Return of spinal reflex after spinal cord surgery for brachial plexus avulsion injury

Case report

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Motor but not sensory function has been described after spinal cord surgery in patients with brachial plexus avulsion injury. In the featured case, motor-related nerve roots as well as sensory spinal nerves distal to the dorsal root ganglion were reconnected to neurons in the ventral and dorsal horns of the spinal cord by implanting nerve grafts. Peripheral and sensory functions were assessed 10 years after an accident and subsequent spinal cord surgery. The biceps stretch reflex could be elicited, and electrophysiological testing demonstrated a Hoffman reflex, or H-reflex, in the biceps muscle when the musculocutaneous nerve was stimulated. Functional MR imaging demonstrated sensory motor cortex activities on active as well as passive elbow flexion. Quantitative sensory testing and contact heat evoked potential stimulation did not detect any cutaneous sensory function, however. To the best of the authors’ knowledge, this case represents the first time that spinal cord surgery could restore not only motor function but also proprioception completing a spinal reflex arch. (DOI: 10.3171/2011.7.JNS111106)

Key Words • root avulsion • spinal cord surgery • regeneration • plasticity • H-reflex • cortical functional magnetic resonance imaging • peripheral nerve

SEGMENTAL intramedullary afferent and efferent connections are interrupted in the “longitudinal” spinal cord injury caused by avulsion of the spinal nerve roots to the brachial plexus. If untreated, the patient is left with a monoplegia and typically severe, devastating pain. An active surgical approach to this type of spinal cord injury in which avulsed roots or nerve grafts are implanted into the spinal cord results in the recovery of function and the alleviation of pain.2

The useful return of muscle activity from ventral root reconnection to the spinal cord after spinal root avulsion injury was first reported in 1995. 3 This type of spinal cord surgery, in which motor but not sensory conduits are reconstructed, is currently performed in patients with complete or subtotal brachial plexus avulsion injuries, with a good outcome in terms of hand function.2,4 Recent studies of CNS activities in patients with restored motor function without sensation have demonstrated cortical plasticity and the use of preinjury-established cortical sensory programs for motor performance.5 Several attempts to restore sensation and the spinal cord reflex arch by implanting avulsed or cut dorsal roots have been made only experimentally with an unpersuasive outcome. Good regeneration of the sensory neurons in the dorsal horn of the spinal cord has been established, however, through medullary implantation of a nerve graft connected distally to the sensory part of the spinal nerve after removing the DRG.3

Here, we describe the assessment of sensory recovery 10 years after the reconnection of avulsed peripheral nerves with motor and sensory neurons within the spinal cord after a complete brachial plexus injury. The objective in this case was to analyze the extent of sensory recovery from the repair of a spinal cord injury that had severed transverse segmental spinal cord connections.

Case Report

History. This 35-year-old man sustained a total left-sided (nondominant) brachial plexus injury with Horner syndrome in a motorcycle accident. Preoperative neurological examination showed neither motor nor sensory function in the hand, arm, or shoulder.

Abbreviations used in this paper: CHEPS = contact heat evoked potentials stimulation; DRG = dorsal root ganglion; fMR = functional MR; H-reflex = Hoffman reflex; QST = quantitative sensory testing.
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At surgery performed 1 week after the accident, no somatosensory evoked potentials could be elicited. Complete avulsions of the roots at C-5, C-6, and C-7 and subtotal avulsions of the roots at C-8 and T-1 with 1 or 2 remaining ventral rootlets were noted when the lower cervical spinal cord was exposed. The ipsilateral sensory branch of the radial nerve in the forearm and the medial cutaneous nerve of the forearm were harvested as nerve grafts. Before implanting the grafts into the spinal cord, small 2- to 3-mm longitudinal slits were made in the pia mater.

The avulsed C5–7 ventral roots were connected via the nerve grafts implanted 1- to 2-mm deep to the pia mater near the ventral root exit zone for motor recovery. After removing the DRGs, the sensory part of C-7 was connected to the pertinent spinal cord segment through implantation of the nerve graft into the dorsolateral sulcus of the spinal cord near the dorsal root entry zone to reconnect the dorsal or sensory part of the spinal cord with the periphery. The position of the tips of the nerve grafts in the spinal cord was retained with fibrin glue, which was also used for distal attachment of the graft. The grafts were approximately 5–8 cm in length.

Clinical Assessment. The patient did not attend postoperative appointments, but he appeared at a clinical conference about 10 years after the accident and subsequent surgery. Controlled shoulder and elbow movements, without any signs of synkinesia, were noted. Shoulder abduction and forward flexion to 90° as well as good external and internal rotation were demonstrated. Full elbow flexion was strong enough to lift a weight of 8 kg. There was control of pronation and supination. Useful finger and thumb flexion could also cause wrist flexion. There was no active elbow extension, no activity in wrist flexor or extensor muscles, and no finger extension or intrinsic hand muscle activity. A tendon reflex could be elicited from the biceps muscles but not from the triceps or brachioradialis muscles. There was sensation only in the C-5 dermatome, probably due to overlap from the adjacent dermatome. There was perception of movements in shoulder and elbow joints. The initial severe and classic avulsion type of pain in the arm had been reduced in time along with reinnervation of the muscles at 1 year postoperatively, when the patient had returned about 10 years after the accident and subsequent operative appointments, but he appeared at a clinical conference about 10 years after the accident and subsequent surgery. Controlled shoulder and elbow movements, without any signs of synkinesia, were noted. Shoulder abduction and forward flexion to 90° as well as good external and internal rotation were demonstrated. Full elbow flexion was strong enough to lift a weight of 8 kg. There was control of pronation and supination. Useful finger and thumb flexion could also cause wrist flexion. There was no active elbow extension, no activity in wrist flexor or extensor muscles, and no finger extension or intrinsic hand muscle activity. A tendon reflex could be elicited from the biceps muscles but not from the triceps or brachioradialis muscles. There was sensation only in the C-5 dermatome, probably due to overlap from the adjacent dermatome. There was perception of movements in shoulder and elbow joints. The initial severe and classic avulsion type of pain in the arm had been reduced in time along with reinnervation of the muscles at 1 year postoperatively, when the patient had returned to his previous work and could drive an ordinary car. He was enjoying mountain biking in his spare time.

Laboratory Assessments. A CHEPS device (Medoc Ltd.) with a thermode area of 572.5 mm² was used, and the stimulation protocol we followed was described previously. Ten 51°C stimuli (with an interstimulus interval of 7 seconds) were applied to the C-5 and C-6 dermatomes on both arms and the left side of the face. Evoked potentials were recorded from 7 electrodes (FCz, Cz, C3, C4, Pz, P3, and P4) by using a protocol similar to that described previously. The ground electrode was placed on the left temporal region, and the implicit reference was located in the Fz position. An infraorbital electrode was also used to enable ocular correction. Electrode impedance was maintained below 5 Ω throughout the recording. Electroencephalography activity was recorded and digitized at a sampling rate of 500 Hz; a low pass filter with a frequency of 0.15 Hz and a high pass filter of 100 Hz were applied to the recording. The recorded electroencephalography data were analyzed using Vision Analyzer Version 1.05.001 (Brain Products GmbH). The data were filtered, semiautomatically corrected for ocular artifacts (Gratton and Coles method), segmented around the contact heat stimulus, and averaged. Latencies (N2) and amplitudes (N2-P2) of Aδ evoked potentials from the Fz position following contact heat stimulation were normal from the unaffected right arm and left side of the face but absent from the affected left arm.

Functional MR imaging was conducted while motor tasks were performed. Four sessions were acquired, each with the active phase as follows: 1) left arm volitional movement (active left); 2) left arm passive movement (passive left); 3) right arm volitional movement (active right); and 4) right arm passive movement (passive right). Each session was self-paced approximately every 3–4 seconds in blocks of 30 seconds alternating with baseline blocks for a total of 85 volumes per session.

Images were acquired on a Siemens Verio 3T scanner with a 32-channel head coil. An echo planar gradient echo sequence was used for the MR images (TR 3 seconds, TE 30 msec, 36 contiguous slices acquired interleaved, 4 mm thick, field of view 220 mm², matrix 64 × 64, resolution 3.4 mm × 3.4 mm × 4 mm, and acquisition time 4 minutes 26 seconds). Three-dimensional T1-weighted high-resolution structural data scans were acquired prior to the fMR images.

Functional MR images were spatially realigned, normalized to match the echo planar template, and smoothed with a Gaussian filter of 6 mm, using SPM5 (http://www.fil.ion.ucl.ac.uk/spm). Statistical parametric maps were created for each session (active phase > baseline) by using a height threshold of p < 0.05 corrected for multiple comparisons across the brain volume.

The contralateral precentral gyrus was activated in all 4 conditions. Additional areas were activated when the patient moved his left arm, including the cerebellum, contralateral temporal gyrus, superior frontal gyrus, and supplementary motor area.

Neurophysiological recordings of tendon stretch or the H-reflex were made on a Medtronic Keypoint electromyography machine. The musculocutaneous nerve was stimulated in the upper arm/axilla by applying a single electrical stimulus with a current duration of 1 msec. Surface recordings were made from the biceps muscle with the patient activating the muscle to about 20% of maximum power. At a low stimulation strength, a reproducible H response (latency of about 16 msec) was recorded. As the stimulus strength was increased, the H-reflex disappeared and a much higher-amplitude biceps M wave appeared.

Muscle and skin biopsy specimens for histological assessments of regenerating motor and sensory fibers were immunostained with antibodies to the structural nerve marker PGP 9.5. Tissue from skin and muscle were immersion fixed in Zamboni fluid for approximately 2 hours and then rinsed and stored in phosphate-buffered saline containing 15% w/v sucrose and sodium azide.
The immersion-fixed samples were embedded in optimal cutting temperature compound and snap frozen in melting isopentane suspended in liquid nitrogen. Endogenous peroxidase was blocked by incubation in industrial methylated spirit containing 0.3% w/v hydrogen peroxide for 30 minutes. After rehydration, sections were incubated overnight with primary antibody. Sites of primary antibody attachment were revealed using nickel-enhanced avidin-biotin-peroxidase compound (Vector Laboratories), as previously described. Sections were counterstained for nuclei in 0.1% w/v aqueous neutral red and mounted in xylene-based mountant (DPX; BDH Merck Ltd.).

**Test Results.** Neither QST nor CHEPS for the evaluation of cutaneous sensory nerve fibers registered any response from the affected arm, except for the C-5 dermatome during QST, which showed elevated sensory thresholds. In biopsy specimens from the upper arm, the pan-neuronal marker PGP 9.5 showed abundant fibers in the biceps muscle but very few subepithelial fibers in the skin (Fig. 1). Neurophysiological testing demonstrated an H-reflex from the biceps muscle on stimulating the musculocutaneous nerve of the affected arm (Fig. 2). Functional MR imaging showed extended sensorimotor cortex activity on active elbow flexion, but also S1 (primary somatosensory) cortex activity on passive flexion of the affected arm (Fig. 3).

Informed consent was obtained from the patient to study the tissues and to study the sensory mechanisms via fMR imaging. Ethics approval was obtained from the Royal National Orthopaedic Hospital as well as the Hammersmith Hospital (approval number 07/H0706/78).

**Discussion**

The biceps tendon reflex, H-reflex, and fMR imaging studies verified the return of proprioception after spinal cord surgery. However, exteroception could not be demonstrated by QST, CHEPS, or tissue histochemistry. Might the return of proprioception in the present case be attributable to something other than nerve implantations into the dorsal part of the spinal cord? There are several possibilities, such as collateral growth from adjacent intact or avulsed DRG neurons; however, extensions of supernumerary dendrites or dendraxons from dorsal horn neurons into implanted peripheral nervous system conduits should be considered, as has previously been demonstrated for motoneurons. New growth or plasticity from intraspinal neurons is most likely, as the DRGs were removed during surgery in the featured patient. The return of muscle function follows from ventral root implantation into the spinal cord. The absence of extensor muscle function, even though a graft was implanted into the C-7 segment, most likely depends on aberrant and nonspecific motoneuron reinnervation, as documented in basic and clinical studies. Sensory function cannot be regained by implanting avulsed dorsal roots, as DRG neuron axons are unable to regenerate into the adult spinal cord. Sensory nerve cells in the spinal cord could, like CNS motoneurons, potentially elongate new processes into a peripheral nervous system graft implanted into the dorsal spinal cord to reconnect with the periphery. The return of the muscle stretch reflex, despite the missing primary Ia sensory neurons, could depend on spinal cord plasticity with new peripheral extensions from spinal cord interneurons with excitatory properties normally involved in multisynaptic segmental reflexes. Basic science
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Fig. 3. Coronal (left) and axial (right) fMRI images demonstrating activation during active and passive arm movements. Red, left arm active; yellow, left arm passive; blue, right arm active; and green, right arm passive.

studies are certainly necessary to reveal the mechanisms behind clinical observations of surgically related spinal cord regeneration and plasticity of sensory systems. The restoration of a spinal reflex arch from surgery—in the present case, a “longitudinal” spinal cord injury—could serve as a model in future clinical trials to improve function after spinal cord injuries.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Carlstedt, Anand. Acquisition of data: Misra, Papadaki, McRobbie, Anand. Analysis and interpretation of data: Misra, Papadaki, McRobbie, Anand. Drafting the article: Carlstedt, Anand. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Carlstedt. Administrative/technical/material support: Anand. Study supervision: Carlstedt.

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