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CLINICAL NOTES
Spinal Myoclonus After Spinal Cord Injury

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Abstract

Background/Objective: In the course of examining spinal motor function in many hundreds of people with traumatic spinal cord injury, we encountered 6 individuals who developed involuntary and rhythmic contractions in muscles of their legs. Although there are many reports of unusual muscle activation patterns associated with different forms of myoclonus, we believe that certain aspects of the patterns seen with these 6 subjects have not been previously reported. These patterns share many features with those associated with a spinal central pattern generator for walking.

Methods: Subjects in this case series had a history of chronic injury to the cervical spinal cord, resulting in either complete (ASIA A; n = 4) or incomplete (ASIA D; n = 2) quadriplegia. We used multi-channel electromyography recordings of trunk and leg muscles of each subject to document muscle activation patterns associated with different postures and as influenced by a variety of sensory stimuli.

Results: Involuntary contractions spanned multiple leg muscles bilaterally, sometimes including weak abdominal contractions. Contractions were smooth and graded and were highly reproducible in rate for a given subject (contraction rates were 0.3–0.5 Hz). These movements did not resemble the brief rapid contractions (ie, "jerks") ascribed to some forms of spinal myoclonus. For all subjects, the onset of involuntary muscle contraction was dependent upon hip angle; contractions did not occur unless the hips (and knees) were extended (ie, subjects were supine). In the 4 ASIA A subjects, contractions occurred simultaneously in all muscles (agonists and antagonists) bilaterally. In sharp contrast, contractions in the 2 ASIA D subjects were reciprocal between agonists and antagonists within a limb and alternated between limbs, such that movements in these 2 subjects looked just like repetitive stepping. Finally, each of the 6 subjects had a distinct pathology of their spinal cord, nerve roots, distal trunk, or thigh; in 4 of these subjects, treatment of the pathology eliminated the involuntary movements.

Conclusion: The timing, distribution, and reliance upon hip angle suggest that these movement patterns reflect some elements of a central pattern generator for stepping. Emergence of these movements in persons with chronic spinal cord injury is extremely rare and appears to depend upon a combination of the more rostrally placed injury and a pathologic process leading to a further enhancement of excitability in the caudal spinal cord.

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Key Words: Spinal cord injuries; Spinal myoclonus; Spasticity; Spinal central pattern generator; Electromyography

INTRODUCTION

The cat's lumbosacral spinal cord includes all the necessary circuitry for the generation of rhythmic, alternating stepping movements of the hind limbs, in the absence of supraspinal control (1–3). This circuitry is often referred to as the central pattern generator (CPG). Properties of this CPG can be influenced by afferent feedback (4–6), pharmacologic manipulation (6–9), and electrical stimulation of brainstem regions (2,10,11). Activity-specific training can also influence stepping probability in the spinalized cat (7,12) and rat (13) hind limb. This approach is the basis for a number of clinical studies using a combination of body weight support and treadmill locomotion to improve walking ability in persons after traumatic spinal cord injury (SCI) (14–19).

In spite of these clinical initiatives, absolute proof for a CPG in humans remains elusive (20). Several inves-

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tigators have described rhythmic contractions and/or stepping-like leg movements brought about by continuous electrical stimulation of the lumbosacral spinal cord in the adult human (21–23), but results do not necessarily reflect the action of an intrinsic CPG for stepping (24,25). Stimulus-conditioning reflex studies in persons with chronic SCI support the existence of a central pattern generator (26,27), as do split-treadmill studies in infants (28), but neither have demonstrated this CPG acting independently or spontaneously.

Spontaneous and involuntary contractions of abdominal, paraspinal, and lower limb muscles in persons with SCI (29–32), spinal cord tumors (33,34), or other spine disorders (35–37) have been reported as examples of spinal myoclonus. In an earlier publication, we described involuntary rhythmic, alternating stepping movements in the legs of a person with chronic SCI; we suggested that these movements could reflect the action of a CPG for stepping (38). We now add to this single case report the findings from studies of an additional 5 subjects who share many or all of the same properties as described previously (38). Factors common to all subjects include a history of chronic cervical SCI and a significant pathologic condition affecting the low back, hips, thigh, or spinal cord. These additional clinical data allow us to address the following question: "Do such movements also fall into the category of spinal myoclonus?"

MATERIALS AND METHODS

The findings from 6 subjects presented herein emerged from electrophysiologic studies of many hundreds of subjects with chronic SCI, in which we concentrated on plasticity of motor function caudal to the region of injury. Each of the 6 subjects studied had reported episodes of involuntary and rhythmic leg movements, and at the time these movements began, all but one described their level of spasticity as being the worst he or she had ever had. Typically, subjects wanted to know why the leg movements had started and whether or not we could do anything for them to reduce their spasticity. Therefore, there were no formal inclusion criteria other than a history of involuntary spontaneous and rhythmic leg movements. The study protocol was approved by the University of Miami Institutional Review Board, and all subjects signed an informed consent prior to examination.

Subjects were examined on a treatment table or dental chair, beginning in a seated posture with hips flexed (~110°) and knees extended (between 170° and 180°). After cleaning (alcohol) and abrading the skin, pairs of self-adhesive gel surface electrodes (S'Offset, Graphic Controls, Buffalo, NY) were positioned (3–5 cm apart) over multiple muscles bilaterally. Muscles were selected to represent major flexors and extensors of the hip, knee, and ankle bilaterally. These always included the psoas (hip flexors), quadriceps (knee extensors); hamstring (knee flexors), tibialis anterior (TA) (ankle flexors), and soleus (ankle extensors) muscle groups. Additional muscles examined in some cases included abdominals, paraspinals, gluteal, and hip adductors. All electrodes for each subject were placed by the author. Electromyography (EMG) was amplified (2024F, Intronix Technologies, Bolton, Ont., Canada; gain = 1K or 10K), filtered (100–5,000 Hz), and stored on digital tape (Vetter 4000 AS) for later analysis. All waveforms were monitored both audibly (Rane SM26B splitter to Yamaha MS101 speaker/monitor) and visually (Toshiba T6400 laptop and RC Electronics Computerscope, Santa Barbara, CA) during recording sessions. In one subject, an electroencephalogram (EEG) was recorded with paste-filled disc surface electrodes using the same Intronix amplifiers but different filter and gain settings (gain = 100K; 0.5–100 Hz).

For all subjects, electrical stimulation pulses were delivered to the skin in an attempt to influence movements. A Grass S88 stimulator coupled to an SIU5 stimulus isolation unit was used to deliver stimulation through a pair of self-adhesive surface electrodes (Cleartrace, Conmed, Utica, NY). Stimulus sites included both the plantar and the dorsal surface of each foot (electrodes about 5 cm apart) and the abdomen (pair of electrodes ~5 cm lateral to the umbilicus on both left- and right-hand sides; stimulation was applied to one side at a time). Trains of square-wave, constant-voltage stimulus pulses were used (150 V, 1-ms duration). Within a train, stimulus rates were 500 Hz. Train duration varied from as few as 3 pulses to as many as 25 pulses.

After electrode placement, subjects were asked to attempt an isolated voluntary contraction in each of the muscles being examined. The seatback upon which the subjects were reclining was then lowered, bringing subjects to a supine position with hips extended to approximately 180°. Spontaneous activity was recorded with subjects lying in this position for a period of 10 to 20 minutes. Next, various manipulations and sensory inputs were examined for their effect on EMG activity. Joint movements (one limb at a time) were imposed at the hip, knee, ankle, and toes, with testing applied to both lower limbs. Other sensory inputs to the abdomen, legs, and feet included (a) gentle skin stroking with a blunt wooden probe to the plantar and dorsal surfaces of the foot, the circumference of the shank, the medial, lateral, and ventral surfaces of the thigh, and the abdomen; (b) vibration (Ling Dynamic Systems 203, 80 Hz, ± 2-mm displacement) of the plantar surface of the great toe, the Achilles tendon, the patellar tendon, and the abdomen; (c) rubbing with ice over the same distribution as for skin stroking; and (d) electrical stimulation (sites and parameters described above). Sensory testing was applied bilaterally in all cases, one side at a time.

Reflective markers were positioned at the hip, knee, and ankle on the right leg of one subject who demonstrated bilateral stepping movements of her legs. For kinematic analysis of joint angles, a video recording was made of leg movements under different conditions of

Table 1. Characteristics of 6 Patients with Spinal Myoclonus

Subject #	Age (y)	Sex	SCI Level	ASIA Score	Movement Types	Pathology	Treatment
1	25	M	C5/C6	A	Simultaneous	C6-L1 SC syrinx	Surgery: shunted cyst, SC untethering, and duraplasty
2	28	M	C4/C5	A	Simultaneous	HO in R hip; resected	None attempted
3	33	M	C5/C6	A	Simultaneous	L5/S1 HNP and stenosis	Surgery: laminectomy, diskectomy, and fusion
4	22	M	C4/C5	A	Simultaneous	Bilat ischial flaps post-PU	None attempted
5	37	M	C5/C6	D	Reciprocal and alternating	R hip OA and subluxation	Rest
6	56	F	C6/C7	D	Reciprocal and alternating	Strained L hamstring	Ice, rest

SC = spinal cord, HO = heterotopic ossification, HNP = herniated nucleus pulposus, OA = osteoarthritis, PU = pressure ulcer.

activation. Joint angles were determined in frame-by-frame analysis of this video record (SMART System Pro, Enterprise Consulting Inc, Norwood, Massachusetts) for 12-second periods of leg movements.

EMG records were acquired via Computerscope (RC Electronics) and analyzed for interburst interval, using cursers positioned at successive activity peaks of whichever muscle demonstrated the best-defined onset and offset of activity. At least 30 seconds of rhythmic contractions were examined for determining the average interval between bursts.

RESULTS

The 6 subjects' characteristics are summarized in Table 1: (a) clinical injury level, (b) neurologic status (ASIA scale) at time of testing, (c) description of muscle movements within a limb (agonists/antagonists recruited simultaneously vs in a reciprocal manner) and between limbs (left- and right-leg muscles activated simultaneously vs in an alternating manner), (d) site of identified pathology believed to be contributing to leg movements; and (e) treatment (if attempted) that led to cessation of the involuntary movements. All had sustained traumatic injury to the cervical spinal cord at least 3 years prior to examination. Based on the International Standards classification (39), subjects 1 to 4 were ASIA A. Subjects 5 and 6 were neurologically incomplete (ASIA D) and capable of limited independent ambulation. Note that other findings from subject 5 were featured in a prior publication (38). We compare features of his findings to those of others included within this report.

Subject Characteristics

Beyond a common history of cervical SCI, each of the 6 subjects had additional pathology that we feel contributed to the expression of leg movements. This pathology was known at the time of testing in subjects 2, 4, and 6 and had not yet been discovered when testing subjects 1, 3, and 5.

One week after subject 1 was examined, magnetic resonance imaging MRI revealed a spinal cord syrinx extending from vertebral C6 down to T12 (ie, ~S1 neurologic level). Surgical treatment (Table 1) eliminated the rhythmic leg movements.

At some point (timing uncertain) after his SCI, subject 2 had developed severe heterotopic ossification of the right hip. This was treated with surgical resection of the acetabulum, resulting in a 3-inch length difference between legs. According to the subject, rhythmic leg movements developed several months after his surgery to the hip and had persisted for a period of more than 2 years, occurring whenever he fully extended his hips.

Within days of examining subject 3, we found him to have a herniated disk at L5/S1, with bilateral compression of the nerve roots and thecal sac. After surgical decompression (laminectomy, discectomy, and fusion with pedicle screw instrumentation), the involuntary leg movements ceased.

Shortly after his spinal cord injury, subject 4 had developed bilateral grade IV pressure ulcers on his sacrum, which were repaired surgically. There was extensive scar tissue and atrophy around his pelvis and gluteal surfaces. He reported that his involuntary leg movements developed some months after his surgical treatment of the pressure ulcers and could be reliably brought on by fully extending his hips.

A detailed history of subject 5 is provided elsewhere (38). Briefly, he developed involuntary stepping-like movements within a week of beginning an intensive exercise program at 17 years post injury, which included prolonged periods of standing and walking. Radiologic examination of his right hip revealed arthritic degeneration and subluxation. Involuntary stepping was interrupted for approximately 20 minutes after infusion of his

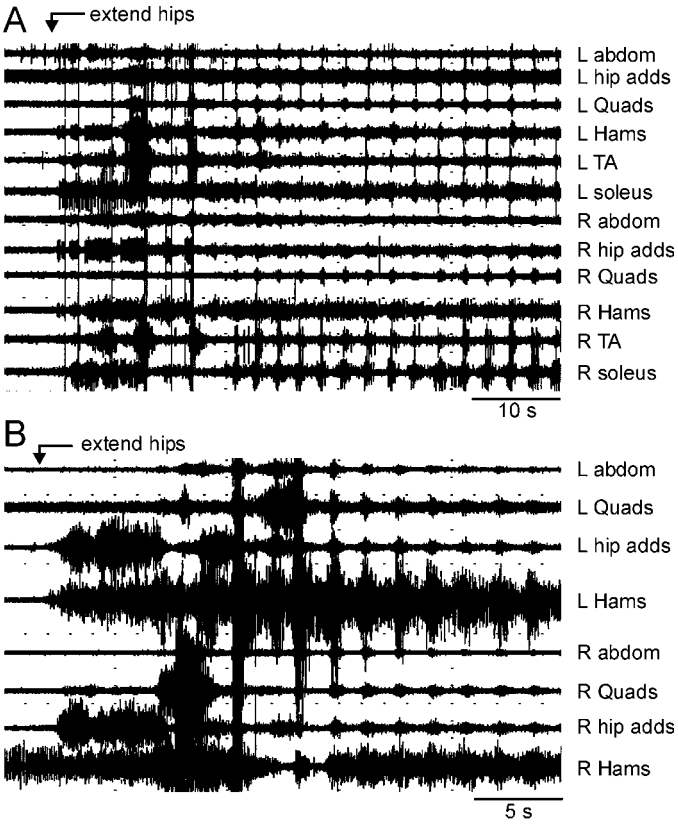

Figure 1. EMG records from multiple muscles in subjects 2 (A) and 4 (B). Recordings began while both subjects were in a seated position; then the chair back was lowered (vertical arrows), causing hip extension and an assumption of a supine posture. In each case, the early stages of repositioning elicited a strong spasm, which evolved into rhythmic contractions across most or all of the muscle groups illustrated. Note the different time scales for the 2 panels.

Abdom (abdominal), psoas (hip flexor), hip adds (hip adductor), quads (quadriceps, knee extensor), hams (hamstring, knee flexor), TA (tibialis anterior, ankle flexor), soleus (ankle extensor).

right hip capsule with lidocaine, confirming a role of afferent input from his hip in mediating these stepping movements. His involuntary stepping movements ended entirely about 2 weeks after he discontinued his daily exercise routine.

At the time of examination, subject 6 had recently sustained an acute strain in her left hamstring brought on by walking in a training-related study. This injury caused her considerable pain and a sense of "tightness" in the back of her left thigh. Despite this injury, this subject denied any significant exacerbation of her spasticity. She went for a 5-day period without any further walk training and frequently applied ice to her sore thigh. With a reduction in pain, the subject resumed her walk training, and involuntary stepping movements did not recur.

Movement Characteristics

None of the subjects had experienced spontaneous rhythmic leg movements while seated in wheelchairs. However, lowering the back support of the examination surface to put subjects in a supine position (ie, extending their hips) resulted in an immediate onset of rhythmic involuntary contractions of lower limb (always) and abdominal muscles (sometimes) in 5 of the 6 subjects examined. Figure 1 shows examples from subjects 2 (top A) and 4 (bottom B). Because the hips were extended from sitting to lying, there was a marked increase in EMG activity within multiple muscles of both subjects. This activity evolved over a period of seconds into simultaneous, rhythmic, and bilateral contraction/relaxation cycles in multiple muscles. Sometimes this waxing and waning of muscle activity was superimposed upon tonic muscle activity (eg, L Hams record of Figure 1B). During the peak of contractions, the legs of subjects 2 and 4 appeared to stiffen, but joint angles at the knee and ankle did not change appreciably, because both joints were already extended. There was also slight internal rotation at the hips in both subjects. There was no reciprocal organization of agonist vs antagonist muscles in the same limb. In fact, nothing about the limited leg movements caused by these contraction patterns resembled stepping movements of the legs, except for the highly reproducible period and rate of contractions. Because of the limited angular joint excursions caused by these rhythmic contractions, video analysis of these movements in subjects 1 to 4 was not carried out.

Once these movements had started, different forms of sensory stimulation sometimes modulated the amount of EMG activity for a given burst but were not effective in eliminating the pattern. An example of short-term influence of electrical stimulation on the involuntary movement pattern is illustrated in Figure 2. The upper records (Figure 2A) show an example of spontaneous, bilateral, and simultaneous contractions in leg and trunk muscles, in this case from subject 3. We found that this pattern could be interrupted by a brief, high-frequency train of electrical pulses applied to this subject's right-side abdomen, provided stimulation occurred just prior to or during the EMG burst (Figure 2B; stimulus trains applied at the arrows). Each train halted the next expected contraction but did not "reset" the underlying rhythm because contractions resumed at the expected time once train stimuli were discontinued (eg, last 3 "beats" of Figure 2B). (Similar observations made in subject 5 were previously reported [38; see Figure 7].) Electrical cutaneous stimulation at other sites, including the plantar surface of the right foot, failed to influence the spontaneous contraction pattern, as shown in Figure 2C. Rubbing the skin of the foot or leg with ice usually caused a modest enhancement of the involuntary movement frequency and vigor in this and other subjects but did not fundamentally change the pattern's distribution or timing. Vibration had no obvious effect on

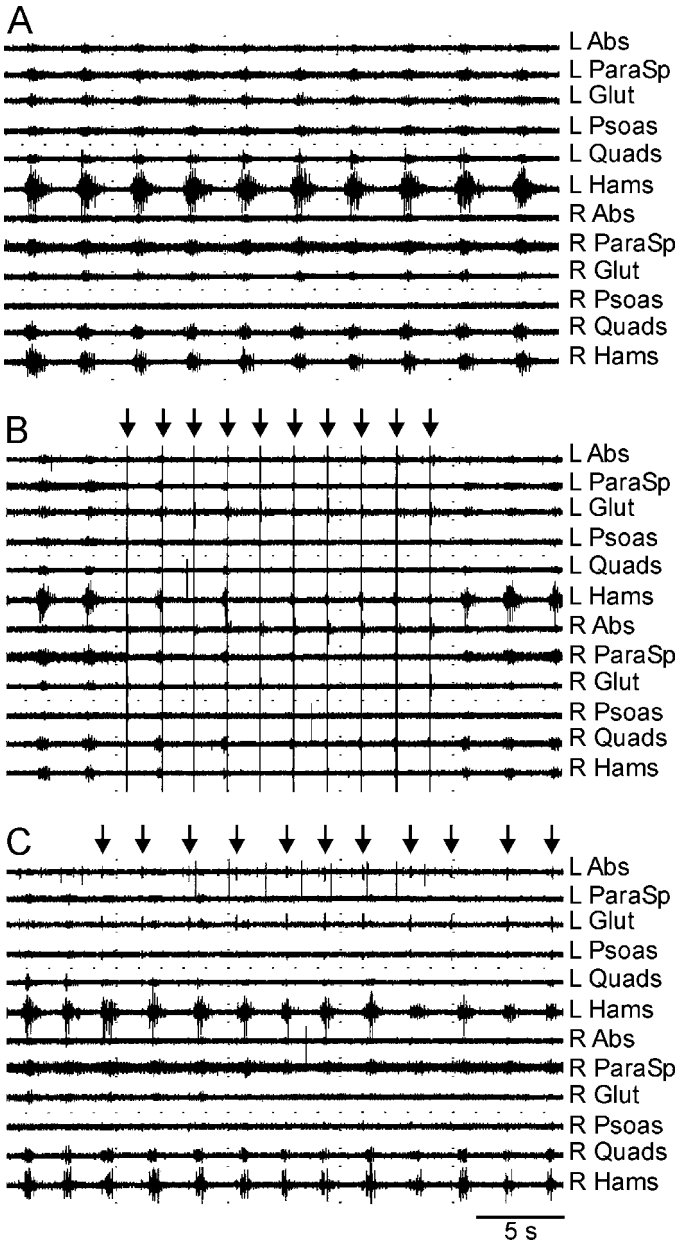

Figure 2. EMG records from multiple muscles of subject 3, in all cases while he was lying supine with hips extended. The top-most panel (A) illustrates spontaneous activity while in this position. In B, brief trains of electrical stimulus pulses were applied to the skin on the subject's right abdomen at the times indicated by arrows. Each stimulus pulse halted the EMG associated with that contraction without affecting the timing of the next contraction. In C, comparable stimuli applied to the subject's right foot (plantar surface; stimulus train onset at the arrows) had no effect on the spontaneous contractions.

Abs (abdominal), paraSp (paraspinals, back extensor), glut (gluteal, hip extensor).

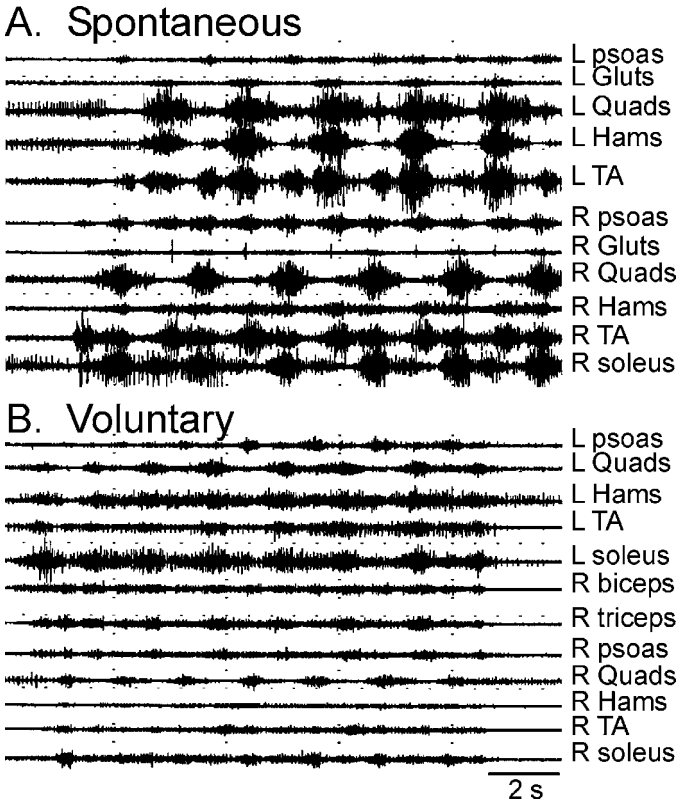

Figure 3. EMG records from multiple muscles of subject 6 while she was lying supine with her hips extended. The upper panel (A) shows activity that was involuntary and spontaneous in onset (ie, it did not begin in response to cutaneous or electrical stimulation). In the lower panel (B), the subject was asked to replicate the involuntary leg movements by rhythmically contracting and relaxing the appropriate muscles. Modulation was poorly defined relative to that illustrated in panel A, with a greater overall amount of co-contraction between different muscle groups of the left and right sides. Note that the muscle identities are not consistent across the 2 panels, in that panel B includes several upper limb muscle sites.

Biceps (biceps brachii, elbow flexor), triceps (triceps brachii, elbow extensor).

movement patterns or magnitude in any subject, regardless of the site of application, nor did gentle stroking of the skin.

Records shown in Figures 1 and 2 were taken from subjects with neurologically complete SCI. In contrast, records in Figure 3 were obtained from subject 6, who was able to walk (ie, ASIA D) but still relied upon a wheelchair for her primary mobility. In her case, moving from the seated to supine position did *not* result in an immediate onset of involuntary leg movements. Instead, the involuntary activity shown in Figure 3A developed only after she had been supine for about 20 minutes, and contraction/relaxation cycles did not persist indefinitely, once started. In some cases, the activity started and

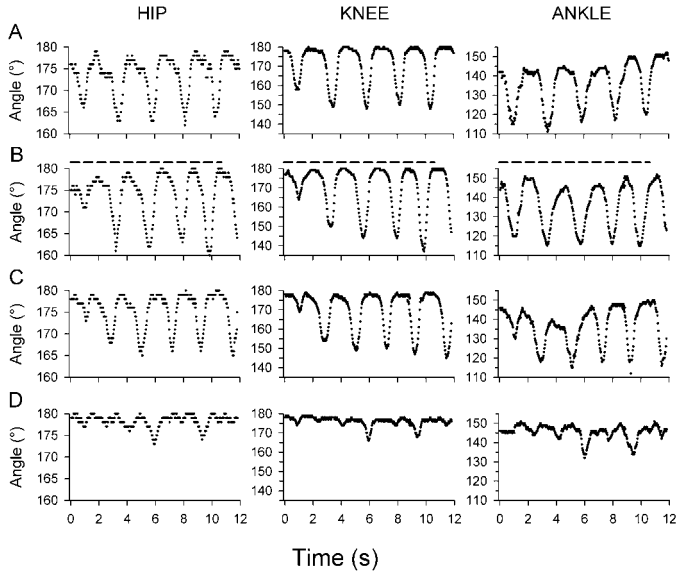

Figure 4. Joint angles vs time for 4 different episodes of leg movements in subject 6, all taken from her right leg and sampled from videotape (~30 frames/second). A 12-second period of activity is included for each condition, with sampling beginning at the onset of movement (approximated from the videotape record). The upper panel (A) shows involuntary activity that was spontaneous in onset. In B, rhythmic movements were caused by rubbing the subject's left foot (plantar surface) with a towel; rubbing began about 10 seconds before movement onset and was continued for most of the record shown (the dashed horizontal line indicates when rubbing was being applied). Panel C shows involuntary movements triggered by a brief train of electrical stimulus pulses applied to the subject's left foot (plantar surface). The lower-most row of records (D) illustrates joint angles associated with the subject's attempts to voluntarily contract and relax her leg muscles to replicate the involuntary stepping-like movements that she had just experienced.

stopped spontaneously. In others, it was triggered by afferent stimulation to the plantar surface of her left foot (eg, gentle rubbing of the skin, electrical stimulation). Regardless of how it was initiated, these contractions stopped spontaneously within 1 minute of onset.

During these periods of involuntary contractions, this subject's legs looked like they were stepping: the muscle activation pattern showed a reciprocal and alternating organization within and between her lower limbs (just as was seen in subject 5). Hamstring and TA activation showed 2 phases per "step" (this was especially pronounced in the left TA). Finally, the phase relationships of these activation patterns were shifted by approximately 180° relative to activation of right-side muscles. The combination of large contraction magnitudes and reciprocal timing between agonist and antagonist muscle groups resulted in substantial changes in hip, knee, and ankle joint angles.

Subject 6 attempted to replicate her involuntary muscle contraction patterns (Figure 3A) with voluntary contractions, the EMG results of which are shown in Figure 3B. For all lower limb muscles, the EMG interference pattern was of smaller amplitude, recruitment modulation within the same muscle was less evident, and there was greater cocontraction between agonist and antagonist muscle groups (ie, less reciprocal activation). The double burst of TA activity seen during the involuntary, spontaneous contractions (Figure 3A) was absent during the subject's attempts to replicate these movements (Figure 3B). Visually, there was little angular change around the joints during most of these voluntary movement attempts, as shown.

Figure 4 illustrates angular displacements of the right-side hip (left column), knee (middle column), and ankle (right column) for subject 6 during 4 different episodes in which stepping-like movements were observed. In all cases, the zero point of the x-axis coincides with the onset of movement. In the top row (Figure 4A), the movement onset was spontaneous (the corresponding EMG traces are shown in Figure 3A). In Figure 4B, movement was precipitated by rubbing a terrycloth towel on the plantar surface of the subject's left foot. Rubbing was initiated about 10 seconds prior to the onset of movement (ie, the starting point of Figure 4 records) and continued for about 10 seconds after movement onset (as illustrated by the dashed horizontal line above each of the 3 traces of Figure 4B). In Figure 4C, a brief train of electrical stimulus pulses was delivered to the plantar surface of this subject's left foot (9 pulses at 500 Hz), beginning about 1 second prior to the zero point of this record. Finally, the lowest panel (Figure 4D) shows joint angular changes when the subject was attempting to replicate, through voluntary contractions, her involuntary stepping movements (the EMG during these voluntary efforts is shown in Figure 3B).

Each of the 3 involuntary stepping periods shown in Figure 4 (A–C) led to substantial changes in flexion/extension angles across all 3 joints of the right leg of subject 6. The magnitude of angular change was largest for movements brought on by continued rubbing of her left foot. Also, the first "step" in each of the top 3 records of Figure 4 had the smallest magnitude and a slightly longer duration than did subsequent "steps." In contrast, most of the stepping movement attempts illustrated in Figure 4D resulted in little angular change around the hip, knee, or ankle. There were 2 visibly distinct contraction/relaxation cycles in which the joints appeared to be suddenly released from cocontraction, resulting in modest flexion around all 3 joints. Even so, this degree of movement was considerably less than that seen for any of the 3 involuntary stepping conditions illustrated in panels A, B, and C of Figure 4.

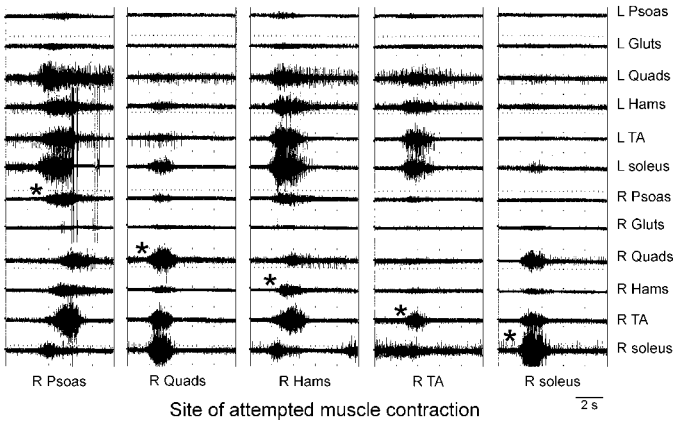

Figure 5. EMG records from multiple muscles when subject 6 was asked to make an isolated, isometric contraction in the muscle indicated at the bottom of each of the panels (and indicated by an asterisk adjacent to that muscle's interference pattern). For example, when asked to contract her right hamstring (middle column of records), she was successful, but there were also varying amounts of activity in each of the other muscles being recorded (on both left and right sides). Thus, she was able to voluntarily contract each of the 5 right-side muscles indicated, but in all cases this contraction was accompanied by co-contraction across multiple ipsilateral and (with the exception of her right soleus) contralateral muscle groups. Note that we did not ask subjects to contract gluteal muscles, because their position at testing (supine) was not conducive to making or assessing such a contraction.

Attempts by subject 6 to make voluntary, isometric contractions of individual muscles in her right leg are illustrated in Figure 5. She *was* able to recruit motor units in each of the muscles examined but could not do so in isolation. Instead, each contraction attempt was accompanied by strong co-contraction of multiple other lower limb muscles on both ipsi- and contralateral sides.

Subject 5 claimed that his stepping-like movements woke him up numerous times each night, causing him to feel sleep deprived during the summer that these involuntary movements appeared (details of these involuntary movements in this subject are provided elsewhere) (38). We examined the relationship between his state of arousal and his involuntary leg movements during a sleep study carried out in his apartment. Given his limited mobility and strong extensor spasticity, this subject struggled to achieve a side-lying position in which hips and knees were flexed. Once positioned this way, his involuntary leg movements ceased, and he quickly fell asleep. Brief (~1-second duration) muscle contractions in his left leg would lead to limb extension and a shifting to the supine position (ie, with hips now extended), yet he remained asleep and his legs did not resume their stepping-like movements. However, in 3 cases during our 2-hour observation period, spontaneous EMG in his left TA muscle was more intense and prolonged (upper arrow in Figure 6; left TA record). This led to EMG in other leg muscles and a disruption of his EEG sleep pattern (ie, a cognitive state of arousal; lower arrow in Figure 6; Fp1–F3 record). Once he was in this state (the midpoint of Figure 6), the rhythmic leg contractions began, leading to a state of complete wakefulness (seen by intense artifact in the EEG traces of Figure 6).

As previously illustrated, persons with neurologically complete SCI (subjects 1–4) showed bilateral and simultaneous contractions in flexors and extensors of the legs during periods of involuntary contractions, whereas movements were reciprocal (between agonists and antagonists) and alternating (between left and right sides) for the 2 subjects with neurologically incomplete injury. Despite this fundamental difference in movement expression, the period between involuntary contractions was similar between subjects. Figure 7 illustrates this finding, for which the average period of at least 10 successive contraction/relaxation cycles is shown, along with the standard deviation of this mean. (For subject 6, both the involuntary [Figure 3A] and voluntary [Figure 3B] periods of leg movements are included.) The average period varied from a low of about 1.9 seconds (ie, ~0.5 Hz) to a high of about 3.5 seconds (i.e. ~0.3 Hz) across the 6 subjects. Note also that for each subject, there was remarkably little variability in the EMG burst rate, as illustrated by the small standard deviations of these means.

DISCUSSION

We have described involuntary, spontaneous, and rhythmic leg movements in 6 subjects with a chronic

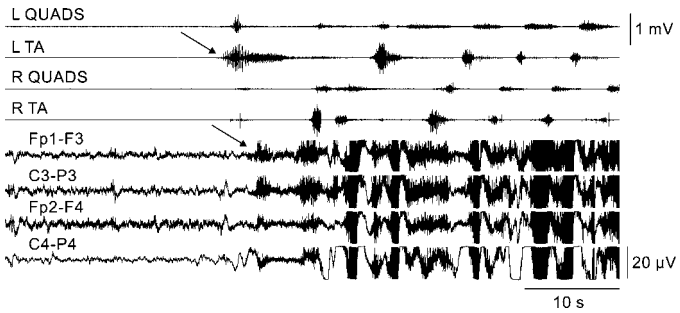

Figure 6. EMG (top 4 traces) and EEG (bottom 4 traces) from subject 5 during a sleep study carried out in his apartment. The subject was supine throughout this record with his hips extended. Despite this positioning, there was no spontaneous EMG from his leg muscles until he had a strong contraction in his left TA (upper arrow). This contraction interrupted his sleep pattern, leading to a state of arousal as shown on the EEG record (lower arrow). Once he was in this state, rhythmic contractions ensued in his leg muscles, causing him to fully awaken (with the dramatic increase in EEG artifact associated with movement and speech).

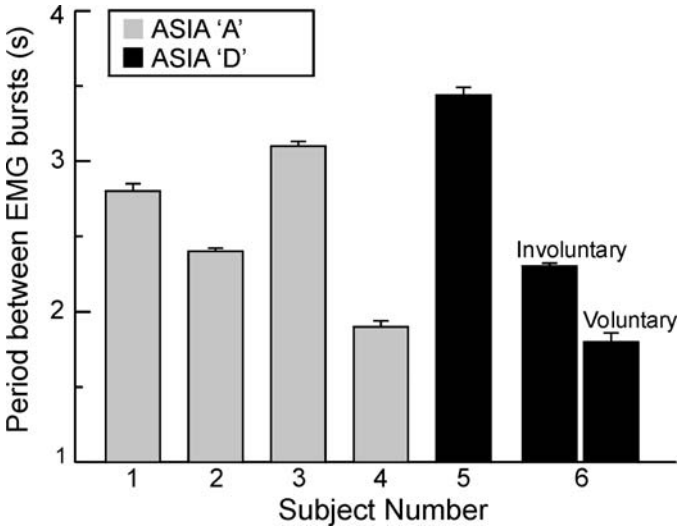

Figure 7. Mean and standard deviation of the period (seconds) between successive involuntary movements for each of the 6 subjects examined. In all cases, subjects were lying supine, and no specific sensory stimuli were being delivered during this determination. Two values are included for subject 6: the first is the period of involuntary movements whose onset was spontaneous, and the second is the period associated with her voluntary attempt to replicate the movements (based on the EMG records in Figure 4B). A distinction is made between neurologically complete (gray fill) and neurologically incomplete (solid fill) subjects, showing a similar range of movement periods, despite this difference in injury severity.

history of traumatic cervical SCI. In the following sections, we will examine these movements in light of other published reports, arguing that they likely reflect some elements of a spinal pattern generator for stepping.

Spinal Myoclonus

Two main forms of spinal myoclonus—segmental and propriospinal—have been reported. Definitions for either entity are not absolute, however, such that there is overlap in the characteristics attributed to both. This may be because these 2 "types" of myoclonus may coexist in the same individual and share the same spinal generator (40), with the overall spinal cord excitability being the determining factor as to which form is expressed.

Segmental (or rhythmic) myoclonus is characterized by brief, jerk-like movements that are localized to a few neurologic segments (ie, myotomes), either with or without a rhythmic component (when present, the rhythm varies widely in rate). The movements are relatively unaffected by sensory input or patient actions and can be seen when both awake and sleeping. Although such movements have been reported in the arms (33,41,42), they are more common in leg muscles and have been termed "periodic leg movements" (43–48). These movements have been likened to spontaneous expressions of the flexion reflex (45,49), reflecting diminished spinal inhibition and/or increased spinal excitability (42,50–52). The burst of EMG in the left TA of Figure 6 in the present study (upper arrow) represents an example of this type of involuntary contraction.

Propriospinal myoclonus involves rhythmic contractions predominantly in muscles of the trunk and is thought to spread via long propriospinal neurons to motoneurons innervating leg muscles (32,37,42,53,54). Thus, a larger number of myotomes are involved with propriospinal myoclonus compared with segmental myoclonus. The rate of contractions is more consistent from burst to burst than is typically reported for segmental myoclonus. There have been multiple reports of propriospinal myoclonus after SCI (30,32,45).

In balance, the involuntary movement patterns described in the present study are more consistent with the propriospinal form of myoclonus vs the segmental form, reflecting the high level of spinal cord excitability most subjects reported at the time the involuntary movements were present (40). However, neither form fully and adequately accounts for the relationship between movement expression and hip angle or for the presence of alternating and reciprocal spontaneous stepping movements in the 2 subjects with incomplete (ASIA D) SCI of this study's cohort.

The involuntary movement patterns seen in subjects 5 and 6 are probably mediated by a central pattern generator for stepping. Muscles were activated in a reciprocal manner between agonists and antagonists in the same leg, and movements alternated between left and right legs. Contractions were graded and smooth, as evidenced by both EMG records and joint-angle records (from subject 6). Tonic afferent input (via hip joint angle) clearly played a role in expression of these movements. Phasic afferent input modulated the movements seen in subject 5 (described in more detail elsewhere [38]) but could not be reliably tested in subject 6 because of the relatively brief periods ($<$1 minute at a time) that her involuntary stepping movements persisted, once under way. The rate of spontaneous contractions showed remarkable consistency in timing from step to step for the same subject and were consistent with a slow walking pace.

Subjects 1 to 4 shared similar movement frequencies as those seen in subjects 5 and 6, as well as a common requirement for hip extension (to 180°) for spontaneous movements to emerge. Thus, the involuntary movement patterns seen in subjects 1 to 4 of this study are also thought to reflect activity of a spinal pattern generator, despite an absence of reciprocal activation (of agonist and antagonist muscles) and left/right alternation. Although comparable movement patterns were not evident, other studies have also concluded that their descriptions of spinal myoclonus may reflect activity of a pattern generator in the spinal cord (29–31,40,45,55).

There are other reports that spinal myoclonus is either expressed or enhanced when subjects are placed supine, with their hips extended (48,56,57). Brief episodes of reciprocal stepping movements in a human with complete SCI were halted by flexing the hips bilaterally (29). Hip angle has been shown to be an important factor modulating CPG output in the cat (4,5,58), and segmental reflexes in the human lower limb are modulated by changes in both hip and knee angle (59–62).

Spinal Cord Excitability

Changes in hip angle alone are clearly not sufficient for eliciting rhythmic and involuntary leg movements in most persons with chronic SCI, given the paucity of reports on this topic. Instead, 5 of the 6 subjects examined in the present study reported having severe spasticity at the time of our investigation. In each case, the spasticity, as well as the involuntary movements we documented, was thought to be due to pathology involving (a) the spinal cord or nerve roots (subjects 1 and 3), (b) the hip joint (subjects 2 and 5), or (c) soft tissue around the pelvis or thigh (subjects 4 and 6). None of subjects 1 to 4 described pain from the suspected pathologic site because each was neurologically complete and had no sensation below the level of their cervical SCI. Subject 5 described a dull ache from his right hip, but sensation in his legs was diminished. Nevertheless, lidocaine-induced elimination of afferent input from his right hip joint led to a temporary cessation of stepping movements in his legs (38). Only subject 6 had near-normal sensation in her left lower limb; at the time of examination, she had been complaining of pain and tenderness in her posterior thigh subsequent to an especially strenuous walking session in which she was a research participant.

The presumed relationship between nociceptor inflow to the spinal cord and the expression of involuntary leg movements described herein is consistent with an often-reported strategy using intense stimulation of the tail (eg, kinking) or perineum (eg, genital squeeze) to cause or enhance hind limb stepping in the cat (63–66), rat (67), or dog (68). Equivalent spinal cord input caused by electrical stimulation of group III or group IV muscle afferents was found to enhance fictive locomotion in the cat (6). In humans with SCI and who demonstrated spinal myoclonus, foot pinch (54) or toe twisting (29) exacerbated the movements. Stepping movements caused by epidural electrical stimulation of the cauda equina in humans with SCI (21–23,69) may reflect similar mechanisms of afferent activation.

Treatment and Recurrence

Table 1 indicates that the systemic pathology suspected of causing the stepping movements was successfully treated in subjects 1, 3, 5, and 6. In each case, treatment resulted in a cessation of the involuntary movements. Moreover, in 3 of these 4 cases, treatment was accompanied by a marked reduction in spasticity (subject 6 did not have an increase in spasticity at the time her involuntary leg movements began, and she was also the only subject in whom involuntary contractions did not begin immediately upon moving from a sitting to a supine position).

Three of these 4 subjects experienced a recurrence of their symptoms (involuntary leg contractions, increased spasticity) some time later. Subject 1 required a revision of a subperitoneal shunt of a spinal cord syrinx 2 years after his first surgery. This second surgical procedure eliminated his symptoms, and he has been symptom free for the past 8 years. Four years after subject 3 was first treated for spinal myoclonus by spine fusion, resumption of severe extensor spasticity and myoclonus caused his doctors to look immediately to the spine, where a L3/4 pseudoarthrosis was diagnosed. A second spine fusion was carried out and his symptoms of spasticity and myoclonus were relieved; they have not recurred 2 years since this second surgery. Finally, involuntary stepping movements could be temporarily halted by infusion of local anesthesia into the right hip capsule of subject 5 (described in detail elsewhere) (38). These movements ceased altogether about 2 weeks after subject 5 discontinued his regimen of lower-limb exercise. Eight months later this subject reinitiated a vigorous daily workout, including weight bearing through his legs. On the second night after resuming this activity, his involuntary stepping movements reappeared, virtually identical in properties to what he had experienced the previous summer. They persisted during the months this subject was working out and then ceased once he discontinued regular exercise.

Differences Between Complete and Incomplete Injuries

Most reports of CPG activity in the spinal cat concentrate on highly rhythmic, alternating movements (or nerve activation patterns) between hind limbs. However, there are reports in both cat (8,70) and marmoset (2) of widespread variability in the activation pattern of spinal cord circuitry, even when using identical methods of excitation. In the rat spinalized at birth, movements showing simultaneous muscle activation between limbs could, through recruitment of descending serotonergic pathways, be switched to ones showing interlimb alternation (67). Brustein and Rossignol (8) attributed substantial differences in drug-induced hind limb movements in the spinal cat to whether or not the spinal lesion was complete.

We propose that the presence of reciprocal alternation in movement patterns seen in subjects with neurologically incomplete injury in the present study was due to residual supraspinal influence over lumbosacral spinal circuitry in subjects 5 and 6. Their inability to mimic these movements through voluntary effort argues

against corticospinal tract as being the source of this innervation (71). By default, this leaves either vestibulospinal tract or reticulospinal tract (the latter via descending propriospinal axons [72]) as the likely source of input causing a "switch" from simultaneous to alternating movements in these 2 subjects.

Further indirect support of a role for supraspinal influence on mediation of alternating movements comes from the sleep study performed in subject 5. It became evident to us that contrary to his own belief, involuntary leg movements did *not* occur when this subject was asleep, even though his hips were fully extended. Instead, it was only when subject 5 was aroused by a particularly strong periodic leg movement that the "stepping" began. Because he was technically not fully awake at this point, it was understandable for him to conclude that the stepping movements woke him up. The absence of stepping movements in this subject when asleep argues that some tonic descending signal associated with his state of arousal was a necessary component to trigger these movements. This hypothesis is supported by a recent study of alternating contractions within TA muscles during sleep, in which it was noted that these movements were especially common during arousals (55).

CONCLUSION

We believe that the 6 examples of spinal myoclonus described in this report are consistent with some elements of a central pattern generator for stepping in humans (20,26,73). The intrinsic excitability of this rhythm generator appears to be much lower in humans than in primates, rats, or cats (20,70,74,75), requiring significant supraspinal and/or segmental afferent input to become evident. As a result, its spontaneous expression in humans is rare. In fact, these 6 subjects represent the only cases of such activity we have encountered in our detailed examinations of more than 600 people with a history of traumatic SCI (including 229 with acute injury [76]). Such a low incidence appears to reflect a requirement for a combination of SCI and particular types of nociceptor input to the lumbosacral enlargement, both of which can increase spinal cord excitability. On a practical note, the development of spinal myoclonus in patients with a history of chronic SCI should alert the health care specialist to look for specific triggering factors reflecting some occult pathology or process (35).

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