Modification of spasticity by transcutaneous spinal cord stimulation in incomplete spinal cord injured individuals

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Abstract:

Context/objective: To examine the effects of transcutaneous spinal cord stimulation (tSCS) on lower-limb spasticity.

Design: Interventional pilot study to produce preliminary data.

Setting: Department of Physical Medicine and Rehabilitation, Wilhelminenspital, Vienna, Austria.

Participants: Three subjects with chronic motor-incomplete spinal cord injury (SCI) who could walk ≥10 m.

Interventions: Two interconnected stimulating skin electrodes (Ø 5 cm) were placed paraspinally at the T11/T12 vertebral levels, and two rectangular electrodes (8 × 13 cm) on the abdomen for the reference. Biphasic 2 ms width pulses were delivered at 50 Hz for 30 minutes at intensities producing paraesthesias but no motor responses in the lower limbs.

Outcome measures: The Wartenberg pendulum test and neurological recordings of surface-electromyograph (EMG) were used to assess effects on exaggerated reflex excitability. Non-functional co-activation during volitional movement was evaluated. The timed 10-m walk test provided measures of clinical function.

Results: The index of spasticity derived from the pendulum test changed from 0.8 ± 0.4 pre- to 0.9 ± 0.3 poststimulation, with an improvement in the subject with the lowest pre-

stimulation index. Exaggerated reflex responsiveness was decreased after tSCS across all subjects, with the most profound effect on passive lower-limb movement (pre- to post-tSCS EMG ratio: 0.2 ± 0.1), as was non-functional co-activation during voluntary movement. Gait speed values increased in two subjects by 39%.

Conclusion: These preliminary results suggest that tSCS may elicit similar results as epidurally delivered stimulation for spasticity control, without negatively impacting residual motor control in incomplete SCI. Further study in a larger population is warranted.

Introduction

Partial injury of descending spinal cord tracts alters the supraspinal motor control over the lumbosacral neural circuitry that is normally preserved caudal to the lesion. The consequences of such injuries are usually paresis or paralysis and spasticity of the lower extremities.[1,2] Also, when present, spasticity can negatively impact otherwise sufficient residual motor control.[3,4]

Treatment modalities used for spasticity target the segmental pathophysiological changes within the spinal cord after the injury as well as changes in the muscle-tendon complex.[5] They range from oral medication and physical interventions to motor nerve block injections and intrathecal drug delivery.[5,6] Yet, therapeutic control of severe forms of spasticity while maintaining or even enhancing residual motor capacities has remained difficult.[10] Surgical treatment of spasticity is based on the concept that spinal reflex circuitry becomes hyperactive after being deprived of supraspinal inhibitory control. By cutting the posterior roots, Otfrid Foerster, 1909, interrupted afferent inputs to the spinal cord to reduce the excitability of segmental neural circuits.[7] More selective posterior root entry zone procedures were developed to decrease lower limb hypertonia and improve ambulation.[8] However, such surgical approaches create permanent lesions within the neural tissue and have the potential to damage surviving neural function and a high incidence of recurrence of spasticity was reported.[9]

The emergence of epidurally delivered electrical spinal cord stimulation (SCS) provided an alternative way to reversibly modify motor control in patients with upper motor neuron disorders.[11-15] Richardson, McLone and colleagues described the alleviation of severe lower limb spasticity in clinically complete thoracic spinal cord injury (SCI) by epidural stimulation applied over the lumbosacral spinal cord and cauda equina.[16,17] In patients with motor complete and incomplete SCI, epidural SCS was applied below and above the lesion at vertebral levels ranging from C2–T10 and at stimulation frequencies of 30 Hz–1500 Hz, with variable results.[18-22] Dimitrijevic and colleagues suggested that the diversity of physiological conditions after SCI and the placement of the epidural electrodes determined the efficacy of SCS in spasticity control.[23,24] While interest in this technique declined in the 1990s, Pinter and colleagues revisited its use in chronic SCI individuals.[25] They showed a significant suppression of severe lower limb spasticity when the epidural electrodes were placed over the lumbar posterior roots and the stimulation frequency was in a range of 50 Hz–100 Hz. The

suggested mechanism was the modification of the excitability of neural circuits within the lumbar spinal cord through continuous posterior-root activation.[25-27]

We previously described a transcutaneous stimulation method to depolarize large-diameter afferent fibers of the L2–S2 posterior roots in humans.[28-30] These input structures to the segmental neural circuits are hence (at least a sub-population of) the same neural targets as electrically stimulated by epidural implants over the lumbar spinal cord.[22,30] In the present exploratory work we hypothesized that transcutaneous SCS (tSCS), when applied in a continuous mode at 50 Hz, can be used to modify the central state of excitability of lumbar neural circuits, and reduce spasticity.

Methods

Subjects and clinical data

After informed consent was obtained, three subjects (mean age 32.7 ± 4.1 years; 1 female) with chronic (10.7 ± 1.2 years post-onset) sensory- and motor-incomplete SCI were studied (Table 1). The participants were otherwise healthy adults. All subjects had spastic muscle hypertonia in the lower limbs and exhibited clonus but were able to complete the 10-meter walk test without braces and were not taking anti-spasticity medications. The study was approved by the Ethics Committee of the City of Vienna, Austria, and conforms to the Helsinki Declaration of 1975, as revised in 2000.

Table 1. Subject characteristics.

Subject no.	Sex	Age	Years post-injury	Level of SCI	AIS	lower limb motor scores		WISCI	Device
						left	right		
1	m	38	9	C5	D	13	12	13	walker
2	m	32	12	C5	D	12	17	16	crutches
3	f	28	11	T9	D	11	13	16	crutches

ASIA Impairment Scale (AIS) category, Walking Index for Spinal Cord Injury (WISCI), assistive devices needed for gait (Device).

Transcutaneous spinal cord stimulation (tSCS)

tSCS was applied using self-adhesive electrodes (Schwa-medico GmbH, Ehringshausen, Germany). A pair of stimulating disk electrodes ($\varnothing = 5$ cm) was placed over the T11 and T12 spinous processes, manually identified by palpation, with one electrode on either side of the spine (Fig. 1A). A pair of rectangular reference electrodes (8 cm x 13 cm each) was placed over the lower anterior abdomen, in symmetry to the umbilicus. The two electrodes of each pair were connected together so as to function as single, larger electrodes. A constant-voltage stimulator delivered charge-balanced, symmetric, biphasic rectangular pulses of 2 ms width (1

ms per phase). Electrode placement was confirmed by eliciting posterior root-muscle reflexes (PRM reflexes) in lower limb muscles with the subjects relaxed in the supine position (Fig. 1B).[29-31] The requirement was that single stimuli evoke PRM reflexes in the L2-L4 innervated quadriceps (Q) at lower thresholds than in the L5-S2 innervated triceps surae (TS).[25,26,32] Paraspinal electrodes were relocated, up to 3 cm in either the rostral or caudal direction when needed to achieve this required PRM response distribution. Double-stimuli at interstimulus intervals of 30 ms, 50 ms, and 100 ms were applied to test the presence of post-stimulation attenuation of the detected responses to verify the stimulation of afferent fibers (Fig. 1C).[29,33]
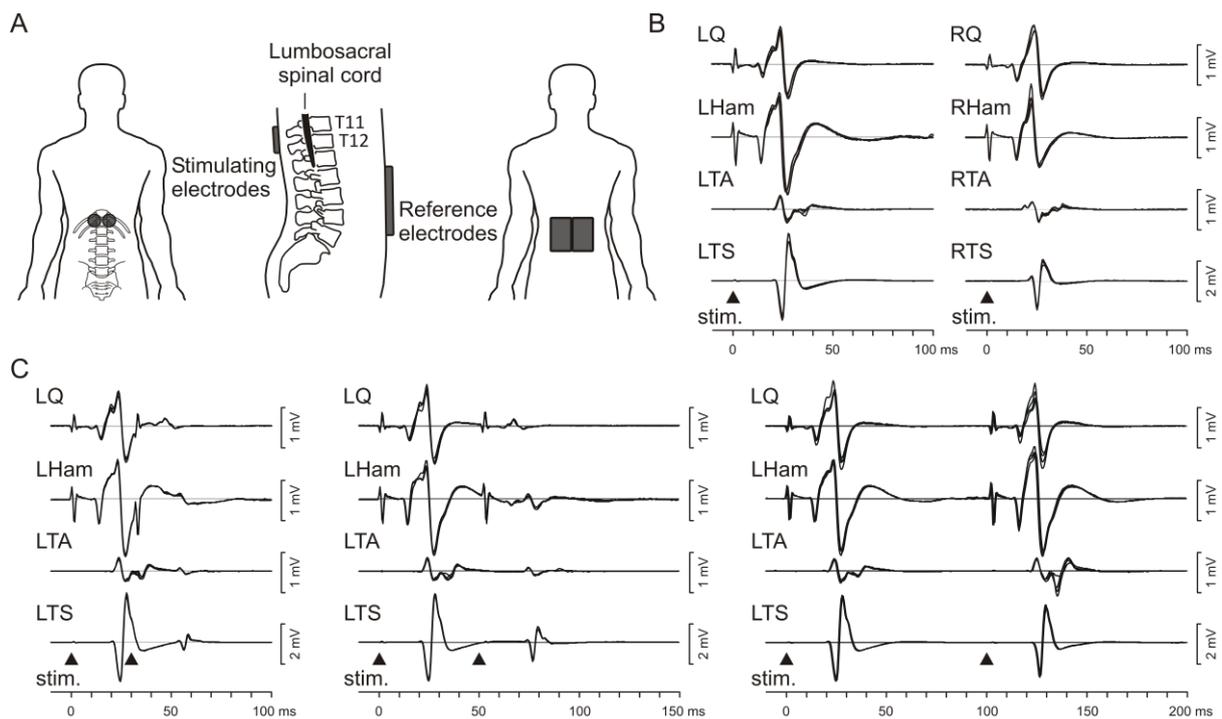

Figure 1. Transcutaneous spinal cord stimulation. (A) Sketch of the placement of the stimulating and reference skin electrodes over the back and the lower abdomen, respectively, relative to the spine and the lumbosacral spinal cord. (B) The elicitation of posterior root-muscle reflexes in left (L) and right (R) quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS) was used as electrophysiological criterion to confirm the position of the stimulating paravertebral electrodes over the lumbar spinal cord. (C) The stimulation of posterior root afferents was verified by testing the recovery cycle of the evoked responses using double-stimuli at interstimulus intervals of 30 ms, 50 ms, and 100 ms. Electromyographic data derived from subject 2 in the supine position.

To induce the hypothesized neuromodulative effect on lumbar spinal neural circuits, tSCS was applied at a frequency of 50 Hz.[25] With the subject lying comfortably supine on an examination bed, the stimulation intensity was slowly increased starting from 0 V to allow for adaptation to the stimulation-induced effects. These effects included, in sequence of their occurrence with increasing stimulation: sensory perception of the stimulation under the paraspinal and subsequently the abdominal electrodes, contraction of the paraspinal and abdominal muscles, and paraesthesias in the lower limbs. tSCS was applied for 30 minutes at

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intensities producing paraesthesias in most of the lower limb dermatomes, yet subthreshold for generating lower limb motor activity. Particularly, the average intensity applied amounted to 20 V ± 2 V (per phase of the biphasic stimulation pulse), corresponding to 68% ± 16% of individual lower limb PRM reflex threshold.[19,24] Discomfort during the stimulation was not reported by any subject.

Assessments

All assessments were performed prior to and immediately following the 30-minute session of 50-Hz tSCS.

The Wartenberg pendulum test (WPT) is a quantitative method for the assessment of spastic hypertonia of the Q muscle.[34] With the subject in a sitting position, reclined at approximately 45°, the examiner lifted the relaxed test limb to a horizontal position, then released it and let it oscillate passively until it stopped in a gravity-neutral position. The test was repeated 3 times on each side.

Electromyographic (EMG) recordings from Q, hamstrings (Ham), tibialis anterior (TA), and TS muscles bilaterally were acquired using pairs of silver-silver chloride recording electrodes (Intec Medizintechnik GmbH, Klagenfurt, Austria), each placed centrally over the muscle bellies and oriented along the long axis of the muscles with an inter-electrode distance of 3 cm.[35] Inter-electrode impedance was reduced to below 5 kΩ using abrasive paste. EMG signals were amplified (EMS-Handels GmbH, Korneuburg, Austria) with a gain of 502, filtered to a bandwidth of 10 Hz to 500 Hz and digitized at 2048 samples per second per channel. Electro-goniometers (Penny & Giles Biometrics, Ltd., Gwent, UK) were used to measure knee and ankle movements. The goniometric data were synchronized to the EMG, bandpass-filtered between 0 Hz and 100 Hz and sampled at 2048 Hz.

Reflex activities and motor tasks tested included, in the supine position, passive unilateral hip and knee flexion and extension movements, the manual elicitation of ankle clonus by rapid stretch of the Achilles tendon, and foot withdrawal by non-noxious mechanical plantar stimulation. Each of the maneuvers was repeated three times on each side, separated by phases of relaxation. In the sitting position, rhythmic voluntary unilateral ankle dorsi- and plantar flexion attempted at a self-selected speed was performed 5 times on each side.

The 10-meter walking speed was acquired with subjects using walking aids (Table 1) as required for safety.[36] Each test was videotaped for offline visual examination.

In subjects 1 and 2, all segments of the assessment were completed in a single recording session. In subject 3, passive lower limb movements and plantar stimulation were performed in one session, and ankle clonus, volitional ankle movement, and the timed 10-meter walk test were accomplished in a second session. The WPT was repeated in both sessions, and the respective measures were averaged, hence contributing single values per leg to the group results.

Data analysis

Data were analyzed offline using WinDaq Waveform Browser playback software (Dataq Instruments) and Matlab 6.1 (The MathWorks, Inc., Natick, MA, USA).

Wartenberg pendulum test. The "index of spasticity," R_{2n}, was calculated as described by Bajd and Vodovnik[37]:

$$R_{2n} = \frac{(peak\ knee\ flexion\ angle\ of\ first\ swing) - (starting\ knee\ angle)}{1.6 * [(final\ resting\ knee\ angle) - (starting\ knee\ angle)]}$$

Scores ≥ 1 signify non-spastic conditions, while $R_{2n} = 0$ is obtained in case of extreme spasticity. The index correlates well with the clinical evaluation of muscle hypertonia graded on the Ashworth scale, and provides a more objective and finely graded measurement.[38] Here, mean R_{2n}-values were averaged over the three repetitions on each side.

Additionally, the magnitude of total ipsilateral lower limb EMG activity generated during the pendulum test was calculated as the sum of the root mean square (RMS) of the EMG activity across the four ipsilateral muscle groups, between the onset of the maneuver, drop of leg from horizontal position, and the time when the resting angle was reached. Data for each muscle were baseline-corrected by subtracting the RMS calculated from a 1-second period preceding the maneuver. Mean values of the three repetitions for each limb were evaluated. The corresponding value after tSCS was then individually normalized to the value before stimulation and normalized mean group results $\bar{A}_{total}$ of these ratios (derived from n = 6 lower limbs) were calculated.

Volitional ankle dorsi- and plantar flexion. The total maneuver-related magnitudes of ipsilateral muscle activation during five consecutive flexion and extension phases (identified by ankle goniometric data) were calculated based on the RMS values as described above and averaged. Agonist muscle activity during each movement phase was normalized to the total activity recorded across all ipsilateral muscles. Thus, the amount of TA activity (RMS_{TA}) relative to the total magnitude of ipsilateral muscle activation (RMS_{total}) during dorsiflexion was individually calculated as RMS_{TA}/RMS_{total}, and group results were obtained across the subjects. Accordingly, the relative TS activity during plantar flexion was computed as RMS_{TS}/RMS_{total}. Mean peak angles of the ankle movement for the five repetitions were also obtained.

Passive lower limb flexion-extension, ankle clonus, and plantar stimulation. In case of passive lower limb flexion and extension movements, base-line corrected RMS from ipsilateral muscles were calculated between the onsets and offsets plus 3 seconds for the movement identified by knee goniometric data. For ankle clonus and plantar stimulation, RMS of ipsilateral lower limb EMG activity was computed for 5-second time windows following the initiation of the maneuvers. Mean values for the maneuver-related magnitude of ipsilateral muscle activation were obtained from the three repetitions of each task, and normalized group mean results $\bar{A}_{total}$ were calculated from the available data sets.

10-m walk test. The time required to walk a distance of 10 m before and after stimulation with the same walking aids was measured.

Results

Pendulum test

The average spasticity index R_{2n} was 0.8 ± 0.4 before and 0.9 ± 0.3 after tSCS. The group result $\bar{A}_{total}$ of the magnitude of ipsilateral muscle activation after stimulation normalized to the corresponding value before stimulation was 0.9 ± 0.0. The EMG activities produced during the WPT were decreased evenly across all subjects after stimulation, while the R_{2n} score improved in subject 3 only, who had the lowest pre-stimulation scores, with no changes in the R_{2n} in subjects 1 and 2. The R_{2n} scores obtained in subject 3 in the two sessions were reproducible for both lower limbs and the pre- and post-tSCS assessments, respectively. Before stimulation, the pendulum test documented restraints in the free-swinging movements of the lower leg in subject 3 (Fig. 2, left). The passive, gravity-driven movement toward the gravity-neutral end-point position was interrupted by numerous short bursts of stretch-elicited Q activity, accompanied by activation of Ham and, to some extent, of TA. After stimulation, activation of the Q only occurred during the initial two flexion-extension oscillations of the leg and the knee movements were a pseudo-sinusoidal, damped motion (Fig. 2, right).
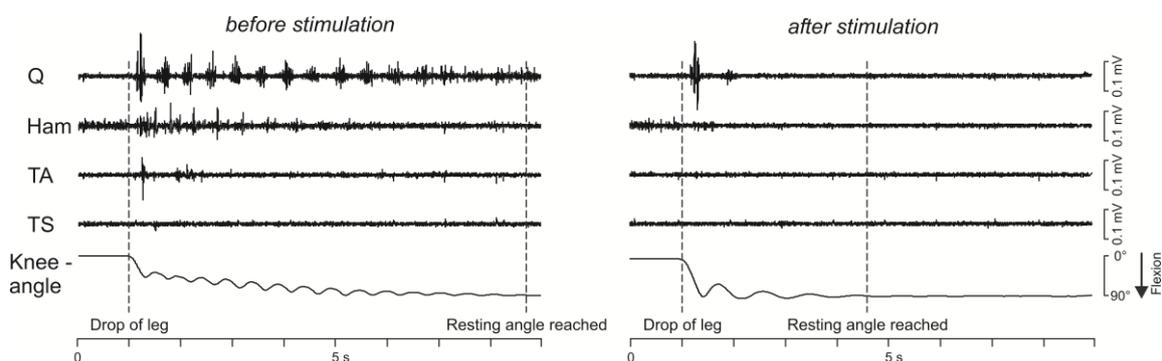

Figure 2. Wartenberg pendulum test. Electromyographic (EMG) activity from quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS) along with knee goniometric data before and after transcutaneous spinal cord stimulation in subject 3. Dotted lines mark the drop of leg from the horizontal position and the final resting knee angle reached. After stimulation, EMG activity is clearly reduced and the knee angle oscillations are a damped, pseudo-sinusoidal motion.

Effects of tSCS on exaggerated reflex responses

Passive hip and knee flexion and extension movements (Fig. 3A) before tSCS induced responses with a spread of EMG activity to all ipsilateral lower limb muscles. These responses were almost completely absent in the post-tSCS assessment. Pre-tSCS, a brisk manual stretch of the calf muscle elicited clonus-like activity in TS that spread to Ham and TA in the example given in Fig. 3B. After tSCS, no muscle activities except for a brief stretch-related reflex response in TS were detected when the same maneuver was performed.

Non-noxious, cutaneous stimulation to the plantar surface of the foot with a blunt probe (Fig. 3C) resulted in withdrawal-reflex EMG activity in all ipsilateral lower limb muscles but after tSCS, was largely diminished.

The general decline in exaggerated reflex activities was reflected by the group results $\bar{A}_{total}$ of the maneuver-related magnitudes of ipsilateral lower limb EMG activity obtained for the post-tSCS assessment normalized to the corresponding values before tSCS (Fig. 3D). The post-tSCS RMS values were considerably reduced across all maneuvers and lower limbs, with the exception of the values derived from the ankle clonus tested in the respective left lower limbs of subjects 1 and 3. Specifically, $\bar{A}_{total}$ amounted to: passive lower limb movement, 0.2 ± 0.1; ankle clonus, 0.7 ± 0.3; and plantar stimulation, 0.4 ± 0.1.
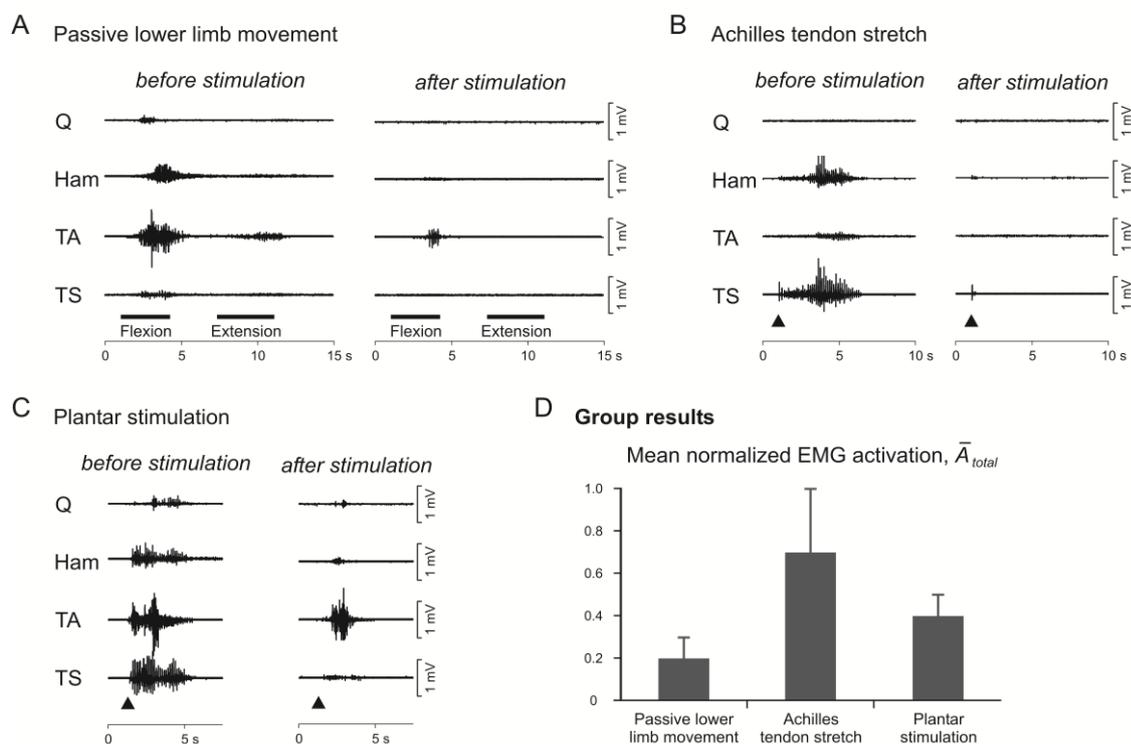

Figure 3. Assessment of different manifestations of spasticity before and after transcutaneous spinal cord stimulation (tSCS). (A) Manually performed hip and knee flexion and extension movements; (B) the attempt to elicit an ankle clonus; and (C) a light stroke of the plantar surface with a blunt rod. Arrow heads in (B) and (C) depict onsets of the respective mechanical stimuli. Exemplary recordings were derived from subject 2. (D) Group results (n = 6) of maneuver-induced magnitudes of ipsilateral lower limb muscle activity after tSCS relative to corresponding values before tSCS. Note the general decline in exaggerated reflex activity in the post-tSCS assessment.

Effects of tSCS on voluntary movements

The EMG activity during volitional ankle dorsi- and plantar flexion performed before stimulation was generally characterized by co-activation patterns in the TA and TS muscles during both phases of movement (Fig. 4A, left). After stimulation, this co-activation was decreased (Fig. 4A, right). Furthermore, active range of motion for dorsiflexion was increased. The mean total range of ankle movement of the different subjects was increased

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after stimulation by a factor of 1.2 ± 0.1. In addition, clonus-like activity in TA and TS that occurred in subjects 1 and 2 during the execution of the voluntary motor task was eliminated after tSCS (Figs. 4A,B).

Group results (Fig. 4C) revealed that the magnitude of ipsilateral EMG activity during dorsiflexion remained almost unchanged compared to that from before stimulation ($\bar{A}_{total}$ = 0.9 ± 0.4). Yet, a more selective activation of the ankle flexor TA during dorsiflexion was observed in the post-tSCS assessment, as reflected by the group mean results of RMS_{TA}/RMS_{total} (0.6 ± 0.1 before stimulation and 0.8 ± 0.2 afterwards; Fig. 4D, left). During plantar flexion, the magnitude of ipsilateral EMG activity was reduced after stimulation ($\bar{A}_{total}$ = 0.5 ± 0.2). There was no increase in selectivity in agonist muscle activation, with the relative TS activity RMS_{TS}/RMS_{total} remaining at a low level (0.3 ± 0.2 before and 0.2 ± 0.2 after stimulation; Fig. 4D, right).
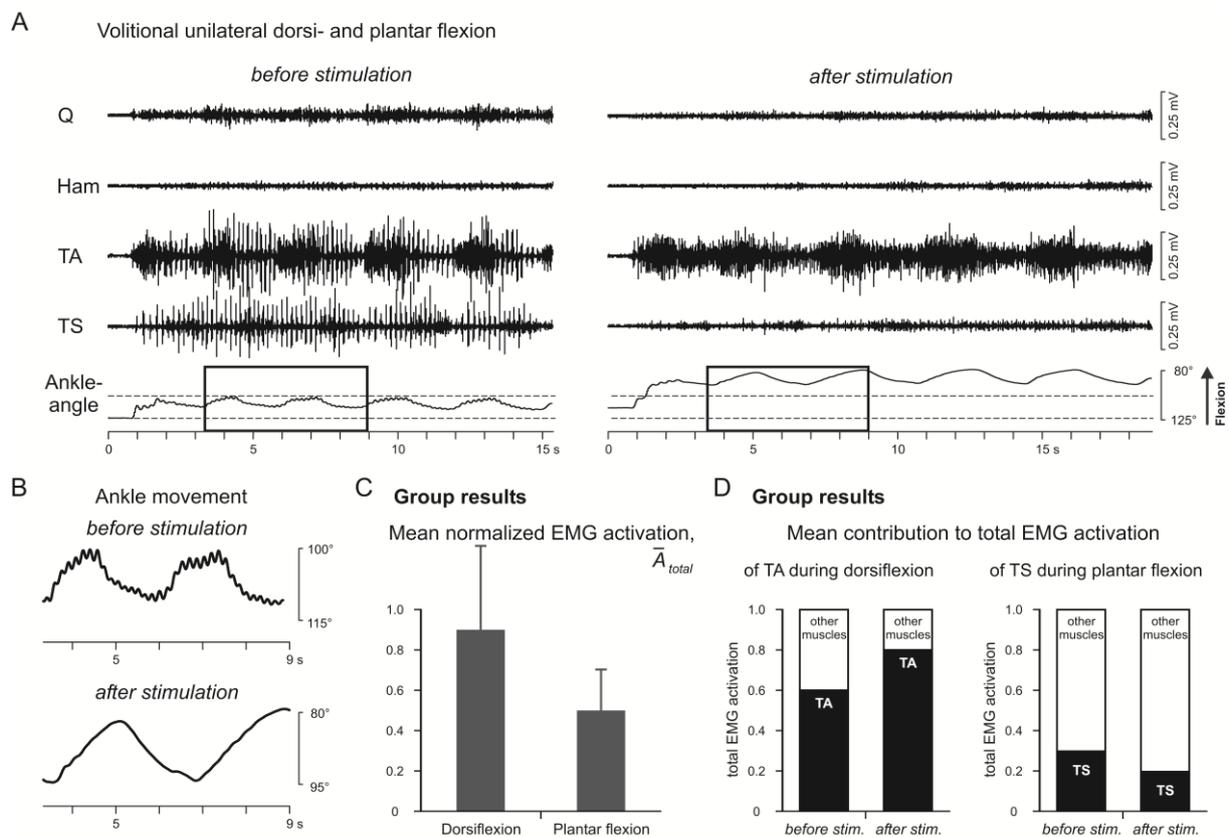

Figure 4. Volitional unilateral dorsi- and plantar flexion in sitting position. (A) EMG patterns showing co-activation and ankle clonus (left) are reduced post-stimulation (right). Dotted lines superimposed on the ankle goniograms show the range between the neutral extended position of the ankle at rest and maximum dorsiflexion before stimulation, and a flexion bias of the rhythmic movement after stimulation is documented by the shift of the goniometric trace. Boxes are displayed with enlarged scales in (B) depicting the interference of clonus-like activity before stimulation that is eliminated after stimulation. (C) Group mean magnitudes of ipsilateral EMG activity during dorsi- and plantar flexion after stimulation normalized to the corresponding values before stimulation. (D) The contribution of TA to the total magnitude of ipsilateral muscle activation during dorsiflexion was increased after stimulation. TS activity during plantar flexion was at a low level before and after stimulation.

Effects of tSCS on the walking ability

Two of the three participants increased their over-ground walking speed after stimulation. Times required to walk 10 m at a self-selected fast, yet secure speed were 54 s before and 34 s after stimulation for subject 1, and 54 s vs. 32 s for subject 2. Clonus-like activity interfering with the subjects' ability to walk before stimulation was visibly reduced after stimulation in these two subjects. Subject 3 had the fastest 10-m time prior to stimulation and did not show any increase after stimulation (23 s vs. 23.5 s).

Subjects' reports

Apart from the anti-spastic effect, the participants described a feeling of lightness of the lower limbs, and increased sensation, especially of the foot sole during ground contact. The anti-spastic effects were subjectively reported to have persisted for two to six hours after tSCS. No negative effects were reported.

Discussion

We described the effects of a 30-minute session of 50-Hz transcutaneous lumbar SCS in three motor-incomplete SCI subjects with clinically evident spasticity. We observed that the responsiveness to muscle stretch, both tonic and phasic was decreased, as was the response to non-noxious, cutaneous stimulation of the plantar surface of the foot. Also, TA was more selectively activated during volitional dorsiflexion movements after tSCS. Finally, two of the three subjects increased their walking speeds considerably after tSCS.

To understand these observations, we must first look to the neuroanatomy stimulated by tSCS. The electrode set-up and stimulation frequency of tSCS resemble that of transcutaneous electrical nerve stimulation (TENS). However, clinical TENS therapies normally excite more superficially located neural structures, and the major application is in the treatment of localized pain conditions. On the other hand, tSCS targets deeply located neural structures within the vertebral canal with the aim to provide bilateral multi-segmental input to the spinal cord and subsequently modify the excitability of its circuits.[22] Within the vertebral canal, large diameter afferent fibers of the L2-S2 posterior rootlets to spinal cord junctions have the lowest thresholds for direct, electrical depolarization.[29] The ligaments and discs between the vertebral bones reduce the transverse electrical resistance of the thoraco-lumbar spine and allow some current to flow through the vertebral canal.[30,39,40] The excitation thresholds for the posterior root fibers are considerably reduced at their point of entry into the spinal cord due to non-uniformities of the anatomy and its electrical conductivities along the fiber paths and changes of the fiber path direction with respect to the generated field.[30,39,40] Among the fibers within the posterior roots, the Ia afferents have the largest fiber diameters. It is known that the Ia afferents, presumably among the fibers depolarized during tSCS, make strong synaptic connections to Ia inhibitory interneurons.[41] Independently, there is indirect evidence in humans that epidural SCS can activate spinal circuitries mediating reciprocal inhibition.[32,42]

Reciprocal inhibition might be one of the mechanisms sub-serving an inhibitory plurisegmental network situated within the lumbar spinal cord that was thought to be involved in the amelioration of severe lower-limb spasticity in a group of clinically complete mid-thoracic SCI people when epidural electrodes were placed over the lumbar posterior roots.[25]

Another potential source of the effects observed here can be drawn from the reports that stimulation of the long tracts of the spinal cord reduces responsiveness to muscle spindle afferent input after spinal cord lesioning in cat models and SCI in humans.[23,24,43,44] Here, we applied tSCS with adequate intensity to produce paraesthesias that are generally associated with posterior-column depolarization during epidural SCS.[45-47] Modeling of tSCS-induced currents, however, has shown that posterior column fibers have considerably higher thresholds than the posterior root fibers.[40] Thus, at the intensities applied here, tSCS was probably not depolarizing long-tract fibers directly. Posterior roots contain fibers from cutaneous mechanoreceptors and their depolarization can also produce such sensations.[48] Therefore, the report of parasthesias experienced here and the incomplete nature of the lesions in this study support the possibility that long loop, spinal-brainstem-spinal mechanisms might be involved in the suppression of segmental excitability.[23] Such combined posterior roots' activation and increased descending inhibition via brainstem loops in the control of spinal spasticity was suggested by other human studies.[17,23,25,49] Therefore, the most likely explanation for the effects seen in the three subjects reported here is a combination of both direct activation of local inhibitory circuits by posterior root fibers and the potentially more complex involvement of descending activation of presynaptic inhibition brought by long-loop mechanisms. This would also explain the observed reduction in the excessive withdrawal-like response elicited by non-noxious stimulation of the plantar surface of the foot, interpreted as a sign of decreased descending inhibitory control and altered intraspinal processing due to SCI.[50] Finally, a generalized reduction of motor outputs by post-synaptic inhibition only is less probable since there was no deterioration of the voluntary activation of motor neuron pools during single ankle joint movements and walking. The improvements in the 10-m walk test in two of the three incomplete SCI participants after tSCS were partially attributable to the reduced clonus-like activity interfering with gait. The influence of a practice effect was less probable since the increase in gait speed of the two subjects was definitely beyond the normal variability of the subjects' condition.

To what extent the above discussed mechanisms contribute to the temporarily persisting modifications of the spinal cord neural circuits' excitability as assessed after tSCS was ended remains to be elucidated. Yet, this carry-over effect and its subjectively reported persistence for two to several hours after cessation of stimulation were not unexpected. In epidural SCS in motor disorders, it was repetitively observed that degradation of the improved function after withdrawal of stimulation could take hours or days.[13,19,23,24] Temporary carry-over effects were also described in functional electrical stimulation of peripheral nerves.[51-53] However, proposed physiological mechanisms underlying these carry-over effects are speculative and

include activity-dependent, temporarily persisting changes of synaptic transmission such as long-term potentiation and long-term depression behavior of spinal motor neurons.[54]

The results were derived from few individuals and thus, generalization to a population with a variety of SCI profiles should be cautioned.[55] Further, the obvious sensory effects of the active stimulation limits the applicability of more conclusive study designs such as crossover studies with sham stimulation. Yet, we conducted thorough and quantitative assessment of many parameters of a highly integrative sensory-motor system.[55] The antispastic effect of tSCS was apparent from complementary biomechanical, neurophysiological, and clinical evaluations and there were no discrepancies of the modifications across the parameters after stimulation. The promising results justify a clinical study with a statistically appropriate subject population with different severities of SCI. The close investigation of the carry-over effects as well as methods for prolonging this beneficial period, e.g. by several sessions of tSCS over a longer period of time, should be also addressed.

Conclusion

Independent from the specific mechanisms, the present results suggest that 50-Hz tSCS for 30 minutes leads to the diminution of pathophysiology (spasticity) and the improvement of normal physiology (voluntary motor control). If shown to be of wide prevalence, it is possible that this therapeutic approach could be used instead of systemically applied medications or ablative treatments with their unfortunate and long-lasting side effects. The temporary relief of spasticity with tSCS could be a non-invasive treatment of use for even short periods, perhaps prior to a physical therapy session where decreased co-contractions and dysynergias and improved voluntary control could be better trained.

Thus, this report serves as evidence that more study designed to characterize the extent and potential mechanisms of tSCS effect on motor neuron excitability is needed. Taken together, these results suggest that tSCS may be able to modify spinal motor responsiveness to external inputs from muscle, tendon, joint and cutaneous receptors while maintaining its responsiveness to input from spinal motor processing generated from within the CNS.

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