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Case Report

Progression of Bladder and Sensory Recovery in a Case of Transverse Myelitis

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Abstract

This is a case of a 45 year old man, diagnosed with transverse myelitis of the thoracic spine [T4-T9], who had unexpected gains in bladder function and sensory outcomes during activity-based lower extremity neuromuscular electrical stimulation [LE-NMES]. While transverse myelitis, characterized as a non-traumatic, inflammatory lesion of the spinal cord, can result in sensory, motor and autonomic deficits, bladder dysfunction often remains one of the most common and disabling consequences. This case report compares urodynamic outcomes [bladder capacity, pressure, voiding efficiency, and uroflow parameters] over three consecutive annual time points as the individual participated in a spinal cord injury [SCI] outpatient rehabilitation clinic and community-based fitness and wellness center. Sensory improvements were assessed in accordance with the International Standards for Neurological Classification of Spinal Cord Injury. Improvements in voiding efficiency, bladder pressure and compliance as well as lower extremity sensation coincided with activity-based LE-NMES. The results of this case report have therapeutic implications by providing physiological outcomes that may help direct future NMES rehabilitative approaches, especially for those with bladder dysfunction. Additional research is warranted to elucidate optimal LE-NMES parameters that may facilitate urologic and sensory recovery for different SCI presentations. Since NMES is highly accessible in the clinical setting, future work could inform how this therapy is implemented in a broader context.

ABBREVIATIONS

ASIA: American Spinal Injury Association; AIS: ASIA Impairment Scale; CFW: Community Fitness and Wellness; DLPP: Detrusor Leak Point Pressure; EMG: Electromyography; FSF: First Sensation of Fullness; ICS: International Continence Society; ISNCSCI: International Standards for Neurological Classification of Spinal Cord Injury; LE-NMES: Lower Extremity Neuromuscular Electrical Stimulation; MC: Micturition Command; MDP: Maximum Detrusor Pressure; MRI: Magnetic Resonance Imagaing; ND: Normal Desire; Pabd: Intra-abdominal Pressure; Pdet: Detrusor Pressure; Pves: Intra-vesical Pressure; PFP: Peak Flow Pressure; Qura: Urinary Flow; SCI: Spinal Cord Injury; UDS: Urodynamics; VE: Voiding Efficiency

INTRODUCTION

Transverse myelitis is characterized as an inflammatory lesion of the spinal cord that can result in bilateral sensory, motor and autonomic dysfunction [1,2]. The onset of symptoms and signs of transverse myelitis can develop over the course of hours to days and clinically manifest as weakness and/or paralysis, numbness and paresthesias, and notably, bladder and bowel dysfunction. Depending on the lesion level, respiratory and cardiovascular dysfunction may be involved as well. Identifying the etiology of transverse myelitis may be challenging as it can be associated with autoimmune disorders, infectious conditions [viral and bacterial] or even the initial symptom of an underlying central nervous system demyelinating disease. In some cases, the cause is not known and is therefore referred to as an isolated "idiopathic" entity. Although most of the recovery occurs in the first 3 months after onset, long-term outcomes have reportedly been varied from individuals recovering with little to no sequelae, moderate disability [difficulty with ambulation, urinary urgency and/or constipation, partial sensory deficits] to severe disabilities [unable to ambulate, absence of bladder/bowel sphincter control, severe sensory deficits and chronic pain] [3-6]. In some instances, it has been reported that bladder dysfunction persists after complete motor recovery from transverse myelitis and remains one of the most common and disabling consequences post-injury [7,8].

While acutely, transverse myelitis is treated with high-dose intravenous corticosteroids [9]; long-term management focuses on addressing the numerous secondary complications. Spasticity,

pain, autonomic dysfunction and impairments in mobility and gait are some of the major factors associated with diminished quality of life following a spinal lesion [10,11]. Importantly, as with traumatic spinal cord injury [SCI], the rehabilitation model for transverse myelitis has incorporated a multidisciplinary treatment approach, including activity-based restorative therapies.

Neuromuscular electrical stimulation [NMES] is a neurorehabilitative therapy that has been used for a variety of purposes in individuals with SCI, including improving the ability to stand, increasing muscle mass and bone density, facilitating gait, and providing aerobic exercise via leg cycle ergometry [12-16]. NMES may also provide an avenue in which to optimize activity below the lesion level with patterned input that results in improvements to multiple systems, such as bladder and bowel [17] respiratory [18-20] and cardiovascular [21,22]. Thus, targeted neuromuscular stimulation therapy may be used as a tool to help individuals overcome the various deficits produced by a spinal lesion and help maintain the integrity of different systemic functions.

Here, we describe a case of an individual diagnosed with transverse myelitis, who had improvements in multiple bladder parameters and sensation coinciding with activity-based lower extremity NMES [LE-NMES] rehabilitation. Further studies are needed in order to elucidate optimal stimulation parameters and electrode locations that may facilitate improvements in urologic and sensory outcomes following incomplete spinal cord injuries. Systematically monitoring and documenting any changes to autonomic systems, such as bladder, during therapy should also be encouraged. Given that NMES is highly accessible in the clinical setting, future work could inform how NMES therapy is implemented in a broader clinical base.

CASE PRESENTATION

Study design

This is a retrospective case report using medical records data from the University of Louisville and KentuckyOne Health - Frazier Rehab Institute. The individual provided written, informed consent, and the research was approved by the Institutional Review Board [University of Louisville, Louisville, KY].

Case presentation

An otherwise healthy, 45 year old man presented to the emergency room with a sudden onset of chest pain, progressive lower extremity dysesthesias and bilateral leg weakness, which progressed to paraplegia within 24 to 48 hours, in November of 2013. He subsequently developed urinary retention, for which a Foley catheter was placed in the emergency room. He reported that he developed right ear pain 5 days earlier, sought treatment at an urgent care facility and was prescribed the antibiotic Ciprofloxacin and reported this had been taken for 3 days. A complete blood count, liver function tests, coagulation profile, renal function tests, urinalysis, metabolic panel and cardiac chemistries were all within normal ranges. Serological testing ruled out viral infection and cerebrospinal fluid testing revealed no evidence of oligoclonal banding, zero white blood cells and normal protein and glucose levels. Electrocardiogram showed normal sinus rhythm with no acute process or ischemia. A chest x-ray showed no active disease. However, magnetic resonance imaging [MRI] testing of the thoracic spine revealed hyper-intensive cord signal lesions from T4 to T9. Additional MRIs of the brain, cervical and lumbar spines were negative for both intracranial abnormality and abnormal cord enhancement.

An initial inpatient neurological examination revealed he had sensation to pain and temperature above the umbilicus at the T9 level bilaterally. Vibratory sense was moderately reduced on both feet [10/25 seconds on big toe to tuning fork]. Deep tendon reflexes were absent on both upper and lower extremities and there was no response to plantar stimulation on both sides. Motor strength of both the upper extremities was normal and equal. Lower extremity motor strength is indicated in Table 1. Coordination was normal and tested with finger to nose and rapid alternating movements. Cranial nerve function was also intact. Gait was unable to be tested. Given the individual's history, physical examination findings and imaging results, a diagnosis of acute transverse myelitis of the thoracic spinal cord from T4-T9 was made. He was then immediately started on intravenous, high-dose corticosteroids that lasted for 5 days. Additional medications initiated at SCI discharge included Neurontin [gabapentin] for neuropathic pain, Mobic [meloxicam] for inflammation as well as Flomax [tamsulosin] to assist with urination. Flomax was discontinued after inpatient rehab and the individual was not taking any other bladder medication during therapy. He did report that Neurontin was used as needed, occasionally at night before bed, while participating in outpatient rehabilitation.

Clinical evaluation

The individual received a clinical evaluation in order to assess motor and sensory status [Table 1 and Table 2, respectively]. At transverse myelitis onset as well as following outpatient therapy, two physical therapists independently performed the International Standards for Neurological Classification of Spinal Cord Injury [23] in order to classify his injury using the ASIA [American Spinal Injury Association] Impairment Scale [AIS].

Urodynamics evaluation

The urodynamic data were obtained from standard urodynamic evaluations [24] performed annually using the Solar [Medical Measurement Systems [now Laborie, Williston, VT]] urodynamic investigation system. The following uroflow parameters were obtained: maximum flow rate [ml/s], flow time [mm:ss], time to peak flow [mm:ss], pressure [cmH_2O] at peak flow, peak pressure, mean pressure and closing pressure, as well as voided volume [ml] and post void residual volume [ml]. Bladder capacity was calculated as the volume of leaked or voided fluid plus any residual amount removed from the bladder. Voiding efficiency [VE] was calculated as: VE = [volume voided/ [volume voided + residual volume] X 100]. Compliance was calculated by dividing the volume change [ΔV] by the change in detrusor pressure [ΔPdet] during that change in bladder volume and was expressed in ml/cm H_2O [25]. The intra-vesical pressure [Pves] at which involuntary expulsion of water/urine from the urethral meatus was observed was considered the detrusor leak point pressure [DLPP]. Maximum detrusor pressure [MDP]

was identified as the peak detrusor pressure during the voiding phase of the cystometrogram, while peak flow pressure [PFP] was the detrusor pressure at peak flow during voiding. Detrusor pressures were calculated by subtracting the intra-abdominal pressure [Pabd] from the intravesical pressure [Pves].

Neuromuscular electrical stimulation

Electrical stimulation was delivered using the SAGE RT60 stimulator [Restorative Therapies, Inc [RTI], Baltimore, MD] and XCite software to manage stimulation parameters. Pre-gelled skin surface electrodes [PALS® Platinum Neurostimulation Electrodes, Restorative Therapies, Inc] were placed bilaterally on the individual's lower leg muscles [tibialis anterior, gastrocnemius and soleus muscles]. A protocol consisting of: 3000μs pulse width, 100pps pulse rate, 33.3Hz frequency, and 7:6 duty cycle was used for 60 minutes, 5 days/week [completing 64 sessions by the last Urodynamics evaluation]. Stimulation intensity was adjusted to maximize the individual's conscious perception of the stimulation, while remaining below motor threshold. The initial purpose of choosing NMES for this individual was to improve sensation in his lower legs, specifically proprioception and kinesthesia, to improve confidence and safety during ambulation [as he often felt as if his legs could "give out" at any moment] and to return to his prior level of function, which included running, cycling, and recreational tennis. Therefore, NMES intensities were maintained just below the motor threshold. The individual was acclimated to LE-NMES prior to training to find the maximum tolerable level of stimulation. Pulse width and frequency were selected to maximize the electrically evoked sensory volley [26,27].

Therapy progression

The individual's symptoms and paraplegia began to improve daily after he began corticosteroid treatment. By 9 days post-transverse myelitis onset, he was admitted to inpatient physical and occupational therapy and received core and lower extremity strengthening, balance and gait training for approximately 1 month [Table 3]. He was able to ambulate 10-12 feet with Maximum Assistance of two people and a rolling walker at admission to inpatient rehab. By discharge, he was able to ambulate 300 feet with Modified Independence and a rolling walker. However, he continued to have partial urinary retention with decreased awareness of the need to empty his bladder and reduced or altered sensation for light touch, pain and temperature to bilateral lower extremities. He later transitioned to outpatient physical therapy beginning December 2013 [Table 3]. Upon examination, he still presented with gait deviations, difficulty with transfers and impaired standing balance. Outpatient therapy also consisted of both locomotor step and stand training [LT] [with and without body-weight support, described most recently in [28]] as well as over-ground gait training and other activity-based tasks. By April of 2014, he regained independent walking without an assistive device. He was then discharged from outpatient therapy for 17 months due to limited approved insurance visits for outpatient therapy. Given the individual still had lower extremity deficits, he was able to resume outpatient therapy in September of 2015 with goals of improving sensation in his lower legs, specifically proprioception and kinesthesia, as well as confidence and safety during ambulation. LE-NMES was initiated while the individual performed challenging dynamic standing and walking tasks over a variety of surfaces.

During LE-NMES therapy, he began to notice marked improvements in bladder function, reporting decreased post-void residual volumes as well as sensory changes, including the ability to distinguish hot versus cold sensations in the lower extremities. The individual initiated a journal noting these urological and sensory changes. Approximately one month later, he was discharged from outpatient NMES therapy after meeting all therapy goals [reducing fall risk] and reaching a plateau in functional recovery. Following outpatient therapy, he continued the same LE-NMES protocol in a community-based fitness and wellness center where he experienced further gains in urologic and sensory function as evidenced by the ISNCSCI [Table 1 and 2], Urodynamic, and uroflow [Table 3] evaluations.

Bladder

The individual presented at the Urology clinic due to incomplete emptying of the bladder 5 months post-transverse myelitis onset. Upon his initial examination in 2014, perineal sensation was diminished [per straight catheter] at S2-S4 and he was unable to void on the initial pressure flow study. Cystometry revealed delayed sensations of filling, but no involuntary detrusor contractions were present. His bladder capacity [500ml] [Figure 1A] was within established normal ranges for adults [29], but he was only able to partially empty his bladder [Figure 1C]. His bladder pressure was also elevated above the recommended standards for detrusor leak point pressure guidelines [<40cmH_2O] [30,31] [Figure 1B]. Following the evaluation, the individual was instructed to continue void attempts as well as perform clean intermittent catheterizations to ensure his bladder was emptied completely.

Precisely 12 days after initiating LE-NMES therapy, the individual began to notice improvements in his post-void residual volumes and documented this in his journal. The April 2015 follow-up Urodynamics assessment and renal ultrasound [US] procedures demonstrate the following objective findings. During catheter placement, it was noted that perineal sensation was intact. Cystometry testing revealed delayed sensations of bladder filling and detrusor instability. Involuntary, uninhibited detrusor contractions were present, but did not result in incontinence. Bladder capacity reached 439ml and voiding efficiency doubled [71.5%] since he was last examined [Figure 1A, C]. However, his maximum detrusor pressure during the filling and voiding cycles was elevated [76 and 149 cmH_2O, respectively]. During this second Urodynamics assessment, his baseline, pre-fill pressure was at 17 cmH_2O and overall compliance was low [9.5 ml/cmH_2O], thus demonstrating poor bladder compliance [32,33]. A bilateral renal US, performed at this time point, was unremarkable, showing normal kidney size and negative for hydronephrosis, shadowing calculi, masses, cysts or cortical loss.

His third annual Urodynamics assessment [April 2016] showed an awareness of bladder filling sensations [first sensation of fullness [FSF], 291 ml; normal desire [ND], 314ml; Urgency, 334ml] at a lower volume of infused water compared to his prior two studies [Figure 2]. Relative to his bladder capacity volume [376 ml], first sensation of filling was apparent

Table 1: ISNCSCI Motor Scores.

Exam Date	Hip Flexors [L2]		Knee Extensors [L3]		Ankle Dorsiflexors [L4]		Long Toe Extensors [L5]		Ankle Plantarflexors [S1]		VAC
	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Y/N
11/19/2013	2	4	4	4	2	4	2	4	2	4	Y
12/09/2013	4	4	5	5	5	5	5	5	4	5	Y
02/08/2016	5	5	5	5	5	5	5	5	5	5	Y

ISNCSCI: International Standards for Neurological Classification of Spinal Cord Injury; L: Lumbar level; Lt: Left; Rt: Right; N: No; S: Sacral Level; VAC: Voluntary Anal Contraction; Y: Yes; Motor Scoring: 5= Active movement, against full resistance; 4= Active movement, against some resistance; 3= Active movement, against gravity; 2= Active movement, gravity eliminated; 1= Palpable or visible contraction; 0= total paralysis; NT= Not Testable

Table 2: ISNCSCI Sensory Scores.

Light Touch	L2		L3		L4		L5		S1		S2		S3		S4-5		DAP
	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Y/N
11/19/2013	2	2	1	2	1	1	1	1	1	1	1	1	2	2	2	2	Y
12/09/2013	1	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1	Y
02/08/2016	1	1	2	2	1	1	1	1	1	1	2	2	2	2	2	2	Y
Pin Prick	**L2**		**L3**		**L4**		**L5**		**S1**		**S2**		**S3**		**S4-5**		
	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	
11/19/2013	0	0	0	1	0	0	0	0	0	1	0	0	1	1	0	1	
12/09/2013	1	1	1	1	1	1	0	1	1	1	1	0	1	1	0	0	
02/08/2016	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	

DAP: Deep Anal Pressure; ISNCSCI: International Standards for Neurological Classification of Spinal Cord Injury; L: Lumbar level corresponding dermatome; Lt: Left; Rt: Right; N: No; S: Sacral level corresponding dermatome; Y: Yes. Sensory Scoring: 0= Absent; 1= Altered; 2= Normal; NT=Not Tested.

Table 3: Therapy Progression.

	SCI	Inpatient Rehab	Outpatient LT	Outpatient LE-NMES	CFW
Time Period	11/6/2013	11/15/13 - 12/10/13	12/16/13 - 4/8/14	9/3/15 - 10/8/15	10/13/15 - 11/23/16
Functional Outcomes	Non-ambulatory	Ambulatory with Max A x 2 to Mod I with walker	Mod I to Independent [no device]	Sensory & Bladder Improvements	*Continued Sensory & Bladder Improvements
Bladder Management	Foley catheter	Intermittent self-catheterization	Voiding + self-catheterization	Voiding + self-catheterization	Voiding + self-catheterization
Uroflow Parameters			April 2014 UDS	April 2015 UDS	April 2016 UDS
Maximum Flow Rate [ml/s]			2.4	9.5	9
Flow Time [mm:ss]			4:17	5:21	1:27
Voiding Time [mm:ss]			16:58	16:06	1:38
Time to Peak Flow [mm:ss]			16:28	14:01	10:15
Pressure @ Peak Flow [cmH20]			52.5	67.6	19.0
Peak Pressure [cmH2O]			106.0	149.0	65.0
Mean Pressure [cmH2O]			20.6	15.9	8.0
Closing Pressure [cmH2O]			35.0	12.7	8.0
Voided Volume [ml]			12.0	314.0	339.0
Post Void Residual Volume [ml]			320.0	125.0	37.0

CFW, Community Fitness and Wellness Center; LE-NMES, Lower Extremity Neuromuscular Electrical Stimulation; LT, Locomotor Training; Max A x 2, Maximum Ambulatory Assistance with 2 people; Mod I, Moderately Independent; UDS, Urodynamics.*Continued sensation improvements noted until 2/21/2016 ["urge to void noted at lower sensory level"].
Data collection stopped at 2/25/2016.

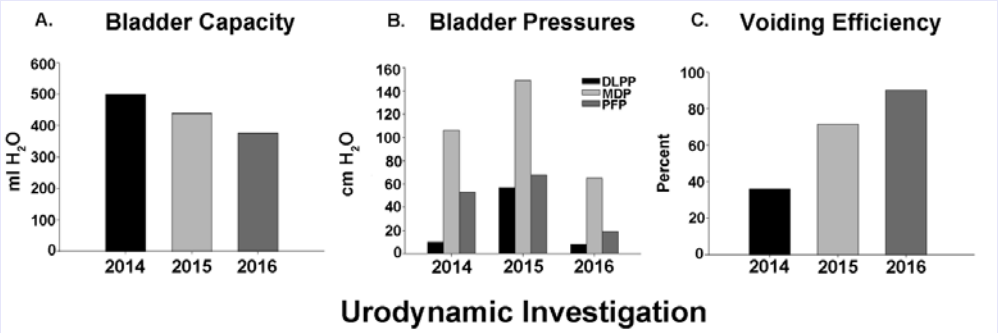

Figure 1 Urodynamic Parameters: Bladder capacity, pressure and voiding efficiency values were tracked over 3 annual time points following the individual's transverse myelitis diagnosis. A. Bladder capacity decreased slightly over time, but still remained within the International Continence Society [ICS] recommended guidelines for normal bladder capacity [30]. B. Bladder pressure [detrusor leak point pressure [DLPP], maximum detrusor pressure [MDP], and peak flow pressure [PFP]] declined to safer values for the upper and lower urinary tract by 2016 [30, 31]. C. Voiding efficiency reached a value within established ICS guidelines of >90% or having less than 25ml post-void residual volume [30].

at 77% of his maximum bladder capacity. He still had detrusor instability and involuntary contractions were identified near bladder capacity, but did not result in incontinence. Importantly, the individual's voiding efficiency increased 2.5 times greater than his initial Urodynamics assessment and reached a value within normal limits [>90%] [30] [Figure 1C]. His peak bladder pressure also decreased to 19 cmH_2O during voiding [Fig.1B] and bladder compliance improved to 51.4 ml/cmH_2O since the 2015 assessment. While bladder capacity slightly decreased overtime, this change likely reflects his ability to voluntarily void, thus conveniently emptying his bladder more often, versus reliance on catheterization and the possibility of over-distention. The follow-up renal US at this time point was also unremarkable with no changes from his last examination in 2015.

Accurate uroflow assessments were also performed at each time point as an overall screening of his lower urinary tract dysfunction. Once the individual was at maximum bladder capacity during cystometry, a successful uroflow was achieved in each instance [Table 3]. For all Urodynamic assessments, the peak flow rate, typically considered a reliable factor in determining abnormal voiding [34], was below normal values [>19 ml/sec for males 40-60 years old] [35] [Table 3]. While flow time [time over which measurable flow occurs] decreased by the third study, it comprised the majority of the voiding time frame, suggesting little delay in bladder emptying. The flow pattern from the initial and second study was intermittent, while the pattern in the third study was continuous, represented by a smoother, bell-shaped curve. A quick spike was noted at conclusion of the uroflow, but is most likely representative of a terminal bladder spasm to rid residual volume versus abdominal straining, as the abdominal channel [Pabd] appears quiescent post-void [Figure 3].

In addition to his personal journal, the individual documented fluid intake and output as well as aspects of bladder management in a standard voiding diary by the American Urological Association [36]. Overtime, his voluntary voids were more frequent, and void volumes became greater than catheterized volumes. However, nocturia was still present at 7 months into LE-NMES treatment. It is unclear if this reflects SCI-induced polyuria [overproduction of urine, commonly seen in SCI individuals [37,38]] or is due to fluid intake 1-2 hours prior to sleeping, as recorded in the bladder diary.

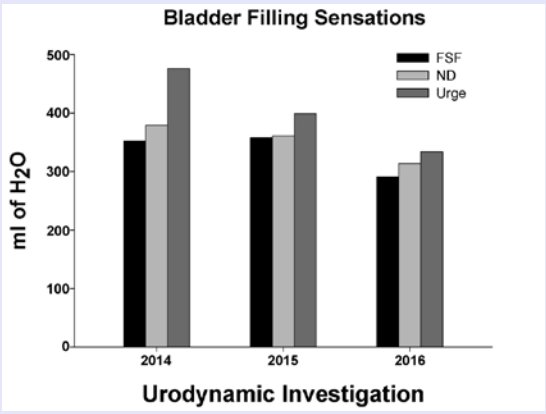

Figure 2 Documentation of Bladder Sensation During Filling Cystometry: The first sensation of fullness [FSF], normal desire [ND], and Urgency were noted at each Urodynamics time point as indicators of the individual's sensation to void at various levels of bladder fullness. Note that these descriptors are subjective and can be influenced by stress or anxiety, but FSF is typically felt at approximately 90-150ml, with a normal desire to void at 200-400ml and a strong urge at 300-600ml [32]. By 2016, the first awareness of bladder filling was considered delayed as it relates to approximate values.

Sensation

The individual demonstrated improvements in light touch at S2 and pinprick sensation at S2 and S4/5 [Table 2]. However, he did not achieve "intact" sensation, as defined by ISNCSCI standards, throughout all regions or even all regions treated with LE-NMES. The shaded areas in Table 2 demonstrate improved sensation determined by increased sensory scores at the final evaluation in 2016 as compared to both prior exams. During outpatient therapy, he logged sensory changes in a personal journal. Precisely 8 days after initiating LE-NMES therapy, he noted increased "sensitivity" to cold sensations, evidenced by decreased tolerance to ice baths from 20-25 minute lower extremity submersions to only 15 minutes. By 2-3 months into training, the application of ice was noted as "very cold and

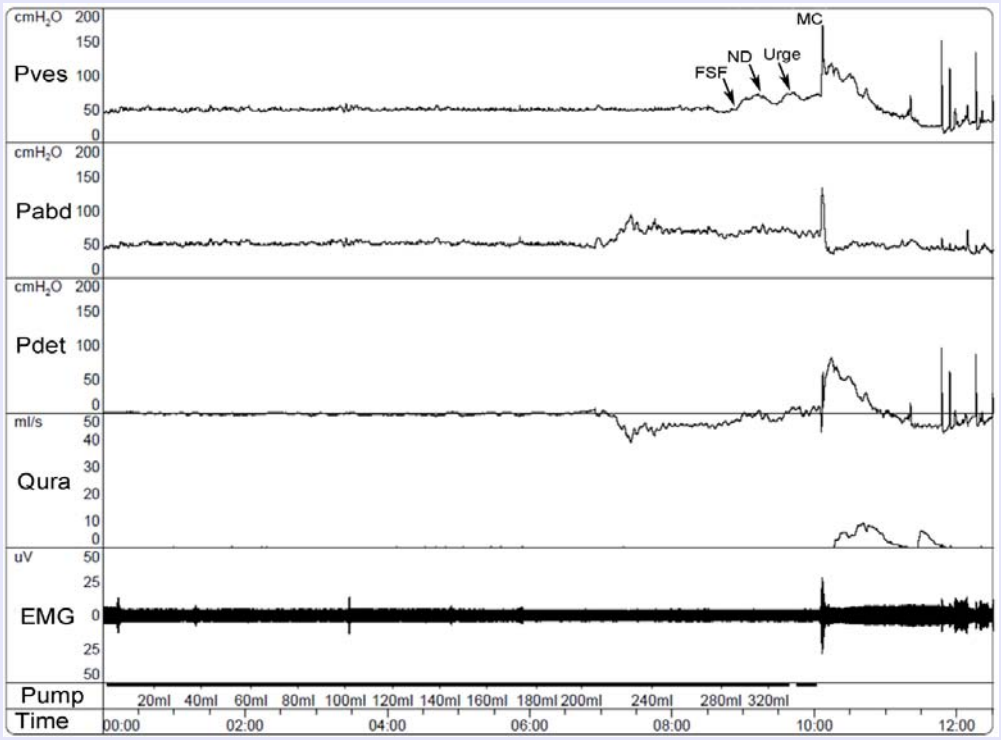

Figure 3 2016 Cystometrogram: A #7 French, air-charged, single lumen catheter,was used to infuse sterile water at a medium fill rate. Intravesical pressure [Pves], was recorded. A rectal catheter [Pabd] was placed to monitor abdominal pressure. The difference between Pabd and Pves is the actual detrusor pressure [Pdet]. First sensation of bladder filling [FSF] was noted at 291ml, normal desire [ND] at 314ml, and Urgency at 334ml. Micturition command [MC] was given once the individual reached capacity [360ml]. Measurement of urinary flow [Qura] demonstrates onset at MC. Electromyography [EMG] indicates a rise in activity just prior to void with relaxation during the void.

unpleasant". Other temperature changes documented at around 1 month into therapy were being able to distinguish the difference between a hot cup of coffee versus a cold beer when placed on the thighs and that the outdoor temperature felt cold when wearing shorts. Importantly, by about 4 months into LE-NMES treatment [between the second and third Urodynamics assessments], the individual reported he was able to feel sensations in the urethra such as, "burning and awareness of the need to go". Prior to these new sensations of bladder fullness, he would either void and/or catheterize by the clock [about every 4 hours] to avoid bladder over-distention or he would time bladder emptying prior to a long drive or work event. At this same time point, the individual noted that as he started an LE-NMES session, he would feel an urge to empty his bladder. He also recorded that as he would run his fingers down the medial aspect of his lower legs, this maneuver would trigger successful urination.

DISCUSSION

This case study presents a possible relationship between LE-NMES treatment and improvements in bladder function and lower extremity sensation. The strongest argument for this relationship is that the individual first noticed improvements in sensation and bladder function [8 and 12 days, respectively] after initiation of LE-NMES. The individual maintained a journal throughout his entire rehabilitation process, and even though he may have been biased to hope for improvement with each new intervention he experienced, journaling was something he had done consistently and was not an isolated activity during LE-NMES treatment alone.

NMES interventions, often combined with a specific functional task, have been shown to improve peripherally related motor outcomes in SCI individuals, such as: [i] increasing muscle mass [13, 39-41], [ii] preventing muscle atrophy [12,13], [iii] improving venous return [42] and [iv] facilitating standing and stepping [43-45]. Secondary benefits to autonomic systems, such as cardiopulmonary function, have also been reported [21,46-48]. NMES therapy is conventionally delivered at constant frequencies between [15-50 Hz] and with a shorter pulse width [50-400 μs], which recruits motor axons preferentially to sensory axons. The nerve fiber recruitment pattern elicited by NMES differs from physiologic mechanisms, which recruits the smallest-diameter neurons prior to larger-diameter fibers [49]. As a result, a commonly reported limitation of NMES therapy is excessive neuromuscular fatigue [50,51]. In order to offset this outcome, but also to preferentially target sensory afferents, a longer-pulse width was employed with the individual's rehabilitation. Longer pulse durations have been shown to depolarize sensory fibers more effectively, largely attributed to the lower rheobase of sensory fibers as compared to motor fibers [52-54]. Long-pulse width parameters have also been used successfully in SCI individuals to produce prolonged motor activity [55,56]. This stimulation parameter emphasizes a "central torque effect," which is thought to maximize the sensory volley to the spinal cord and thus the synaptic recruitment of motoneurons, leading

to a prolonged discharge with increased H-reflex amplitude [57]. The therapeutic implications for longer pulse durations may help individuals sustain longer lasting movements during therapy as well as reduce muscle atrophy by recruiting muscle fibers not typically activated by NMES. This approach may help prevent the SCI induced muscle fiber alterations that commonly lead to rapid muscle fatigability encountered during rehabilitation efforts [26,58].

Given that the individual had recovered lower extremity motor function, the goal of his NMES therapy was to enhance neural plasticity by augmenting existing sensorimotor activation in a task-specific manner in order to facilitate sensory function improvements. By incorporating functional tasks typically encountered in daily life, such as standing over different surface types, we could further promote functionally relevant afferent input to the nervous system. ISNCSCI sensory scores were utilized to objectively support the individual's subjective reports of improved sensation. The authors realize that monofilament testing would have been a more sensitive measure of sensory improvements, however, this case study is retrospective and assigned outpatient therapists did not perform such assessments during the individual's therapeutic progression. The ISNCSCI exam was not performed on a routine basis while the individual was receiving different bouts of outpatient therapy. One of the authors, [KO], performed his third and final ISNCSCI exam while he was participating in CFW LE-NMES training, as his most recent exam occurred upon discharge from inpatient rehab. These authors consider a certain spinal level sensory score to be "improved" if the final score increased compared to the first two scores [because these exams were completed within 1 month of each other and not while the individual was receiving LE-NMES treatment]. Improvements in sensation and tactile awareness may also be expected in this case as sensory fibers are stimulated in addition to motor fibers. In a study assessing hand use in chronic incomplete SCI individuals, NMES therapy was paired with specific task training and resulted in improvements in not only upper extremity functional tasks and strength, but also in sensory scores [59].

Various modes of electrical stimulation have also been used over the years to treat different lower urinary tract dysfunctions. In contrast to more invasive surgical techniques [60,61], bladder activity can be modulated through functional electrical stimulation. Stimulation of larger diameter tibial nerve fibers has been shown to modulate bladder reflex activity, producing an inhibitory effect on the bladder, thus decreasing urinary urgency, frequency and incontinent episodes [62-65]. Further, pudendal afferents can be activated with surface electrodes as a way to suppress bladder over-activity [66-71]. Various animal models have demonstrated that activation of the pudendal circuitry can result in inhibition of reflex bladder contractions and result in increased bladder capacity [72-75].

Although, the mechanisms associated with the progressive bladder recovery shown here are not entirely known, the central activation and excitation driven by the longer-pulse LE-NMES parameters may influence the neural output to the detrusor muscle, causing a more sustained contraction compared to quick bursting contractions, typical of hyperreflexia that would limit bladder emptying. Modulation of reflex mechanisms controlling micturition can arise from spinal convergence of somatosensory input leading to a suppression of the bladder guarding reflex, resulting in improved voiding efficiency. The bladder is also a unique visceral organ in that, in addition to various reflex mechanisms that exist to modulate both the storage and voiding phases [76], it also exhibits predominately voluntary regulation, unlike other visceral organs such as the heart and gastrointestinal tract, which receive tonic neural control. The ability to "turn on" the bladder is facilitated by an amplification of sensory afferent activity, such as fullness and discomfort, which is sufficient enough to initiate effective bladder emptying [77]. In this case, bladder afferent information that travels in autonomic and somatic nerves as well as sensory afferent input from LE-NMES traveling in branches of the sciatic nerve arrives at overlapping spinal regions. Thus, it is possible that electrical stimulation of peripheral tissue projecting to the same lumbosacral spinal segments as those innervating the bladder and urethra, along with descending drive from a conscious desire to void, facilitate synergistic coupling of detrusor and sphincter activity.

A degree of overall neurologic recovery of systems is also expected after transverse myelitis, as individuals with even severe sensorimotor loss can achieve a partial or almost complete recovery, especially if there is some retention of neurological function below the level of injury [78]. As spontaneous recovery may be considered an underlying component in this case, it is important to note that the individual experienced improvements in bladder and lower extremity sensation just days after initiating LE-NMES. Thus, optimizing the therapeutic environment post-injury to promote adaptive changes can help maximize recovery potential. The ability to target neural pathways involved in the micturition cycle is an attractive alternative to the more invasive implantable devices for bladder function, which oftentimes require surgical denervation, abolishing important sensory and genital reflexes. The integration of sensorimotor activity at the level of the lumbosacral cord may be an important factor influencing the urological and sensory changes in this case report.

The clinical applications of rehabilitation strategies in both traumatic and non-traumatic SCI have shifted away from a focus on compensation strategies and towards approaches that can activate the nervous system in order to optimize function and recover abilities thought to be lost as a result of injury. Given that NMES therapy is clinically accessible, an improved understanding of parameters facilitating autonomic and sensory changes is needed. Additional factors to address relate to the long-term effectiveness following the discontinuation of therapy and whether or not a type of home-accessible unit can be applied.

This case report does have limitations, as no controls were utilized to assess the rate or degree of recovery of bladder function without the use of LE-NMES in transverse myelitis. From a validity and reliability perspective, the urinary outcome measures, are considered the gold standard of assessing bladder function within the field of urology [24,79]. However, sensory monofilament testing was not available pre-LE-NMES therapy and thus a more quantitative assessment of the individual's sensory improvements was not possible. In addition, the use of a questionnaire validated in SCI [80] to directly measure the impact

of bladder dysfunction on quality of life will help develop a better understanding of the correlation between urinary symptoms and health-related aspects of life satisfaction.

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