

# Paralysis Lost: The Challenge For Functional Restoration Through Technological Advance

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Neural prostheses have made significant improvements to the management of people with spinal cord injury over the last 30 years. However, the imagination of patients is now turning to complete functional restoration through the exciting possibilities of neural repair. Here we address the future role for neuroprostheses in the light of these high expectations of “overcoming paralysis through a ‘cure’ for spinal cord injury” [1].

## Paralysis

Severe spinal cord injury can lead to a devastating loss of neurological function below the level of injury resulting in multiple system paralysis and dysfunction, but the need for restoration includes more than just locomotion. Indeed, for many patients autonomic nervous system problems dominate their lives after injury, rather than the desire to walk again. Such dysfunctions often include the bladder and bowel control, cardiovascular system, breathing, sweating, sexual function, reproduction, spasticity and the protective roles of temperature regulation and pain sensation. For all of these problems, clinicians and scientists have spent many years developing drugs, new surgical techniques and devices, including neural prostheses, for better control and management. Advances in rehabilitation and reintegration in both the social and working environments have followed. But can all of this be replaced by repair of the spinal cord? Is repair and full restoration of function likely to become a reality?

## Repairing the spinal cord

It was the ancient Egyptians who said that spinal cord injury was ‘an ailment not to be treated’ and even as recently as the late nineteenth century Ramón y Cajal, the acclaimed father of neuroscience, declared that central nerve cells probably could not regenerate. However, the desire to find a “cure” for spinal cord injury is compelling and it is now molecular biology, with substantial funding from dedicated charities such as the Christopher Reeve Foundation and the International Spinal Research Trust, which is attracting the efforts of neuroscientists around the world. They are seeking ways to repair the injured spinal cord through a combination of potential treatments involving early neuroprotection, regeneration and re-myelination in the hope that a “cure” will be found [2] in the not too distant future.

From a recent conference on “Translating promising strategies for spinal cord injury therapy” [3], attended by some of the World’s leading authorities in the field of neural repair, it was clear that there are still many obstacles to transferring any of the existing strategies developed in animal experimentation into trial for clinical application. If so many of the leading authorities are sceptical about current strategy then is it fair that patients should be given such high expectations for imminent success?

Clearly this very important work on neuroprotection, regeneration and repair must continue and will one day become a clinical reality, but in the meanwhile how do we treat and manage patients so that they may have a better quality of life in the period before the ‘cure’ is finally discovered? Is it not the case that drugs, devices and surgery will continue to be the mainstay of treatment and rehabilitative management for most patients with a chronic spinal lesion in the foreseeable future? Even with successful neural regeneration, complete functional recovery will probably remain only partial without assistive devices and so neural prostheses are very likely to continue to play an important role in rehabilitation.

## Restoring Function by Neural Prosthesis

Neural prostheses are devices which can restore very successfully lost functions resulting from damage to the nervous system. They can take the form of both implanted and externally worn aids to restore many different functions in spinal cord injury and provide patients with remarkable improvements to their quality of life. These devices can be powered and controlled through radio links or have their own in-built power and control. The range of such devices now available to patients is considerable, from vital assistive devices such as heart pacemakers and phrenic nerve stimulators for breathing to multi-channel stimulators capable of restoring useful movements. These include standing-exercise programmes in paraplegia [4], hand-grasp in tetraplegia [5] and dropped foot correction in stroke and incomplete spinal cord injury [6]. Many of these implants are now available commercially spawning a variety of industries capable of making the most sophisticated range of implanted devices using micro-miniature electronics. Even more complicated implants incorporating sophisticated microprocessors are being trialled in patients and these are said to be capable of multi-functional stimulation not only for motor control but also for restoring many other functions through one implant.

Interestingly, for people with chronic spinal cord injury the order of priority for functional recovery is not walking, as many able-bodied persons might presume, but reliable control of the bladder and bowel to overcome incontinence. Pain, spasticity, as well as bladder and bowel dysfunction are now some of the most important principal targets for management by neural prostheses.

It is in bladder management where the neural prosthesis has had one of the greatest impacts on improving quality of life in people with spinal cord injury [7]. All of those who suffer a complete supra-sacral injury lose voluntary control of their pelvic floor, sensations from the bladder and develop incontinence caused by a combination of emergent detrusor hyperreflexia and sphincter dyssynergia. Such dysfunction results from reorganisation within sacral segmental pathways following injury of the spinal cord but we know rather little about the specific mechanisms underlying these aberrations. During the past 20 years two key developments using implantable neural prostheses have had a significant impact on treating and managing patients with a neurogenic bladder. The first of these was the Brindley sacral anterior root stimulator with posterior rhizotomy [8] originally developed in the 1970's for bladder emptying in spinal cord injury. The second was the sacral nerve stimulator originally developed by Tanagho and Schmidt for neuromodulating[9] a variety of bladder dysfunctions including the overactive bladder and urinary retention. These two techniques, among others, may in the future be combined using emerging technologies to restore more complete control of the dysfunctional bladder in people with spinal cord injury [10] but without destroying nerves.

### Functional restoration through technological advances: losing paralysis

Current neural prosthetic devices, whether implanted or externally applied, are relatively unsophisticated technologies relying on somewhat un-physiological electrical stimulation of peripheral motor and sensory nerves for their action. However, over recent years a whole generation of new scientific ideas for restoring function is emerging which is based on experimental spinal cord microstimulation of small groups of nerve cells or axons [11]. In this way we might be able to tap into specific excitatory and inhibitory sensory-motor processes within the spinal cord using 'smart' implants. These could both detect neural signals and determine optimal stimulation to rehabilitate segmental reflexes, promote any propensity for regeneration and normalise residual cerebro-spinal connections. For restoring the proper coordination of autonomic and somatic functions, as in the supra-spinal control of bladder-sphincter synergy, this is likely to be a particularly challenging exercise. Even beyond this, micro-miniature implants, in some cases operating at the nanotechnology level, could be imagined interfacing directly with individual cells to influence their neurophysiological and neuropharmacological behaviour. With such advanced technologies we can now begin to see the exciting possibility of how there could be convergence between the neural prosthesis and neural repair to facilitate functional restoration [12].

However, in the meanwhile we must continue to encourage our patients to benefit from many years of successful neural prosthetic development and not let them miss out on proven therapies, which we know can give excellent functional restoration and sound health, whilst we wait for the exciting promise of neural repair to catch up.

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