



Upper extremity motor training of a subject with initially motor complete chronic high tetraplegia using constraint-induced biofeedback therapy

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Abstract

Introduction The purpose of this case study was to determine if a subject with chronic high tetraplegia (C3 AIS A) could learn to use an initially paralyzed upper extremity on the basis of training procedures alone.

Case presentation Initially, an AIS examination revealed no purposive movement below the neck other than minimal shoulder movement. Training was carried out weekly over 39 months. Training began based on electromyographic biofeedback; the electrical activity of a muscle (biceps or triceps) was displayed visually on a computer monitor and the subject was encouraged to progressively increase the magnitude of the response in small increments on a trial-by-trial basis (i.e., shaping). When small, overt movements began to appear; these were, in turn, shaped so that their excursion progressively increased. Training then progressed to enable lifting the arm with the aid of the counterweight of a Swedish Help Arm. Mean movement excursions in the best session were: internal rotation 52.5 cm; external rotation 26.9 cm; shoulder extension 22.1 cm; shoulder flexion 15.2 cm; pronation/supination 120°; extension of index finger (D2) 2.5 cm. Movements were initially saltatory, becoming smoother over time. With the Swedish Help Arm, the subject was able to lift her hand an average of 24.3 cm in the best session with 0.7 kg counterweight acting at the wrist (1.9 J of work).

Discussion Results suggest in preliminary fashion the effectiveness of this approach for improving upper extremity function after motor complete high tetraplegia. Thus, future studies are warranted. Possible mechanisms are discussed.

Introduction

In cases of motor complete high tetraplegia, with usual care, spontaneous recovery of motor function is unlikely to occur >1 year after the injury [1]. Late recovery as a result of treatment is also rare. In one case, a subject with motor complete high tetraplegia [C3 American Spinal Injury Association (ASIA) Impairment Scale (AIS) Grade A] recovered a modest amount of independent upper extremity (UE) function following a treatment regimen that included passive lower extremity (LE) exercise on a functional electrical stimulation recumbent bicycle, UE and LE aquatherapy, and UE and trunk neuromuscular electrical stimulation (NMES) [2]. In two studies, NMES enabled hand-to-mouth movements in subjects with high tetraplegia. Carryover, however, did not occur in the absence of stimulation [3, 4]. Recently, the return of self-initiated stepping has been achieved with lumbosacral spinal cord stimulation from implanted epidural electrodes and some

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training [5]. Similarly, improvement in UE movement has been obtained using implanted epidural electrodes in two subjects with motor incomplete tetraplegia resulting from spinal cord injury (SCI) at the C5–C6 level [6]. However, there have been no reported attempts to directly train UE motor function without electrical stimulation in subjects with motor complete high tetraplegia. A number of phenomena suggest that the potential for substantial motor recovery below the level of injury may remain.

In cats, preservation of just 10% of axons in a spinal segment can support walking [7]. In humans with SCI, preservation of a small portion of the connectivity across the level of injury can make possible limited movement and some recovery [2, 8]. Moreover, many patients with chronic progressive syringomyelia do not experience motor symptoms; Masur et al. [9] found that 9 of 22 (40.9%) patients with syringomyelia showed no signs of motor impairment. Presumably, the redundancy of axonal connections and/or possible neuroplastic growth processes allow preservation of considerable motor function following substantial spinal injury or disease if there is no sudden, traumatic onset.

Constraint-induced (CI) movement therapy (CI therapy) is a neurorehabilitation treatment derived from basic research with primates [10, 11] that has been shown to have efficacy for the treatment of UE motor deficits in subjects with chronic stroke [12–15], traumatic brain injury (TBI) [16], cerebral palsy [17, 18], and multiple sclerosis (MS) [19], as well as LE deficits in motor incomplete lumbosacral SCI [20, 21]. It is regimen based on the performance of self-initiated, active movement; large and functionally significant improvements are reported [14]. CI therapy has also been used in conjunction with the techniques of neurodevelopmental therapy (NDT) to restore considerable functional movement in the initially plegic hands of chronic stroke patients [22, 23]. In the past, we have worked with two subjects with motor incomplete tetraplegia. Their initial motor deficits were similar to those classified as moderately severe (Grade 4) based on active range of motion criteria [22]. The motor improvement for the trained arm was similar to that for subjects with stroke having similar deficits.

Two of the main components of the CI therapy intervention were employed here: intensive training and training by the procedure termed shaping. The latter is a technique in which a behavioral objective, in this case, an improved motor response, is achieved by differential reinforcement of small increments in performance or “successive approximations” in the desired direction [24, 25].

In the present case, self-initiated movement below the level of the neck was not present before training. However, the presence of weak contractions of the upper limb musculature to command indicated that some connections remained intact between the brain and the segmental neural

apparatus of the arm. These would potentially be available for re-enlistment in the innervation of self-initiated movements. However, the use of a physical rehabilitation technique such as CI therapy to achieve this objective is contingent on the presence of observable limb movement. To bridge the critical gap between self-initiated muscle contractions that do not result in observable movement and the performance of overt purposive movement, we used electromyographic (EMG) biofeedback. In biofeedback procedures, the activity of a physiological response system is recorded, amplified, and then transformed into an information display so that the signals or response feedback are easily discriminable by the responding individual. The objective is to enable an individual to self-regulate a physiological system that would otherwise not be susceptible to purposive control.

The rationale for attempting to use a CI therapy approach for enabling movement in the UE of an individual with chronic motor complete high tetraplegia was threefold: (1) the success in applying the CI therapy protocol to subjects with initially plegic hands after stroke, (2) the success in using CI therapy with motor incomplete tetraplegia, and (3) large and significant treatment outcomes for subjects from a variety of different types of central nervous system (CNS) damage.

Case presentation

A 64-year-old right-handed woman sustained a marked C6–C7 hyperextension injury with hematomyelia at C3–C4 and resultant C3 AIS A tetraplegia (Fig. 1) 2 years prior. Physical exam revealed sensation intact to C3 and absent below. She had limited head movement and minimal movement of the shoulders. The latter involved shrug that elevated the elbows ~1 cm from the wheelchair armrests. She was ventilator-dependent and was unable to tolerate >20 min off the ventilator at a time. Although she sustained a mild TBI during the accident, the injury did not affect her cognition.

The study was approved by the Institutional Review Board at the University of Alabama at Birmingham, and informed consent was obtained. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

This subject was given 0.5–2 h in-home sessions weekly for 39 months in which the right arm was trained. She was encouraged to practice the training exercises with caregivers between treatment sessions. For consistency, only data from the weekly sessions with the experimenters were analyzed. To maximize functional gains, training was confined to the subject's right arm; the left arm served as an experimental

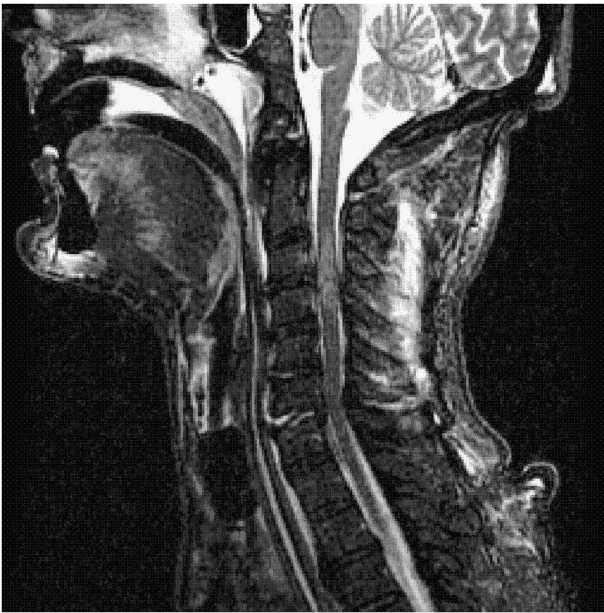


Fig. 1 Magnetic resonance image of the cervical spinal cord demonstrating an acute spinal cord injury with hematomyelia at C2–3 and hyperextension injury at the C6–7 level. Mid-sagittal, STIR (short-TI inversion recovery) image from acute hospitalization. Image acquired on a GE Genesis SIGNA (GE Healthcare, Little Chalfont, UK), 1.5 T, 14 slices 3 mm thick with 1 mm gaps, in-plane FOV = 240 mm × 240 mm, voxel size = 4 × 0.94 × 0.94 mm, TR = 3466.66 ms, TE = 55 ms, acquisition time = ~5 min. NIfTI image displayed with FSLView 4.0.1 (The University of Oxford, Oxford, UK)

control. Motor capacity of the untrained left arm did not improve during the course of this work. Self-initiated muscle contractions were present from the outset, but they were insufficient to produce overt movement.

Treatment began with EMG biofeedback of the weak contractions of the muscles in the subject's right upper arm. The arms were placed on a bedside table positioned to be just above the wheelchair armrest. Electrodes (PALS[®] 5 cm Savare; Axelgaard Manufacturing Co. Ltd, Fallbrook, CA, USA) were affixed to the skin over muscles (biceps or triceps) for 13 sessions over 9 weeks, and the subject viewed the resulting EMG activity on a computer screen (MyoTrac Infiniti module to Biograph Infiniti; Thought Technology Ltd, Montreal, Canada). An experimenter-specified threshold level was represented by a horizontal line on the screen. The subject's task was to exceed threshold, at which point music was added to the visual feedback. Over a period of ~0.5 h, commands were given by the apparatus (MyoTrac Infiniti Clinical System) to "contract" for 20 s and "relax" for 10 s. A variable number of trials were given interspersed with additional rest intervals of variable length, as needed. Initially, response amplitude peaked within the first three trials, dropped to very low levels shortly thereafter, and did not recover after a 5 min rest. This rapid response fatigue

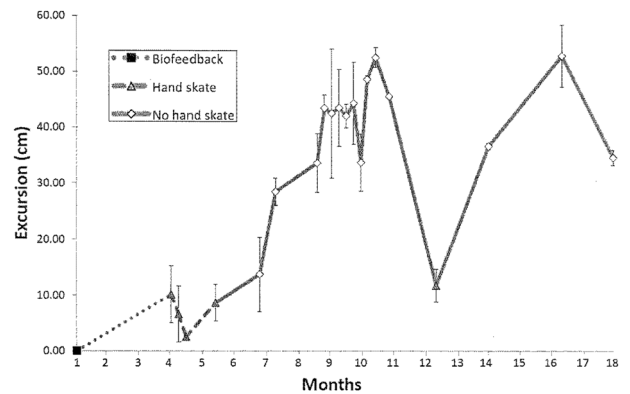


Fig. 2 Mean internal rotation excursion (cm). Patient was asked to internally rotate the upper extremity (UE), initially with the hand attached to a hand skate to reduce friction. Dotted line represents EMG biofeedback training sessions before internal rotation was attempted. Data points represent the mean of all trials in a session. Error bars represent ± 1 SD, but are not visible here if SD was <2.5 cm

limited the length of sessions initially, but with practice the response decrement did not appear for progressively longer periods. The experimenter raised the muscle-specific thresholds in steps from 5 to 30 μ V, usually in 5 μ V increments, when performance exceeded a given threshold over 80% of the time consistently over a series of trials.

Before training, only trace movements of the shoulders were possible; the maximal movement was a shrug of the right shoulder resulting in elbow elevation 0.5 cm from the wheelchair armrest. At session 10, small movements of the whole arm began to appear. During sessions 12–13, a mirror was attached to the bedside table in front of the subject to provide a view of arm movements. In session 14, EMG biofeedback and mirror feedback were eliminated. The subject was then asked to make four standard movements with the proximal arm musculature, not always in the same session: shoulder flexion, shoulder extension, internal rotation, and external rotation. Initially, some movements of limited excursion were made, but they fatigued rapidly and ceased after two to three attempts. In session 17, the subject's lower arm was secured to a hand skate to reduce surface friction. Movement excursion increased and response fatigue decreased, so that by session 19, 10 movements of each type could be made without diminished excursion before the next movement was tested, repeating the pattern previously observed with the EMG responses (see Fig. 2 for internal rotation).

By session 21, the hand skate was eliminated and movements were made with surface friction reduced by talcum powder. Session length was gradually increased to 6 sets of 10 trials with 5 min between sets, though discomfort or response fatigue sometimes led to earlier termination. Between sessions 45–50, daily mean movement excursion achieved for each movement was: internal

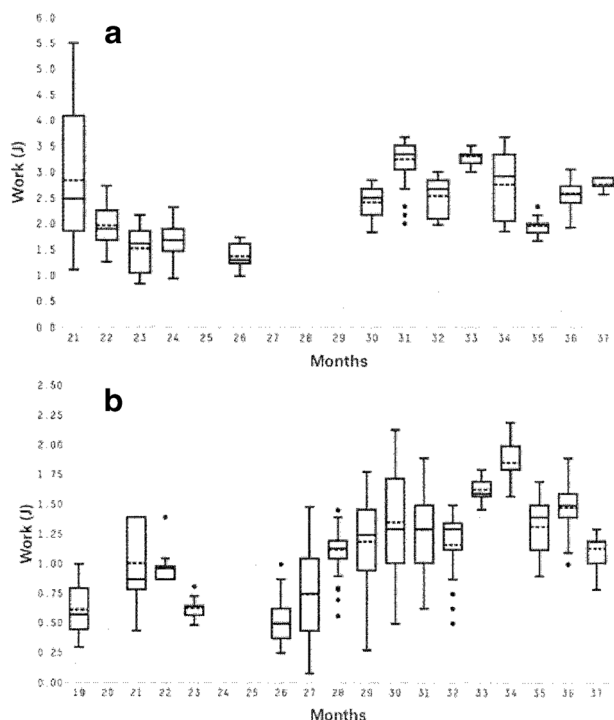


Fig. 3 Raising the arm against gravity. **a** Work produced with counterweight positioned near the elbow (not pictured: four outliers ranging from 8.05 to 9.95 J in month 21). **b** Work produced with counterweight positioned at the wrist. To standardize Swedish Help Arm performance with different amounts of counterweight, work in joules (J) was computed using the formula $W = Fg \times \Delta y$ for all trials up to month 37. Trials are displayed collectively as box plots for each month. Whiskers on box plots indicate ± 1.5 interquartile range; outliers beyond this range are represented as dots. Work with the Swedish Help Arm began 19 months after the beginning of training shown in Fig. 2

rotation—52.5 cm, external rotation—26.9 cm, shoulder extension—22.1 cm, and shoulder flexion—15.2 cm. Movements were initially saltatory with final levels achieved in 3–8 steps. At first, there was considerable contribution from shoulder and torso movements, but as training proceeded there was greater contribution from more distal muscles, especially in the initial movement segments. Movements also became smoother. Shoulder and torso movements, while substitutions for involvement of limb musculature, were not possible before training began. Training of pronation and supination of the hand began in session 21 and was facilitated in session 23 by securing a tennis ball to the palm. Movements, measured with a goniometer, varied from 45° to 120° with the tennis ball and 20° – 30° without this aid. With the digits hanging freely over the edge of a hand skate, finger tapping of digits 2 and 3 (D2, D3) appeared in session 24. In session 30, repeated extensions of D2–D4 were observed. Maximum excursions were: 2.5 cm for D2, 1.8 cm for D3, and 0.5 cm for D5. Thumb adduction of 0.5 cm occurred

beginning in session 31. Active wrist flexion was observed beginning in sessions 29–30.

As isolated UE movements improved, training gradually transitioned to focus on functional movements. To facilitate self-feeding and facial hygiene, training was begun to enable lifting hand to face. A Swedish Help Arm (Stabilis Help Arm, Follo Industrier AS, Oslo, Norway) was used that partially counteracts the influence of gravity by using an adjustable amount of counterweight applied at either wrist or elbow. The focus of the counterweight's action is determined by shifting the location of a sliding fulcrum along a rod from which a lower arm sling is suspended; the rod in turn is suspended from an overhead pulley system through which the counterweight acts. The amount of counterweight was adjusted within and between sessions as part of the shaping process. With the counterweight acting at the wrist, 1.50 kg was required to passively flex the arm at the elbow; 0.70 kg of counterweight eliminated ~47% of the force of gravity for this movement. With the counterweight acting at the elbow, 2.50 kg was required to passively lift the arm; 1.15 kg of counterweight eliminated ~46% of the force of gravity. To standardize characterization of Swedish Help Arm performance with different amounts of counterweight, the work (W) in joules (J) required to lift the arm a certain height (Δy) against the force of gravity (Fg), was calculated using the formula $W = Fg \times \Delta y$. With 0.70 kg of counterweight acting at the wrist, the subject was able to lift her hand an average of 24.3 cm in the best session, which equals 1.90 J of work. With 1.15 kg of counterweight at the elbow, the subject was able to lift her arm an average of 25.9 cm in the best session with 1.15 kg of counterweight at the elbow, which equals 3.43 J of work. Swedish Help Arm performance calculated in joules is presented in Fig. 3. As shown in the figure, the subject's ability to lift her hand and arm improved modestly over 33 sessions.

To increase independence in activities of daily living, the subject was trained to use a standard computer mouse for some computer operations and to control her wheelchair with a hand joystick/goalpost manipulandum. With her hand secured to a computer mouse, the subject was asked to move the mouse cursor to trace the outline or path through a number of geometric shapes on a computer screen and her performance was timed. The subject was also asked to practice typing using the default on-screen keyboard in Windows 7 (Microsoft Corporation, Redmond, WA, USA); clicking was controlled by adaptive software (Dwell Clicker 2; AbleNet Inc., Roseville, MN, USA). After nine sessions of computer mouse training, the subject was able to type simple sentences at a rate of ~1.7 words per min. To practice controlling her wheelchair with a joystick/goalpost, she was asked to navigate an outdoor course drawn on the pavement in sidewalk chalk. The

subject became able to control the wheelchair in outdoor spaces using the joystick, but the wheelchair's hardware configuration lacked sufficient precision for navigation indoors.

At the beginning of training, the subject reported lack of sensation except in her right shoulder; currently, she reports awareness of touch applied to most parts of the upper torso and both arms but not the legs.

Spasticity management was an ongoing effort throughout this study. The subject took baclofen daily, with various dosage timings. She also started taking dantrolene 75 mg daily 27 months into training. In addition, she received 6 rounds of botulinum toxin injections; however, these were to different muscles in five cases, and they did not have any effect quantitatively on the responses being trained. Ongoing spasticity in the paraspinal muscles led to postural issues, including scoliosis. These were addressed in part through various padding adjustments on her wheelchair and bedding. She was fitted for a bivalved thoracolumbosacral orthosis 29 months into training, and she subsequently wore it daily.

Before the beginning of training, this originally ventilator-dependent subject reported being able to stay off the ventilator for a maximum of 20 min, but had stopped exploring this possibility ~1 year earlier. In session 18, the subject was asked to practice staying off the ventilator (monitored by a caregiver) until she felt discomfort or until a finger pulse oximeter indicated that blood oxygen saturation had dropped below 90%. By the next session, 1 week later, she was able to remain off the ventilator for 30 min and progressively increased the ventilator-free period to 19 h on 2 consecutive days 56 weeks later. At session 29, the subject reported being able to activate abdominal muscles to produce a weak cough that gradually increased in strength until incomplete clearance of mucous from the lungs was possible.

Discussion

In this study, we employed CI therapy training techniques to restore some motor function to the pre-injury dominant right arm of a subject with motor complete high tetraplegia (C3 AIS Grade A) who was initially paralyzed from the neck down. We started with EMG biofeedback from the weakly contracting muscles of the right arm and shaped the initial EMG signals to increase their amplitude until overt movement appeared. We then shaped the initial trace movements to increase their excursion so that they could be used for some functional activities.

The current prognosis for individuals with motor complete tetraplegia is no further recovery of motor ability after 12 months post injury. Approximately 94% of individuals

with sensory and motor complete SCI at 1 year remain complete at 5 years post injury [26]. The individuals who do transition to a less severe AIS grade have usually regained some sensation but no motor function below the level of injury. However, through the use of CI therapy techniques, it was possible to restore some functionally useful movement to the trained UE, while inability to move the untrained UE remained unchanged.

Two linked but independent mechanisms have been shown to be associated with the improved motor function produced by CI therapy. The first involves overcoming learned nonuse (LNU) [10, 11, 27], a mechanism proposed to underlie a significant portion of many functional impairments following different types of CNS damage. LNU is a learned inhibition of function that develops in the acute/subacute period due to the temporary depression of neural excitability. If the damage affects motor elements in the brain or spinal cord, there will be a temporary reduction in the ability to move an affected extremity or a complete absence of movement if the damage is severe enough. The resulting motor failure leads to a learned suppression of future attempts to use the affected extremity due to the operation of well-recognized learning processes [10, 11, 27]. Later, after spontaneous recovery of CNS excitability has progressed sufficiently so that movement would again become possible, use of the limb is prevented by the strong previously learned inhibition of movement. However, LNU can be overcome by the application of an appropriate method, such as CI therapy, which induces a subject to move by a number of techniques. A primary method involves intensive training using shaping procedures, and rewarding the initial, impaired movements. The operation of this mechanism and the methods for overcoming it were first observed in monkeys following the surgical abolition of sensation from a single forelimb by dorsal rhizotomy [10, 11]. This work has provided the basis for the development of CI therapy.

A second mechanism associated with CI therapy is the plastic reorganization of the CNS. Multiple experiments employing a variety of different measures indicate that CI therapy produces substantial functional and structural changes in the brain (summarized in Taub et al. [28]).

The same two mechanisms, overcoming LNU and use-dependent plastic CNS reorganization might also be operating in the case of the subject described here. A period of spinal shock and loss of neuronal excitability would supervene following the sudden traumatic insult. During this early post-injury period, the segmental spinal apparatus would not have sufficient excitability to permit overt movements to be made in response to suprasegmental commands. These are similar conditions that give rise to the development of LNU after damage to the brain. Repeated attempts to use an extremity during a period when spinal

cord excitability could not yet support the performance of movement would lead to repeated failure resulting in a learned suppression of attempts to use that extremity. During the subsequent weeks or months, background excitability exhibits a slow spontaneous recovery, presumably as a result of neurochemical changes and neuroplastic processes involving in part axonal sprouting [29] from spared descending fibers and intraspinal elements [30, 31]. Neuroplastic processes would also take place in the brain following a SCI [32, 33]. However, even when spinal cord of excitability spontaneously returns to a level that would support movement because these structural neuroplastic processes and neurochemical changes, the LNU would persist. It would normally be permanent, but techniques such as CI therapy could override the LNU and bring the latent capacity for purposive movement to expression. The increased movement would presumably give rise to further plastic use-dependent CNS reorganization that would support still greater improvement in motor ability. However, in motor complete high tetraplegia, there is an added complication in that the absence of purposive movement over an extended period results in muscle atrophy. This would impede progress in improving movement even though the neural apparatus to make it possible is present [4]. We believe muscle atrophy was responsible for the slow progress of motor improvement in the present case.

This slow improvement probably precludes general clinical application of CI biofeedback therapy (CIBT) to motor complete high tetraplegia until further research uncovers methods to speed up the recovery process, perhaps by such non-invasive means as muscle, peripheral nerve, and/or transcutaneous brain stimulation. However, as noted, CI therapy can produce substantial improvement in individuals with motor incomplete tetraplegia within the same 3-week time frame as it does after brain injury. In addition, Beekhuizen and Field-Fote [34, 35] have found that a massed practice training approach (without shaping) can also improve impaired motor function in subjects with incomplete tetraplegia classified as AIS Grade C or AIS Grade D as have Kim et al. [36]. Consequently, it might be appropriate to consider some issues of clinical relevance to such cases.

The current results and previous results with incomplete tetraplegia suggest that chronicity of injury and absence of purposive movement at C4 and below are not barriers for use of an effective therapy, provided trace movement is present, especially if atrophy is diminished. A related consideration is that in order to avoid disuse atrophy, training of movement should begin acutely soon after the subject has been medically stabilized.

Other nuances regarding future work with patients with motor complete and incomplete tetraplegia bear discussion.

Such patients would appear to benefit from a more rigorous and structured program of therapy than is usually employed. The subject described here was given one session weekly by the experimenters. However, the caregivers were trained in the laboratory's training procedures and carried out an additional two to three practice sessions per week. With regard to the details of this case, we trained the previously dominant right arm. Insofar as it is relevant, in our work with stroke subjects, premorbid dominance was not a factor in magnitude of treatment outcome [12, 14]. Moreover, we do not think the presence of bony injury would have modified the results, if the vertebral column was stabilized.

Another issue relevant to clinical practice is the length of time the training effect will persist after the end of treatment. No relevant data was obtained in the present case. However, data is available on retention of the treatment effect from CI therapy for chronic stroke and MS. If subjects are not contacted for 1 year after the end of treatment, there is a mean 84% retention of treatment effect [13] and a mean 45% retention rate after 4–5 years [19]. However, with the use of "transfer package" techniques [14, 37], there is no loss in retention and even further improvement after 1 year. In this case, due to difference in the severity and etiology of neurologic damage, the prognosis for retention is uncertain.

Invasive methods, such as epidural stimulation with an implanted device [5, 6] and stem-cell implantation [38], have recently shown promising results for the rehabilitation of LE movement in motor complete paraplegia [5, 39] and UE movement in motor complete tetraplegia [6]. However, a recent survey of SCI patients, caregivers, and healthcare professionals indicated that non-invasive activity-based treatment for SCI is currently the number one research priority among these stakeholders [39]. The Swedish Help Arm and EMG biofeedback device (which can also be used for NMES) were purchased for <\$2500 each. This is a cost within the means of most clinical facilities; however, it is unlikely to be covered by most insurance providers. Despite this, our case report suggests that there is potential for some individuals with high tetraplegia to benefit from an activity-based treatment such as CIBT.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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