

NOGO A PROTEIN NEUTRALISATION AND MOTOR CORTEX COMPUTER IMPLANTS: A FUTURE HOPE FOR SPINAL CORD INJURY

Dear Sir,

Spinal cord injury is a horrendous, emotionally devastating event. The morale of spinal cord injury patients can sometimes be improved from learning about ongoing research to cure paralysis. This letter provides a brief introduction for practising physicians and other healthcare professionals.

It had been previously thought that there is regeneration only in the peripheral nervous system (peripheral nerves) but not in the central nervous system (brain and spinal cord), due to the intrinsic properties of peripheral and central nervous system neurons. However, in the early 1980s, it was discovered that it is actually the microenvironment of central nervous system myelin that prevents regeneration. Myelin insulates axons and increases conduction of electrical impulses. Axons from the central nervous system can easily grow over peripheral nervous system myelin, while the growth of peripheral nervous system axons is immediately arrested upon contact with central nervous system myelin.⁽¹⁾ Building on this new understanding, in 1990, it was shown that intracerebral administration of mouse monoclonal antibodies raised against myelin basic protein would allow severed corticospinal axons in rats to regrow over 11 mm (about one quarter the length of a spinal cord) with corresponding improvement in motor function.^(2,3) The antigen neutralised by the monoclonal antibodies has been identified, cloned and sequenced. It has been christened Nogo A – it serves as a “No Go” signal to axons.⁽³⁾

Recent research has sought to identify the active region of Nogo A that produces growth cone arrest.⁽⁴⁾ Peptides which block binding of Nogo A to its neuronal receptor appear to duplicate the regenerative effects of the monoclonal antibodies.⁽⁵⁾ Alternatively, given that monoclonal antibodies against Nogo A have good penetration into the spinal cord following cerebroventricular injection,⁽⁶⁾ they might be used in people after humanisation of the mouse immunoglobulin backbone. It is important to note that Nogo A is not the only molecule that prevents central nervous system regeneration. Several other candidate molecules are under active investigation.⁽⁷⁾ Regeneration might be more efficient if different growth inhibiting molecules were suppressed simultaneously. Glial scarring is another impediment to axonal regrowth that will have to be dealt with, possibly using chondroitinase to inhibit scar formation in the spinal cord.⁽⁸⁾ A key question is whether neutralisation of Nogo A long after spinal cord injury has occurred would be effective. Based on the data in rats, it should be possible to get regeneration, starting treatment weeks or longer after injury, assuming neurons have not degenerated because their axons were transected.

Computer-brain interfaces offer another way to surmount paralysis. In a recently published report, a monkey with implants into the parietal cortex of the cerebrum could literally “think” a cursor across a computer screen.⁽⁹⁾ In other studies, electro-encephalogram electrodes on the scalp of human volunteers created a noninvasive brain-computer interface that also could control a cursor on a two-dimensional screen.⁽¹⁰⁾ In the future, thought-controlled prosthetic limbs or muscle stimulators may be possible; the person would think about a motor action, and artificial limbs could be activated or muscles could be electrically stimulated to contract. Cerebral cortex implants or scalp electrodes could be modulated by sensory information from position sensors on the limbs. One would have to in some way recreate the complicated and dynamic integration of sensory and motor pathways that occurs naturally. Direct neural sensory feedback and control of a prosthetic arm have been achieved in amputees with electrodes implanted in nerve stumps of limb stumps, allowing an amputee to control grip strength and position of a prosthetic arm.⁽¹¹⁾ This technology could be expanded for use in combination with electrodes activated by the cerebral cortex, either brain implants or skull-electrode based systems.

Spinal cord injury patients may or may not be interested in the above details of neurobiology and bioengineering, but they will certainly appreciate knowing that spinal cord regeneration and computer control of movement have been achieved on an experimental basis, setting the stage for future clinical trials. By taking care of themselves now and making maximal efforts on rehabilitation, spinal cord injury patients can increase the likelihood that they personally will be able to benefit from these new breakthroughs.

Yours sincerely,

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