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Book Reviews

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Brain Damage, Brain Repair
JW Fawcett, AE Rosser and SB Dunnett

Publisher: Oxford University Press ISBN: 0-19-852337-8 pp: 466 Price: £29.

Spinal Cord Trauma: Regeneration, Neural Repair and Functional Recovery
L McKerracher, G Doucet and S Rossignol

Publisher: Elsevier ISBN: 0-444-50817-1 pp: 470 Price: EUR 234

These two books landed with a satisfying thud on the Editor's desk. They are both excellent volumes dedicated to the holy grail of CNS regeneration. They both, in their different ways, illustrate the enormous advances in this field. Patrick Wall has pointed out that, up until the Second World War, spinal cord transection was a terminal and lethal condition with the doctor's duty being to supervise the inevitable eventual death. This was changed by the invaluable work of Sir Ludwig Guttmann, who prevented deterioration through good nursing practice, the use of sterile techniques and of antibiotics, by movement and by lifting the morale of staff and patients. This raised the problem of what to do next. An overview of the progress made must include the discovery of nerve growth factor in the 1950s, sprouting of new terminals (boutons termineaux) in the 1950s, unmasking of synapses in about 1978 and, the demonstration that spinal cord nerve fibres regenerate into transplants of peripheral nerves in about 1980. The phenomena of sprouting of new synapses, the unmasking of existing synapses and the alteration of receptive fields have altered our view of the way in which the intact CNS functions, and raised questions pertinent to recovery and to the true nature of the effect of CNS damage in terms of disability. This means that regeneration of damaged or transected CNS fibres cannot be a matter of simply rewiring because, even if successful growth of axons is achieved, they will be growing into a CNS, which has been altered as a result of the lesion.

Neither of these books actually has *synapse* in the Index. This is surprising since the whole point of trying to achieve regeneration of CNS axons is that they will make connection with nerve cells, and the only connection is via synapses. Both books give a good account of sprouting in the injured CNS, but neither book gives an account of the early work in this field. For example, a series of papers in *Experimental Neurology* and *Brain* in 1963, 1964 and 1973, described changes at the motor neurone surface following partial denervation with a progressive glial reaction and sprouting of new synapses from intact fibres, which restored the synaptic zone to normal appearances. The important point here is that the synaptic zones were restored to normal appearances. Recently, Raisman has pointed out (*Journal of The Royal Society of Medicine* 2003; **96**: 259) that 'When nerve cells lose connections, new connections are formed by adjacent nerve fibres restoring exactly the original number of connections that existed before the injury'.

This has two very important implications with regard to the success or otherwise of CNS regeneration. Firstly, sprouting, together with unmasking, means that previously relatively unimportant pathways now become important and previously important pathways now do not exist. How will the growth of axons alter this? Secondly, if axon regeneration is successful and axons grow across the lesion, what will they actually grow on to? The target cell synaptic zone is full. How can the axons possibly make synaptic contact unless they somehow displace existing boutons? If they do displace existing boutons, how can this be achieved and which boutons will they actually displace? This seems to me to be a fundamental problem of CNS regeneration. It may not be a problem or it may be less of a problem in the acute stage where the important topics include the effect of trauma itself, inflammation, scar formation and inhibitory influences and are potentially surmountable. Both of the books address this area extremely well. However, in the chronic state the questions posed by sprouting and the restoration of synaptic zones, unmasking of synapses and altered receptive fields need to be addressed and they are not addressed in either of these two volumes. Perhaps Karl Marx was correct 'Mankind always sets itself only such problems as it can solve: since looking at the matter more closely, it will always be found that the task itself arises only when the material conditions for its solution already exist or are at least in the process of formation'. Or am I being too cynical?

Brain Damage, Brain Repair covers the field of both neuroscience and neurology with sections on mechanisms of Brain Damage, Damage Limitation, Intrinsic Mechanisms of Recovery, Clinical Assessment of Brain Damage, Pharmacology and Rehabilitation, Structural Repair and nine appendices devoted to specific diseases. The diagrams and illustrations are first class (but I

couldn't see any acknowledgement of the illustrator). I would have liked a summary and conclusion at the end of each chapter or section rather than just in some of the chapters. The use of boxes, for example the T-cell classification on p 55 is an excellent addition to an understanding of complex processes. The book is unusual in that it includes both basic science and clinical pathology and clinical description, but the admixture of clinical with basic science is not entirely successful. For example, the section on Management of Patients in Coma hardly seems relevant in this type of book and, like the appendices on specific diseases, although useful and interesting thumb nail sketches, are much better dealt with in standard clinical neurological texts. Some of the clinical features are rather misleading. For example, Chapter 17 refers to pyramidal pattern of weakness and to upper motor neurone and lower motor neurone lesions, but fails to describe the differing pattern of weakness in upper motor neurone, nerve root, peripheral nerve and muscle lesions. Patterns that are as characteristic as spasticity and reflex changes. Chapter 2, *Axotomy and Mechanical Damage* describes events following a lesion of CNS axons and describes changes in the parent cell body and, in some situations, anterograde cell death. In the parent cell, there is a retrograde reaction that leads to most of the synapses on the cell soma retracting and their place being taken by glia. In Chapter 12, on the failure of CNS regeneration, the reader is referred to this process in Chapter 1 (it is actually in Chapter 2), but I could not find what happens to synapses of the cut axons about which, of course, a great deal is known. Chapter 17 deals with anatomical plasticity and sprouting but does not mention degeneration and the fact that degeneration of a critical number of boutons produces a temporary effect on neighbouring boutons which is of relevance in spinal shock.

Spinal Cord Trauma: Regeneration, Neural Repair and Functional Recovery is based on the XXIII International Symposium of the Centre for Research in Neurological Sciences held in Montreal in May 2001. There are 121 contributors to the book and the sections cover spinal cord injuries in patients, in animal models, neuroprotection and transplantation, and molecular targets to promote axon regeneration. Nearly all the chapters have an abstract which is extremely helpful and the book throughout has excellent illustrations. The book covers research on spinal cord injury including clinical aspects in Man and experimental studies in animals, molecular mechanisms, rehabilitation and functional repair, strategies for neuroprotection and regeneration, cell transplantation, etc.

Both of these books give an excellent overview of the current state of the progress in CNS regeneration, particularly with regard to basic research of course. Brain Damage, Brain Repair has a section on pharmacological management that does not mention the use of steroids in spinal cord injury. Spinal Cord Trauma does discuss the use of steroids, but is uncritical and fails to mention the important systematic review of Short, El-Masry and Jones (*Spinal Cord* 2000; **38:** 273–286). This is a pity, because this review is probably the most comprehensive review in the literature. Both of these books are obviously aiming at the eventual use of basic research in the clinical field, but neither of them discusses clinical trials and the problems of assessment in a clinical setting and how a model of physiological and clinical assessment can be established and generally accepted. The initial effect of applying therapy to a spinal-injured person may well be an increase in spasticity or an increase in pain and this must be monitored. Potentially disastrous effects could occur as regards cardiovascular reflexes, and problems relating to abnormalities of bone and muscle. Before any specific therapy can be applied in Man, there must be a period of training and this must be standardised and generally accepted and, the effects of training by itself must be monitored. Complex patterns of movement are encoded within specific groups of connected interneurons – the central pattern generator which contains the complete spatio-temporal pattern of a complex act. It may be that the central pattern generator needs to be reactivated. An important aspect of motor control is the incorporation of sensory input and there are two aspects of this. It is likely that afferent stimulation will play a large part in the management of patients treated with therapeutic manoeuvres aimed at regeneration. Some movements, perhaps all, rely on sensory feedback for their control, but in addition, most movement also relies on a 'feed forward' mechanism, which is a neural process based entirely on an internal model, within the brain, of the required movement. In other words, the motor action has an internal representation and sensory feedback must be used in order to create the brain's internal model of the movement in the first place. By how much is this 'feed forward' mechanism disrupted where there is an absence or a severe deficit of incoming information from the body?

Although I recommend both of these volumes unreservedly and although they serve as a tribute to their Editors and contributors (and to their publishers), on reading these volumes I sometimes had the irreverent feeling, as GK Chesterton put it 'It isn't that they can't see the solution, it is that they can't see the problem'. I hope I am proved wrong.

LS Illis
Editor *Spinal Cord*