Spinal Cord Injuries the Facts of Neuropathology: Opportunities and Limitations

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ABSTRACT

It is essential for research projects which are undertaken to find a “cure” for human spinal cord injury (SCI) to be consistent with the neuropathological facts of the disorder. In this respect there are three main points to be taken into account. Firstly, the researcher should be aware that simple transection of the spinal cord is not a feature of human SCI. The usual lesion is one of compression and disruption with haemorrhage. The second and most important aspect of human SCI is to understand that Wallerian degeneration inevitably ensues following disruption of the axon. Wallerian degeneration is progressive and inexorable and unlike the peripheral nervous system CNS axons do not regenerate. The third and more helpful fact is that in the majority (71%) of SCI autopsies a small amount of white matter, myelin and axons, was found to be preserved at the level of injury. Re-activation of these dormant, axons offers the opportunity for improvement of the SCI patient's neurological status by means of restorative neurology (RN).

Key Words: Human spinal cord injury (SCI), Neuropathology of SCI, “cure” of SCI, Restorative Neurology of SCI.

INTRODUCTION

Spinal Cord Injuries (SCI) pose an enormous problem worldwide socially and in economically. Apart from the overriding humanitarian aspects of SCI the financial burden is considerable. For example, the prevalence of SCI in the USA is estimated to be 282,000 persons with the average lifetime cost of healthcare and living expenses being in the order of US 1 trillion dollars (1). Because of the catastrophic medical consequences of SCI and the associated financial burden there is a great urgency to find a “cure” for SCI despite the fact that it is a daunting task. As a result, there is much research in progress worldwide in the search for a “cure”. Much time and effort are devoted to this cause seemingly more for emotional and altruistic reasons than for the likelihood of a successful outcome. Because of the severity of the disorder SCI research proceeds headlong despite the limitations posed by the neuropathological facts (2).

For instance, it is naïve in the extreme to believe that severed axons can be re-joined analogous to electric wiring. This is so not only because of the extremely delicate nature of the tissues (there are millions of axons, myelinated and unmyelinated, in the normal spinal cord) but especially because Wallerian degeneration has caused the axons distal to the injury to be lost i.e. after injury there are no remaining distal axons to be re-joined. It is the purpose of this review to draw attention to the limitations of current SCI research because of the neuropathological facts of the condition and Inter alia to describe the clinical benefits which may be provided for many SCI patients by the application of Restorative Neurology (RN).
THE ESSENTIAL NEUROPATHOLOGY OF SCI
The first point to be made is that no two human cases of SCI are ever exactly alike. There is no standard lesion, everyone is an individual. This seemingly simple fact means that when an effective treatment is discovered it will need to be customised to suit each affected person.

There are 3 pathological stages in the evolution of SCI following injury, acute, subacute and chronic. In diving accidents and motor vehicle trauma the spinal cord injury arises from hyperflexion, hyperextension and/or rotation of the vertebral column causing fracture. As a result the spinal canal is compromised and the spinal cord is crushed and lacerated. Contrary to popular view complete transection of the spinal cord is rare except for stab injuries. Compression of the spinal cord from subdural or extradural haematoma formation is not a feature of SCI as shown in a large series of post mortem examinations (2,3).

SCI is clinically “complete” when there is total loss of sensation and voluntary motor control below the level of injury. The SCI is clinically “incomplete” when some degree of sensation and/or voluntary movement is retained below the level of injury. There is a third clinical category for which the term “discompletes SCI “has been applied. In this situation there is loss of sensation and voluntary motor controls below the level of spinal cord injury as in clinically complete SCI, but in whom there is neurophysiological evidence of transmission of impulses across the level of injury. This phenomenon is supported by post-mortem examinations which show that there is usually a small quantity of axonal sparing at the level of injury in which case the term “anatomically discomplete SCI” may be used (2,3).

The Acute Stage
Immediately following injury the major change evident to the naked eye is the physical disruption and swelling of the cord at the level of injury present over two or three spinal cord segments. The spinal cord swelling is due to oedema and intra-spinal haemorrhage. Associated is a small quantity of blood in the subarachnoid space. Cross section of the spinal cord at the level of injury reveals central haemorrhagic necrosis with a variable amount of preserved white matter at the periphery.

The Subacute Stage
A few hours after injury polymorphs infiltrate the lesion followed by lymphocytes in a few days and later by macrophages which engulf the necrotic debris. A small amount of traumatic demyelination can be found at this stage limited to the level of injury. Softening (myelomalacia) of the spinal cord is also evident.

The Chronic /End Stage Lesion
At about three weeks after injury macrophages have phagocytosed most of the necrotic tissues so that cavity formation ensues. Reactive astrocytes produce gial fibres within the wall of the lesion and run across the cavity forming gial trabeculae. The final result is a multilocular gliotic cyst within the walls of which are the remnants of white matter containing myelinated axons. Wallerian degeneration follows the disruption of axons.

WALLERIAN DEGENERATION
Wallerian degeneration is the term used for the progressive degeneration of myelin and axons distal to the injury following disruption of a myelinated nerve fibre. Within hours after the injury the myelin sheath breaks up into globules and the axon degenerates distal to the lesion. Wallerian degeneration continues to the next synapse. In the weeks and months following the nerve injury both myelin and axons become lost in this way. The myelinated nerve fibres of the peripheral nervous system also undergo Wallerian degeneration following transection. However there is a great difference in the peripheral outcome compared to the CNS. This is because the peripheral axon has the ability to regenerate contrast to the CNS axons which do not regenerate. Schwann cells which form the peripheral myelin provide the trophic factors for axonal regeneration. Oligodendrocytes which produce central myelin lack this ability.

Thus, once Wallerian degeneration has occurred in the CNS there is no possibility of spontaneous axonal regeneration. It is this lack of regenerative capability which creates the greatest stumbling block in the search for a cure of SCI (4).
CLINICAL ASPECTS OF SCI
Spinal cord injury is associated with clinically devastating effects as it causes complete or partial paralysis of the lower limbs (paraplegia) or if the injury is at a higher level in the neck, paralysis all four limbs (tetraplegia). The loss of voluntary motor function is accompanied by varying degrees of anaesthesia, para-aesthesia, phantom pains and autonomic disturbances. These symptoms are due to disruption of the long, ascending and descending, white matter tracts of the spinal cord. However, damage to the central grey matter from the injury does little neurological harm. This is because the loss of the central grey matter is compensated for by the overlapping territories of the neighbouring spinal segments. The SCI patient’s neurological state usually improves slightly during the first 3 weeks after injury and slower partial recovery continues for up to 2 years post injury (5). SCI patients are disabled for life and in need support for all the requirements of daily living for which medical rehabilitation is addressed.

It should be kept very much in mind that clinical improvement is the norm following SCI. The patient’s neurological state stabilises when oedema and shock subside in the few days and weeks following injury. The final neurological outcome becomes more or less fixed at about 12 months post injury although further slight improvement even after many years may occur (5).

Because of the natural history of SCI proceeds to spontaneous recovery it becomes extremely difficult to evaluate marginal results of experimental therapeutic interventions. Small improvements are often reported in the literature from therapeutic trials but it is difficult to distinguish such outcomes from spontaneous neurological recovery. Furthermore because no two SCI patients are exactly alike controlled human SCI trials are difficult to arrange.

Conservative management of SCI has been shown to more often produce a better clinical outcome than surgical decompressive laminectomy (6,7). Furthermore in a large series of SCI autopsies no space taking lesions were found which would have benefitted from decompression (2,3). Therefore surgical intervention is indicated only for unstable fractures and conservative management of SCI should be the rule (6, 7).

THE DISCOMPLETE SYNDROME
The term clinically discomplete spinal cord injury was first coined by Professor Milan Dimitrijevic to describe the phenomenon of neurophysiological transmissions of signals across the level of injury in SCI patients who were otherwise clinically complete. In his pioneer work rostral transmission of impulses was demonstrable by spinal evoked potentials and caudal transmission of signals was detected by poly-EMG using the Jendrassic manoeuvre. Initially Dimitrijevic’s observations were met with some doubt because they were inconsistent with perceived views of the lesion in complete SCI. However his work was later substantiated by my post-mortem findings. In a series of SCI autopsies it was found that a high proportion of patients had a small amount of preserved white matter consisting of intact myelinated axons traversing the lesion even though in life these patients were clinically complete. In this series of 136 SCI autopsies preserved white matter at the site of injury was present in 97 cases (71%). Forty four of these were clinically incomplete during life and 53 were clinically complete so that the term anatomically discomplete may be used for the latter group. These post mortem findings gave credence to Dimitrijevic’s original neurophysiological observations and the presence of residual white matter is the key to the success of Restorative Neurology (8). The therapeutic methods of RN are directed towards awakening of these dormant residual axons and thus improving the clinical status of the SCI patient. In this way, a previously clinically complete patient may be converted to being clinically incomplete with a subsequent much greater rehabilitative potential (9,10).

RESTORATIVE NEUROLOGY (RN)
The basic principle of RN is to apply various techniques to enhance partially retained, but masked, neurological functions below the level of injury in SCI patients. This approach differs from conventional rehabilitation because it is directed to the affected lower limbs. Conventional rehabilitation is mostly concerned with strengthening the upper limbs to compensate for the paraplegia below.

Conventional rehabilitation and RN complement each other as both address the SCI patient’s emotional and physical wellbeing, their needs of daily living and the treatment or prevention of complications such as muscle contractures (shortening), reflex spasms, pressure decubiti and infections. The end-point of both disciplines is to return the patient to a normal life as much as possible, being independence and with a vocation.
METHODS OF RESTORATIVE NEUROLOGY (RN)

Professor Dimitrijevic first demonstrated by means of neurophysiological assessments that signals may pass through the level of the spinal cord injury in otherwise clinically complete SCI patients. In RN the preserved axons at the level of injury are stimulated electrically and by other means so that dormant nerve fibres become again active. In this way a wheelchair-bound SCI patient may gain sufficient improvement to be able to walk again so that a “complete” patient may be rendered “incomplete”.

Examples of the methods applied in RN for SCI are:

- Extradural electrical spinal cord stimulation.
- Extracranial and extradural magnetic stimulation.
- Neuro-pharmacological agents e.g. baclofen, which suppress reflex contractions (so called ‘spasms’) and thereby unmasking residual neurological functions.
- Intra-spinal opioids to inhibit pain so that with such relief the patient is able to apply covert residual voluntary functions.
- Mesh glove electrical stimulation enhancing cerebral plasticity.
- Able X System of neurorestoration of upper limb movements.
- Other physical methods such as intense massage.
- Electro- acupuncture proving sensory input and thereby activating reflexes.
- Psychological factors related to motivation and mood.
- Music therapy
- Yoga and Meditation.
- Functional electrical stimulation (FES) of body musculature simulating walking movements.
- Robotics, and ‘exoskeleton’ substituting lost functions.
- Restorative neurosurgery by means of peripheral nerve and/or tendon transplantation.

To again emphasise the point, the successful outcome of RN is dependent on the fact that in a high proportion of SCI patients a small quantity of white matter has escaped injury at the level of the lesion both in clinically incomplete and discomplete patients. When re-activated these preserved axons provide clinical benefits in the discomplete group (11).

CONCLUSION

The principal message of this article is for SCI research to be conducted in accordance with the neuropathology of the disorder. Research workers should be especially aware of the importance of Wallerian degeneration. Regrettably in the past much attention has been given to trying to reconnect the severed ends of axons disregarding the facts of the neuropathology of SCI. Reconnecting severed axons is an impossible task because Wallerian degeneration has destroyed the axons distal to the lesion. Although some experimental success has been achieved in the regeneration of severed axons this has been so only for a few mms of regrowth. Such efforts are confounded by the very long distances which need to be covered, up to 20 or 30 cms, to be of any value. Even so if long distance regeneration of axons is ever achieved the problem of restoring normal physiological function would pose a major obstacle. This is because the complex system of reflex connections and neural circuits of the normal spinal cord would need to be recreated for normal function to be re-established.

This review is not intended to discourage SCI research, rather the opposite as it draws attention to the reality of the neuropathology of SCI (12). Armed with this knowledge it is anticipated that SCI research will become more efficient and productive in the future. We live in hope that a cure for SCI will eventually be discovered guided by these comments.

Declaration

There are no conflicts of interest

REFERENCES