Augmentation of Voluntary Locomotor Activity by Transcutaneous Spinal Cord Stimulation in Motor-Incomplete Spinal Cord-Injured Individuals

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Abstract: The level of sustainable excitability within lumbar spinal cord circuitries is one of the factors determining the functional outcome of locomotor therapy after motor-incomplete spinal cord injury. Here, we present initial data using noninvasive transcutaneous lumbar spinal cord stimulation (tSCS) to modulate this central state of excitability during voluntary treadmill stepping in three motor-incomplete spinal cord-injured individuals. Stimulation was applied at 30 Hz with an intensity that generated tingling sensations in the lower limb dermatomes, yet without producing muscle reflex activity. This stimulation changed muscle activation, gait kinematics, and the amount of manual assistance required from the therapists to maintain stepping with some interindividual differences. The effect on motor outputs during treadmill-stepping was essentially augmentative and step-phase dependent despite the invariant tonic stimulation. The most consistent modification was found in the gait kinematics, with the hip flexion during swing increased by $11.3° \pm 5.6°$ across all subjects. This preliminary work suggests that tSCS provides for a background increase in activation of the lumbar spinal locomotor circuitry that has partially lost its descending drive. Voluntary inputs and step-related feedback build upon the stimulation-induced increased state of excitability in the generation of locomotor activity. Thus, tSCS essentially works as an electrical neuroprosthesis augmenting remaining motor control. **Key Words:** Human—Locomotor training—Neuromodulation—Spinal cord injury—Transcutaneous spinal cord stimulation.

Recovery of motor function following spinal cord injury (SCI) is variable, also depending on the severity of injury (1). This recovery can, in some cases, be augmented with rehabilitation therapies that activate sensorimotor pathways and spinal locomotor circuitries below the lesion level using body weight-supported treadmill stepping with therapist assis-

tance or robotic driven gait orthosis (2–4). The mechanical movement and loading of the limbs during such stepping generates multimodal afferent input patterns that can drive neural circuits of the spinal cord to produce sequenced and amplitude-modulated outputs to leg muscles in people with motor-complete SCI (5,6). This peripheral input coupled with surviving translesional activation in individuals with motor-incomplete SCI may improve their response to such training and over-ground walking capability (7). Yet even those clinically classified as American Spinal Injury Association Impairment Scale (AIS) D according to the International Standards for Neurological Classification of Spinal

Cord Injury (8) do not regularly become functional community ambulators after training (4). Such augmented yet insufficient recovery is likely due, in part, to the reduced excitability within spinal locomotor circuitries and their altered physiological state (9). Therefore, there is a need for neuroaugmentative methods to supplement functional locomotor training (7), and epidurally delivered electrical spinal cord stimulation is regarded as a promising way to add excitation (10–12).

Previously, we developed a transcutaneous version of spinal cord stimulation (tSCS) that can be used for the modulation of post-SCI motor control (13–15). Like epidural lumbar spinal cord stimulation, the transcutaneous method allows for the stimulation of afferent structures associated with multiple myotomes and dermatomes of the lower limbs bilaterally. Here, we present data on the immediate effects of 30-Hz tSCS on the rhythmic motor activities generated during active treadmill stepping in three SCI individuals classified as AIS D. Our hypothesis was that tSCS subthreshold to produce motor responses in the lower extremities would enhance the base excitability of the lumbar spinal locomotor circuitry and augment locomotor function during treadmill stepping. Parts of the data presented have been published in abstract form (16).

SUBJECTS AND METHODS

Subjects and clinical data

Three otherwise healthy adults with chronic motor- and sensory-incomplete SCI were studied (Table 1). All subjects were able to complete the 10-meter walk test without braces or manual assistance provided by therapists, but they were not functional community ambulators despite standard-of-care rehabilitation and intensive locomotor training. They regularly practiced standing using a standing frame as well as stepping in parallel bars, and had undergone treadmill training as part of their rehabilitation program. Spasticity, classified according to the (modified) Ashworth scale at hip, knee, and ankle,

ranged from 1 to 4 in subject 1, 0–1 in subject 2, and 2–3 in subject 3. In all subjects, clonus could be evoked manually in the supine position by a brisk stretch of the patellar or Achilles tendons and also occurred in several muscles during stepping, with subject 2 being most severely affected. Subjects were not taking antispasticity medications. The study was approved by the Ethics Committee of the City of Vienna, Austria (EK 06–109-0706). Subjects signed written informed consent prior to their participation.

Treadmill stepping

All subjects stepped actively on the treadmill, secured with a modified parachute harness, but without body weight support. Two therapists were prepared to assist the stepping movements when necessary, mainly to avoid stumbling. Subjects were allowed to make use of the parallel bars attached to the treadmill base for balance support.

Transcutaneous lumbar spinal cord stimulation

tSCS was applied as in our previous studies (13–15). A pair of self-adhesive stimulating electrodes (Ø = 5 cm; Schwa-medico GmbH, Ehringshausen, Germany) was placed paraspinally over the T11 and T12 spinal processes, a pair of indifferent electrodes (8 × 13 cm each) placed paraumbilically. Both electrode pairs were interconnected to function as single, larger electrodes. A constant-voltage stimulator delivered charge-balanced, symmetric, biphasic rectangular pulses of 1-ms width per phase. With reference to the abdominal electrodes, the paraspinal ones acted as anode for the first and as cathode for the second pulse phase. Exact placement of the paraspinal electrodes was monitored via posterior root-muscle (PRM) reflex recordings in the legs with the subjects in upright position on the stopped treadmill. Double stimuli with interstimulus intervals of 30 ms, 50 ms, and 100 ms were applied to assess the presence of postactivation depression and hence verify the selective stimulation of afferent structures (13,18,19). Individual PRM reflex thresholds were documented. The same electrode

TABLE 1. *Subject characteristics*

| Subject no. | Sex | Age | Years postinjury | Level of SCI | AIS | Lower limb motor scores | | WISCI | Device |
						Left	Right		
1	F	28	11	T9	D	11	13	16	2 Crutches
2	M	32	12	C5	D	12	17	16	2 Crutches
3	M	38	9	C5	D	13	12	13	Walker

AIS, American Spinal Injury Association Impairment Scale (8); WISCI, walking index for spinal cord injury (17); Device, assistive devices needed for 10-m walk test.

placement was used to deliver 30-Hz stimulation during treadmill stepping.

Data acquisition

Surface electromyographic (EMG) activity was recorded from the quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS) bilaterally using pairs of silver–silver chloride surface electrodes (Intec Medizintechnik GmbH, Klagenfurt, Austria). Each electrode pair was placed centrally over the muscle bellies and oriented along the long axis of the muscles with an interelectrode distance of 3 cm (20). An additional pair of recording electrodes was placed in horizontal orientation on the right side of the trunk closely below the costal arc to detect stimulus artifacts. To improve signal quality, interelectrode impedance was reduced below 5 kΩ using abrasive paste. A reference electrode was placed over the right fibular head. EMG signals were amplified using a Phoenix poly-EMG system (EMS-Handels GmbH, Korneuburg, Austria) set to a gain of 502, filtered to a bandwidth of 10–500 Hz and digitized at 2048 samples per second and channel. Electro-goniometers (Penny & Giles Biometrics Ltd., Gwent, UK) were used to record hip and knee movements bilaterally. The goniometric signals were filtered to a bandwidth of 0–15 Hz. To detect foot contact, force-sensing resistors (RS Components HandelsgesmbH, Gmünd, Austria) were affixed to the shoe soles below the heel (model FSR 174 [189–5584]), the ball of the great toe, and the ball of the little toe (both FSR 151 [189–5590]). All sensor data were digitized at 2048 samples per second and synchronized to the EMG data.

Signal processing

Stimulation artifacts produced by the 30-Hz stimulation were superimposed on the recorded physiological EMG activities generated during treadmill stepping, with the strongest contamination seen in the Ham-channel (Fig. 1A,B, left). For offline artifact removal, the recordings from the trunk-located electrode pair were used to trigger an adjustable blanking interval of 2–5 ms, beginning with the leading edge of the stimulus. The length was adjusted to cover any die-away effects of the falling stimulus edge as visible in the recorded trace. The derived sequence of blanking intervals was applied to the EMG recordings by setting the traces to zero (Fig. 1A,B, right). We estimated the blanking-induced errors on our target parameter root mean square (RMS) of EMG activities produced during 10 gait cycles of active treadmill stepping in subject 1. We compared the RMS of EMG recordings without tSCS at two different step speeds (1.6 km/h and 0.8 km/h) with the RMS of the same data set with blanking intervals of 5 ms applied for an assumed 30-Hz stimulation train. This validation showed deviations in the RMS of less than 8% for all EMG activities and muscle groups.

Data analysis

Mean RMS values of the EMG activities during stance and swing phases were calculated from 10 gait
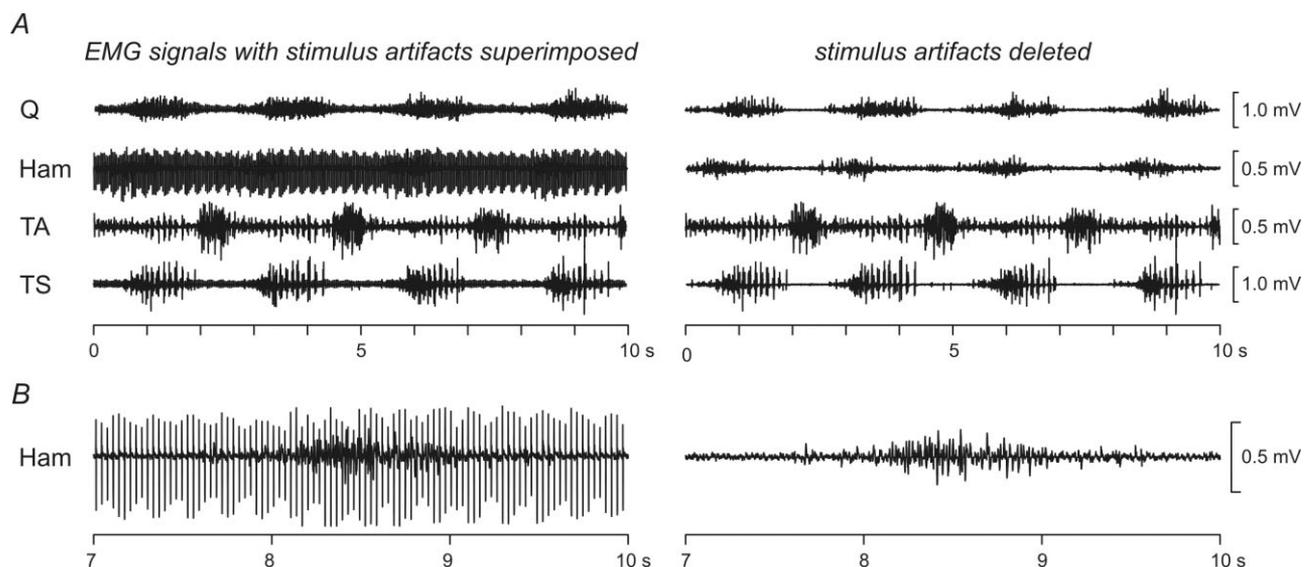

FIG. 1. Removal of stimulus artifacts produced by 30-Hz transcutaneous spinal cord stimulation. A. Electromyographic (EMG) activity of quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS) before (left) and after (right) blanking out stimulation artifacts. B. Recording segment of Ham derived from A in enlarged time scale. Example represents the worst case of artifact contamination observed; subject 2.

cycles for the stimulation-off condition and from 10 gait cycles for the stimulation-on condition after artifact removal. Hip and knee ranges of movement (ROMs) during each of the 10 gait cycles were derived from the goniometric data and subsequently averaged. Mean angle–angle plots illustrating the interjoint coordination during stepping were produced based on the average goniometric signals per gait cycle. Durations of stance and swing phases as well as gait cycle durations were calculated on the basis of the foot switch data.

Data were analyzed offline using MATLAB R2012a (The MathWorks, Inc., Natick, MA, USA).

Study protocol

The main protocol included stepping at a self-selected speed on the treadmill, first without stimulation and then under 30-Hz tSCS below the intensity producing lower limb muscle reflex activity. The self-selected speeds amounted to: subject 1, 1.6 km/h (0.44 m/s); subject 2, 2.0 km/h (0.56 m/s); and subject 3, 1.5 km/h (0.42 m/s). Each session started with 10 gait cycles under the stimulation-off condition. Subsequently, the treadmill belt was stopped and continuous 30-Hz stimulation was turned on, starting from 0 V and with slow gradual increase of intensity to allow the subjects to adapt to the stimulation-induced effects. These effects included, in sequence of their occurrence with increasing intensities, sensory perception of the stimulation under the stimulating and indifferent electrodes, contraction of the paraspinal and abdominal muscles, and paresthesias in the lower limb dermatomes. Target intensities for 30-Hz stimulation were defined as to produce paresthesias covering most of the lower limb dermatomes as perceived by the subjects, yet subthreshold for leg muscle activation. Individually, these target intensities amounted to: subject 1, 18 V (per phase of the biphasic stimulation pulse, corresponding to 86% of the PRM reflex threshold in standing position); subject 2, 27 V (71% of PRM-reflex threshold); and subject 3, 20 V (80% of PRM-reflex threshold). None of the subjects reported discomfort during the stimulation. After reaching the target intensity, 10 gait cycles under stimulation were recorded. Supplementary recordings were conducted in subject 1: The main protocol was repeated with the self-selected speed to test reproducibility as well as with half the self-selected speed (0.8 km/h, 0.22 m/s). In a final recording, treadmill stepping at 0.8 km/h started under ongoing 30-Hz stimulation that was abruptly turned off after 14 steps, while the subject continued stepping. The subject rested for a few minutes between the stepping trials.

RESULTS

Treadmill stepping without tSCS

All subjects could step actively without body weight support on the treadmill. Left heel lift at initial swing had to be occasionally assisted for subject 1 to keep up with the treadmill belt speed, subject 2 intermittently required manual assistance to control left foot placement, and subject 3 walked without manual assistance.

Rhythmic EMG activities with consistent timing during the step cycle were generated in all recorded muscles and subjects, as illustrated in Fig. 2A. Activation of Ham, TA, and TS muscles occurred largely at times that were functionally appropriate for the phases of gait. An exception was found in left TA of subject 1 with its main activity occurring during stance. Q activity occurred during stance phases, and individually yielded a second burst either at the transitions from swing-to-stance or from stance-to-swing. The EMG activities were lower in subject 1 than in the other two participants by a factor of two to three times.

Further, some nonfunctional motor activity was generated during stepping that was partially interspersed within the rhythmic EMG bursts. In subject 1, clonus-like EMG activity occurring bilaterally in TS during the stance phases and brief stretch-reflex like activities in the left Q at each heel-strike was recorded. Subject 2 developed the most severe clonus-like EMG activity occurring in Ham, TA, and TS bilaterally that interfered with the stepping motions as also reflected in the goniometric traces in Fig. 2A. Also, subject 3 developed clonus-like EMG activity that was more often present in the distal than proximal leg muscles, and were more evident on the left side.

Treadmill stepping under 30-Hz tSCS

Stimulation had immediate effects on motor output and kinematics in subjects 1 and 2, making it possible for them to no longer require manual assistance for secure stepping. The main effect on motor output was augmentative, without major changes in the overall EMG patterns (Fig. 2B). An exception was the phase-appropriate generation of rhythmic activity in the left TA of subject 1. Stretch reflex-like responses as generated at heel strike in the stimulation-off condition were largely diminished during 30-Hz tSCS delivery, while clonus-like activities were less modified.

The constant frequency tSCS modulated the amplitude of existing gait phase-dependent motor output (Fig. 3). In subjects 1 and 2, TA activity was
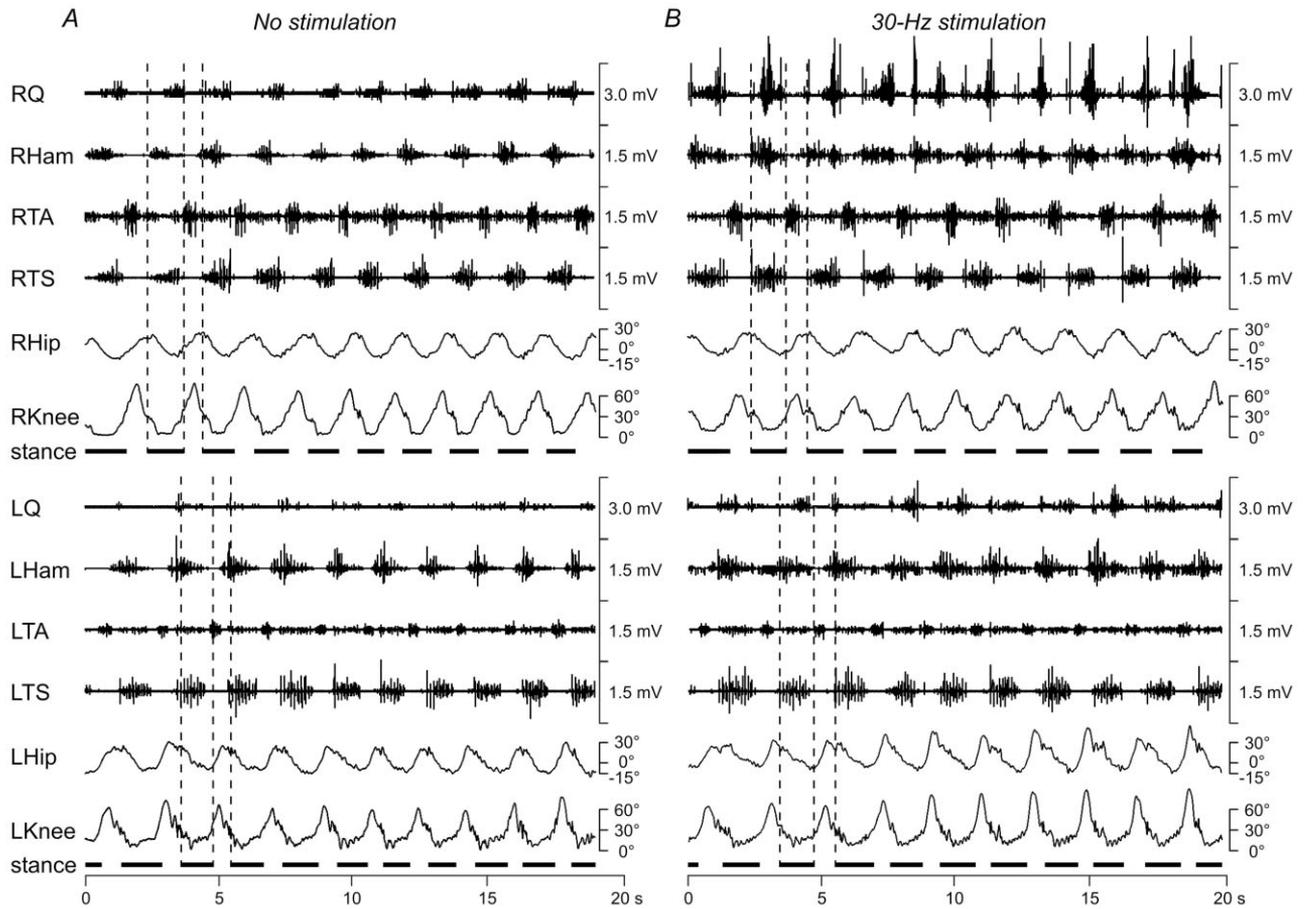
FIG. 2. Electromyographic (EMG) activity and joint movements during active treadmill stepping in an individual with motor-incomplete spinal cord injury, without (A) and with (B) continuous 30-Hz transcutaneous lumbar spinal cord stimulation. Shown are EMG activities of 10 gait cycles, starting with right foot contact, derived from right (R) and left (L) quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS). Black bars indicate stance phases. Vertical dashed lines point out stance and swing phases of one exemplary gait cycle each. Treadmill belt speed: 2.0 km/h; no body weight support; occasional assistance of left foot placement during stimulation-off condition; stimulation intensity: 27 V; subject 2.
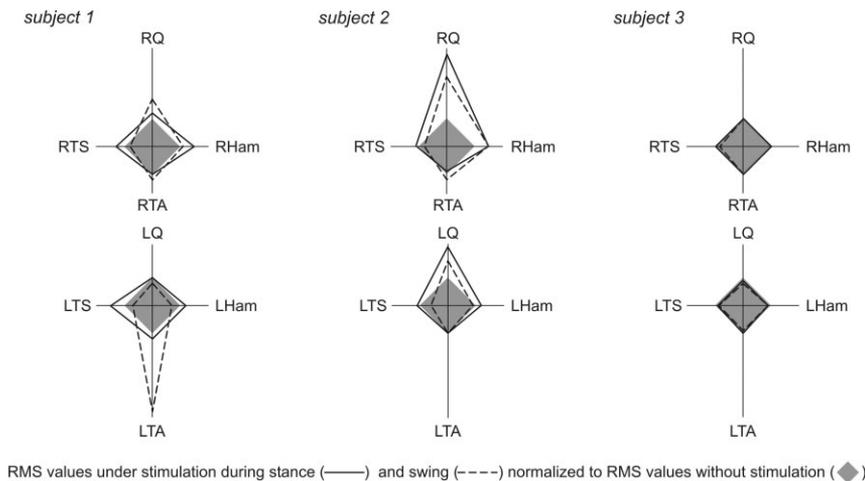

FIG. 3. Stimulation-induced modulation of activation patterns during stance (solid lines) and swing (dashed lines) phases of treadmill gait. The radar charts represent the root mean squares (RMS) of the electromyographic activity for each muscle averaged over 10 steps while receiving 30-Hz stimulation, normalized to the respective values during the stimulation-off condition. Gray-shaded areas are shown for scaling purposes and represent activity during the stimulation-off condition (i.e., spanning values of the ones along the axes). Data from right (R) and left (L) quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS).

TABLE 2. *Stepping parameters and their changes under stimulation*

Subject	1		2		3	
Stimulation-Off/On	No Stimulation	30-Hz	No Stimulation	30-Hz	No Stimulation	30-Hz
R Hip ROM [°]	21.7 ± 1.5	39.0 ± 8.6	36.1 ± 2.0	38.6 ± 4.7	42.6 ± 3.5	45.8 ± 2.2
L Hip ROM [°]	30.1 ± 1.7	38.7 ± 6.5	39.2 ± 3.7	55.2 ± 10.7	61.9 ± 1.8	67.3 ± 5.8
R Knee ROM [°]	56.5 ± 3.6	74.4 ± 7.3	66.8 ± 4.5	56.1 ± 5.9	57.7 ± 2.3	58.8 ± 1.6
L Knee ROM [°]	69.6 ± 3.3	79.3 ± 4.4	61.6 ± 5.7	74.4 ± 8.5	71.6 ± 2.2	71.2 ± 2.0
Step cycle duration [s]	2.55 ± 0.10	2.97 ± 0.22	1.86 ± 0.17	1.98 ± 0.12	2.03 ± 0.09	2.00 ± 0.05
R Stance : Swing	71:29	64:36	63:37	63:37	76:24	79:21
L Stance : Swing	73:27	65:35	65:35	65:35	75:25	81:19

R, right; L, left; ROM, range of movement. Mean values ± standard deviation derived from 10 gait cycles each.

augmented during the swing phase, while TS activity was enhanced during the stance phase. The phase-dependent modifications of the proximal and distal leg muscle activation in subject 1 showed left–right differences, while in subject 2, modulation was more symmetrical with the main effect being the augmentation of the activities in the proximal muscle groups. The stimulation-induced effects on the EMG patterns of subject 3 were minimal, with activation amounting to 90–100% of that during the stimulation-off condition.

30-Hz tSCS also had effects on the gait kinematics. The most consistent finding, observed in all subjects and limbs, was an increase of $11.3 ± 5.6°$ in the maximum hip flexion angle during swing leading to an increased hip ROM in five of the six limbs. In subject 1, the step cycle duration was increased with only the swing phases being prolonged, changing the stance-to-swing ratios toward more normal values. Changes in joint ROMs, step cycle durations, and stance-to-swing ratios with interindividual differences are detailed in Table 2.

The interjoint coordination of hip and knee during stepping is illustrated for all subjects as angle–angle plots in Fig. 4. In subject 1, the stimulation led to a strong flexion bias with exaggerated foot clearance as part of a fluid multijoint movement. Changes toward an augmented flexion component in the gait kinematics were also induced in the other two subjects, even in subject 3 in whom the motor outputs were not augmented.

Supplementary recordings in subject 1

Testing active treadmill-stepping at slow (0.8 km/h) and self-selected (1.6 km/h) speeds showed a tendency for increased motor output to be generated with the higher stepping speed. This output was further augmented with 30-Hz tSCS. Figure 5A suggests interactions between the influences of stepping speed and stimulation-off/on conditions on the generated motor outputs, with a stronger facilitating impact of tSCS during faster stepping. The strongest interaction effects were evident in the left TA. Without stimulation, subject 1 could functionally activate the left dorsiflexor only at the slow stepping speed, but lost this ability during the faster self-selected speed. The functional motor pattern was restored during the self-selected speed under 30-Hz stimulation with an augmented left TA burst during swing. The causal relation between stimulation application and the modification of voluntary stepping is further detailed in Fig. 5B,C. In Fig. 5B, the subject started to step at 0.8 km/h with 30-Hz stimulation. Stimulation was then suddenly turned off, causing immediate degradation of hip and knee movements. Moreover, for both tested speeds, the interjoint coordination of hip and knee during stepping under stimulation differed from the subject's normal walking pattern with its bias toward exaggerated and prolonged flexion movement. These specific walking patterns were reproducible when repeating the recordings at the respective speeds with tSCS (Fig. 5C). With stimulation, the subject reported an effortless, near automatic initiation and execution of the swing phases together with an improved stability during stance.

DISCUSSION

tSCS at 30-Hz with intensities between sensory and motor thresholds for the lower limbs demonstrated acute neuromodulatory effects on the voluntary locomotor activity in three motor-incomplete SCI subjects. Stimulation in conjunction with the subjects' voluntary execution of treadmill stepping caused immediate modifications of spinal motor output, gait kinematics, and the amount of manual assistance required, with interindividual differences in these outcomes. Despite the constant amplitude and frequency of tSCS, the modifications occurred within and appropriate to physiologically specific phases of the gait cycle.
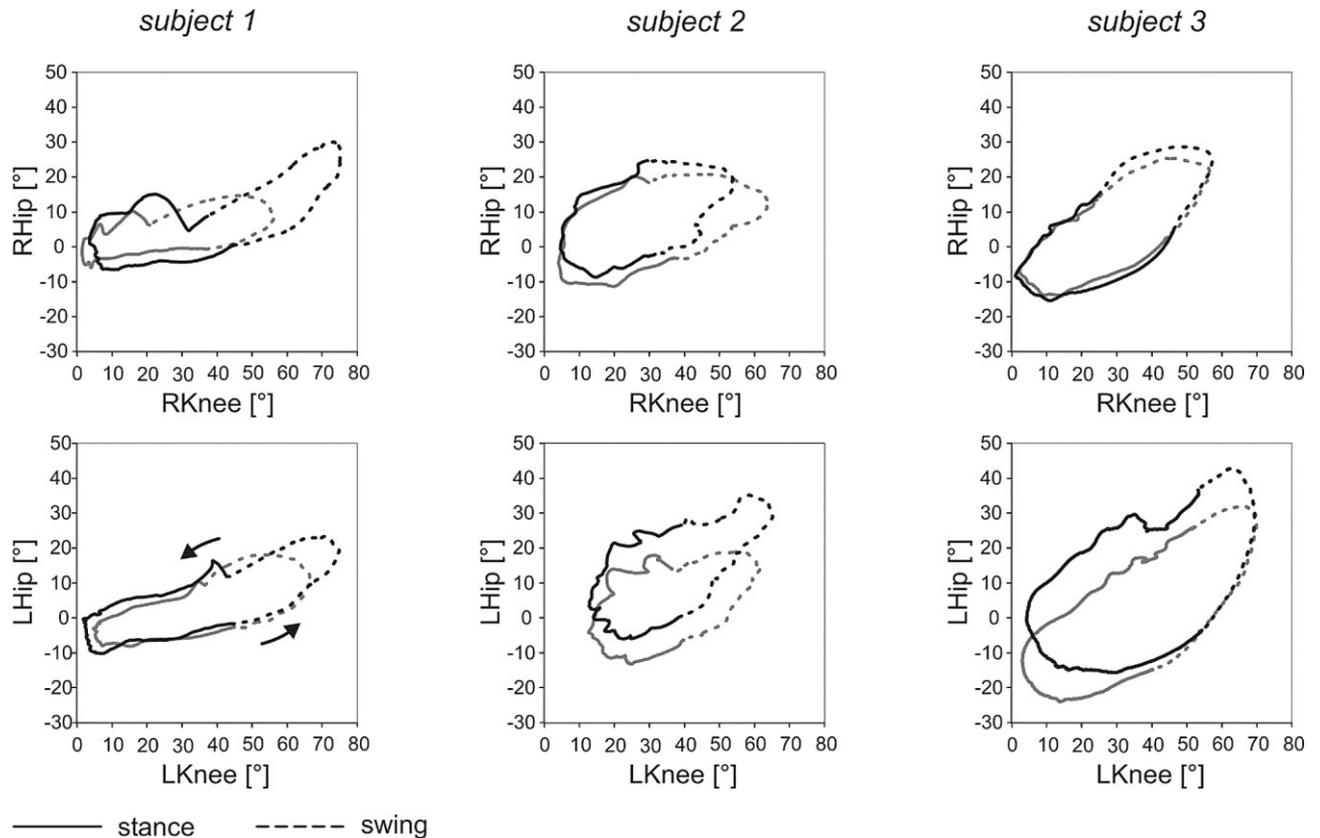
FIG. 4. Angle–angle plots illustrating the coordination of hip and knee movement without (gray lines) and with 30-Hz stimulation (black lines) of right (R) and left (L) side, each averaged from 10 step cycles. Arrows in left lower graph indicate the movement direction.

Stimulation of the type used here has been shown to depolarize afferents of the lumbar and upper sacral posterior roots, including Ia fibers from muscle spindles to produce reflex responses termed PRM reflexes (13,14,19). Further, 50-Hz tSCS induces lower limb paresthesias in sensory incomplete SCI individuals (15). In clinical applications of epidural stimulation, these tingling sensations are normally associated with the depolarization of long ascending fiber branches from cutaneous mechanoreceptors within the posterior columns of the spinal cord (21,22). Computer modeling studies of tSCS have confirmed the depolarization of the proximal portions of posterior root fibers within the vertebral canal, but suggested considerably higher thresholds for the posterior column fiber branches (14,23,24). Therefore, the paresthesias induced by tSCS may have been alternatively initiated in the posterior roots as well (25) (i.e., within the main axons distal to the posterior column branches). It can thus be suggested that the neural structures activated by the stimulation as applied here included fibers from cutaneous mechanoreceptors in the posterior roots and,

less probably, the superficial posterior columns. The paresthesias might have been induced by stimulation of only a small number of cutaneous fibers per dermatome (22). Group I fibers in the posterior roots from lower-limb muscles and tendons must have been depolarized as well, as their larger axons require less stimulus intensity to reach firing threshold (26,27). Yet their activation was subthreshold for reflex output, probably reflecting the need for additional excitatory input for summation within the motor nuclei before discharge may occur (28).

The input provided by tSCS must be rather similar to that of epidural lumbar SCS (14,23,29,30). The highly synchronized action potentials induced in the afferent axons spread to their terminal branches within the spinal cord and trans-synaptically modulate the operation of neuronal circuitry. We recently showed that tSCS modifies spasticity in individuals with motor-incomplete SCI (15), with the stimulation frequency set at 50 Hz, similar to epidural SCS for spasticity control (31). The frequency of 30 Hz applied in the present study was chosen because of earlier epidural SCS work where such frequency
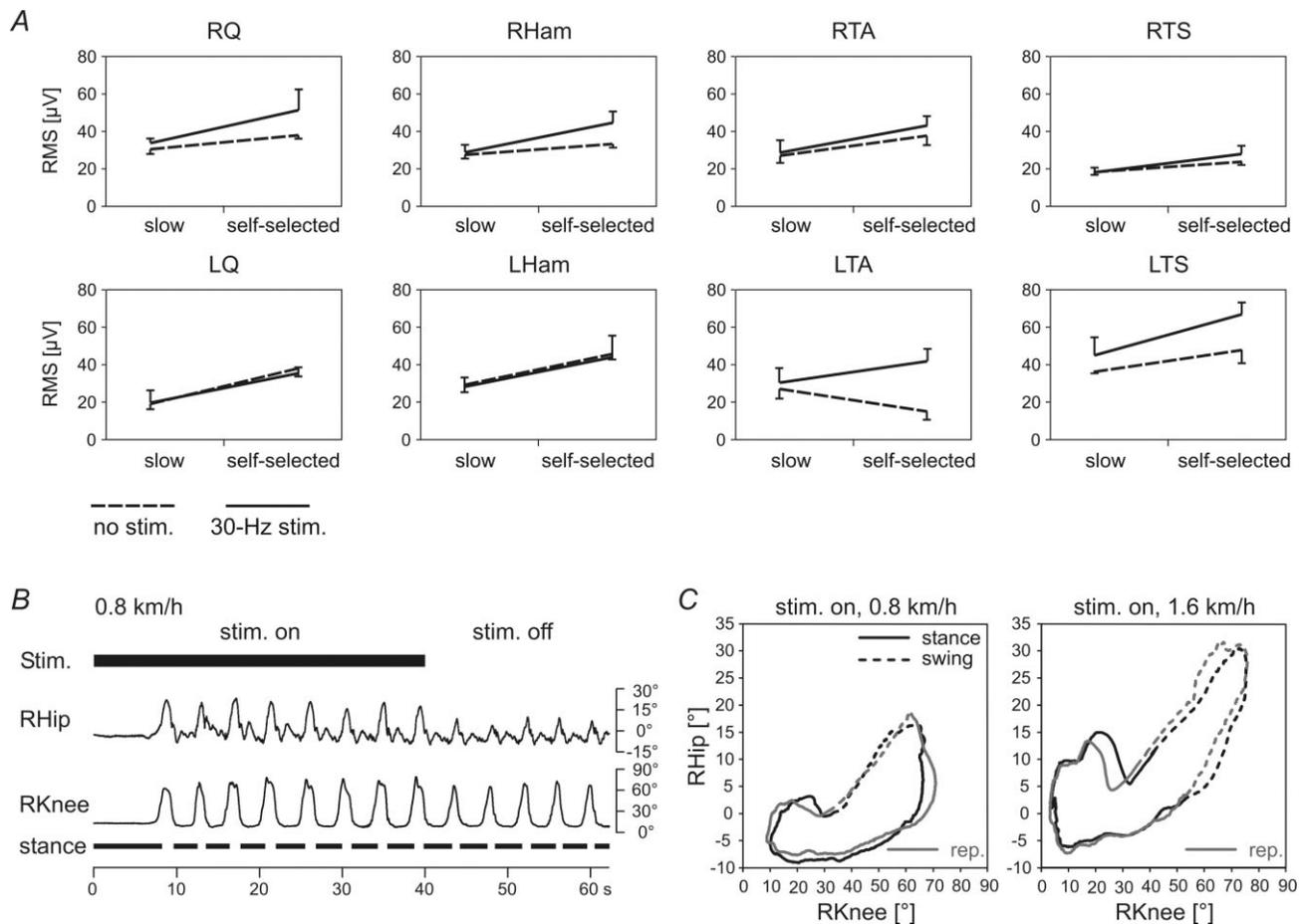
FIG. 5. Supplementary recordings in subject 1. A. Average root mean square (RMS) values of EMG activity, per gait cycle, during stepping at 0.8 km/h (slow) and 1.6 km/h (self-selected) under stimulation-off (dashed lines) and on conditions (solid lines); right (R) and left (L) quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS). B. Right hip and knee joint movements at the transition from standing to stepping at 0.8 km/h under stimulation (stimulation-on; thick vertical black bar) and their modifications after sudden cessation of stimulation (stimulation-off). Broken bars at the bottom are stance phases. C. Angle–angle plots of right hip and knee movements averaged from 10 gait cycles at 0.8 km/h (left) and 1.6 km/h (right) during 30-Hz tSCS. Black lines are derived from first trials each, and gray lines represent the repetitions (rep.).

was shown to activate lumbar spinal locomotor circuitry in motor-complete SCI subjects (10,12,32,33). Consequently, the 30-Hz tSCS was expected to elevate the resting excitability level of locomotor networks of the lumbar spinal cord.

There are supportive observations that this elevated excitability level can be used by residual voluntary control and/or step-related sensory feedback in the generation of motor activities. Improved motor function under stimulation was repetitively reported in previous studies of epidural SCS in numerous patients with various upper motor neuron disorders (34–36). Barolat et al. (37) were among the first to report regained supraspinal control over some movements of the otherwise paralyzed lower limbs after severe SCI that was present only under epidural SCS. There, the stimulation was set to induce

paresthesias in the lower limbs, but was subthreshold for muscle activation. Recently, a case study on an SCI subject who lacked clinically detectable voluntary motor function below the lesion was presented showing a return of some supraspinal control over leg movements with epidural stimulation (12). These observations indicate that even after a severe SCI, a small number of preserved fibers transiting the lesion could be utilized to activate the spinal circuitry that has been brought to an elevated physiological state using epidural stimulation. Moreover, Herman and colleagues applied epidural SCS in two motor-incomplete SCI individuals classified as AIS C to augment the outcome of locomotor training (30,38). Nonpatterned stimulation was applied at 20–40 Hz and intensities set between the sensory and motor thresholds. The combined training improved over-

ground walking, walking speed, step length, and endurance, and reduced the sense of effort for both participants. Yet the acute SCS effects were different in these two subjects, probably due to the exact neuroanatomy stimulated and the individual injury history and residual functions (30). In the first subject, epidural SCS induced phase-shifts in the temporal EMG patterns, without amplifying the muscle activities or changing the kinematics. In the second subject, EMG activities were substantially enhanced under stimulation, and the joint kinematics were altered significantly, including larger hip flexion by approximately 10° during swing (30). The authors suggested that the recruitment of afferent fibers in the posterior roots and/or columns by epidural SCS provided for the modulation of lumbar spinal cord locomotor circuits, which in turn could be utilized by descending voluntary drive and/or step-related peripheral feedback (30).

Our results derived from subjects 1 and 2 demonstrate a striking similarity to the findings in the second subject reported by Herman's group (30). In subjects 1 and 2, the trans-synaptic effects presumably preconditioned the functional state of neural circuits involved in locomotor control at pre-motoneuronal level. At motoneuronal level, the tonic input might have caused a repeated depolarization of their (resting) membrane potentials, bringing the motoneurons closer to firing threshold. Volitional activation and/or step-related sensory feedback then built on this enhanced state of excitability in the generation of the modulated motor outputs. Variations of the stimulation effects between these two subjects could have been due to segmental and side-to-side differences in stimulated input structures as well as the subjects' residual motor function, which was also reflected in the much lower levels of EMG activity produced in subject 1 during stepping and the different manifestations of spasticity.

The changes of gait kinematics with increased ROMs but only marginal changes in EMG activities in subject 3 could be explained by reduced muscle hypertonia under stimulation. An anti-spastic effect of tSCS has been suggested, when applied at 50 Hz (15), and an interindividual variability of the "optimal" parameters for spasticity control is known from the application of epidural SCS (31). Thus, in subject 3, the effect of stimulation with the chosen parameters might have been suboptimal for augmenting locomotor control. The slight reduction of the EMG activities could have been at least in part attributable to the artifact removal procedure, and the increased hip angles during swing could be explained by augmented hip flexor activities not assessed by EMG.

In all subjects reported here, the incomplete nature of the lesion further supports the possibility that beside the activation of local lumbar spinal cord circuits, tSCS acted on brainstem mechanisms as well and evoked long-loop effects (39).

The supplementary recordings in subject 1 suggest that the stimulation effects also depended on the step frequency. Variations of step frequency and thus velocity-dependent afferent information can be interpreted by the human lumbar spinal cord circuitries to adequately adapt motor outputs (6). This input-processing capability of the spinal circuitries could have been augmented under stimulation, thus yielding activation of otherwise quiescent muscles (left TA of subject 1) and proportionally higher EMG outputs with increased step frequency. Yet the particular contribution of feedback inputs and supraspinal drive to the induced augmentation of spinal motor excitability under tSCS during the increased step frequency cannot be determined. The supplementary recordings further confirmed the direct causal relationship between the application of tSCS and the modification of spinal motor output.

CONCLUSIONS

The present results suggest that transcutaneous lumbar spinal cord stimulation can be used as a non-invasive electrical neuroprosthesis to promote locomotor-permissive physiological changes within spinal cord circuitry. Combined with functional training, it may allow for more efficient therapies to facilitate restoration of functional ambulation in severely affected SCI subjects. There is early evidence that such combined training over a prolonged period of time can promote neuroplasticity after SCI (40). Further studies in a larger population are warranted to scrutinize the interaction between the neural input generated by stimulation and the individual profile of residual motor function after SCI.

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