the challenges for brain repair in Alzheimer’s disease and spinal cord injury. A special emphasis is given to the mechanisms by which neural transplants may exert their restorative capacity, e.g. by local release of trophic molecules (e.g. GDNF, NGF) and/or neurotransmitters (e.g. dopamine, GABA), by the establishment of afferent and efferent connections, by serving as relay bridges as in the spinal cord or a combination of these factors. Recent developments, such as methods for monitoring graft survival in vivo using sophisticated neuroimaging techniques in patients and animal studies, are also included.

In the last part of the book, two further important aspects of brain repair are considered in more detail. Due to the limited availability and the complex ethical issues implicated with the use of human embryonic material, it is now generally accepted that the exploration of alternative cell resources is one of the major issues determining the further successful translation of neural transplantation and restoration strategies into more widespread clinical applications. Currently, these include progenitor and stem cells immortalized cell lines, as well as xenogeneic tissue; the authors discuss the individual advantages and limitations of each. Last, but not least, psychological factors in graft function are addressed, highlighting the potential influence of training and experience of the host, which may ultimately foster restorative processes by which the host ‘learns to use the transplant’ effectively. This, in turn, may have important implications for the design of rehabilitation programmes for transplanted patients.

An extensive and up-to-date reference list, a comprehensive glossary for the student and helpful author and subject indexes complement this 339-page book. Furthermore, the individual chapters are well illustrated and clearly written.

Overall, the book by Barker and Dunnett represents a comprehensive and excellent overview of brain repair concepts and strategies ranging from the experimental basis to clinical applications. It can be highly recommended to both non-specialists and experts in the field, as it provides easily accessible information together with in-depth reviews of most of the important areas of brain plasticity and restoration.

In summary, Neural Transplantation: An Introduction and Neural Repair, Transplantation and Rehabilitation represent two quite different approaches to a similar topic, and it is up to the interested reader to choose which route he or she wants to travel along this fascinating landscape of the still evolving field of brain repair.

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