Transcutaneous spinal cord stimulation

Background – Epidural spinal cord stimulation

Spinal cord stimulation is currently used to control neurological pain and impaired motor functions. In these clinical applications, epidural spinal cord stimulation-systems are being used with the electrode (or 'lead') being surgically placed in the epidural space (the outermost part of the vertebral canal outside of the meninges covering the spinal cord). The electrode delivers electrical stimulation to the posterior aspect of the spinal cord from a close distance of a few millimeters. Epidural spinal cord stimulation works through the principle of neuromodulation, i.e. the modulation of altered neural circuits' activity of the spinal cord.

Epidural spinal cord stimulation has been repetitively reported to be effective in suppressing spasticity in patients with spinal cord injuries (Richardson & McLone, 1978; Dimitrijevic et al., 1986a; 1986b; Barolat et al., 1995). Pinter and colleagues (2000) demonstrated that epidural spinal cord stimulation is highly effective to control severe lower limb spasticity of patients with traumatic spinal cord injury. There was a remarkable antispastic effect across thigh and leg muscles when stimulating the lumbar posterior roots with frequencies of 50 Hz–100 Hz. In patients with motor complete (i.e. functionally complete or discomplete) spinal cord injury in supine position, continuous constant epidural stimulation of the same site of the spinal cord (with frequencies of 25 Hz–50 Hz) could generate automatic, stepping-like activity in the paralyzed lower limbs (Dimitrijevic et al., 1998; Gerasimenko et al., 2002; Jilge et al., 2004; Minassian et al., 2004; 2007a). Figure 1 shows an example of such rhythmic electromyographic activities recorded from the lower limb muscles of a patient with chronic complete spinal cord injury.

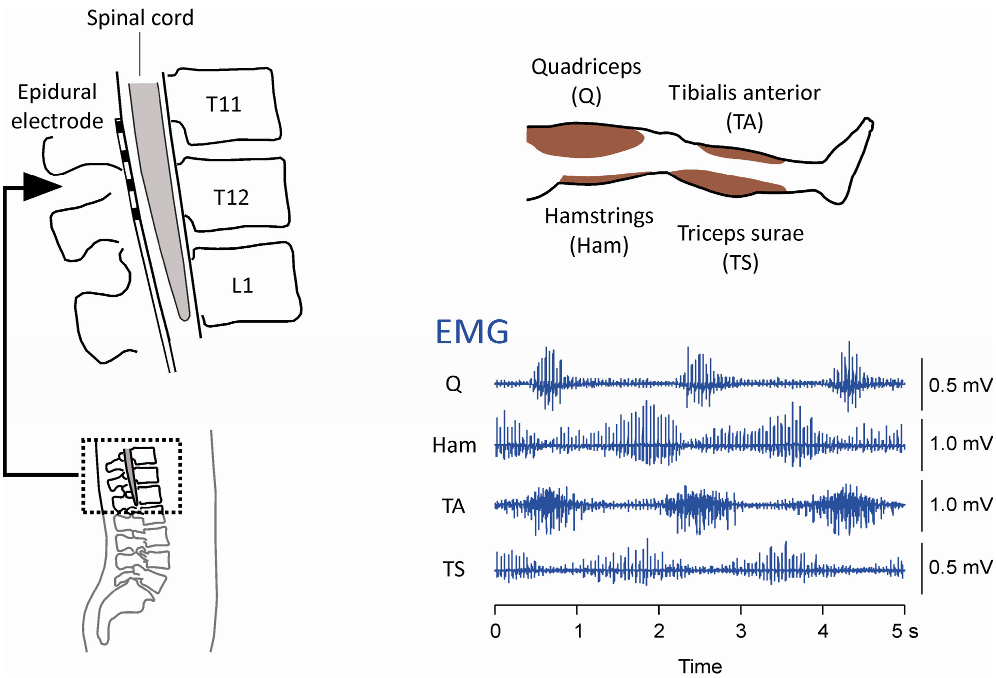

Figure 1: Rhythmic electromyographic (EMG) activity produced in paralyzed lower limbs with a so-called locomotor-like pattern, i.e. reciprocal activation of antagonistic muscles. Left: Sketch of epidural electrode and its position with respect to the vertebrae and the spinal cord. Right: Studied lower limb muscles and corresponding EMG recordings. The continuous, constant epidural stimulation (10 V, 22 Hz) of the lumbar spinal cord produced rhythmic muscle contractions. The subject had a chronic, motor complete spinal cord injury and was lying supine on an examination bed.

Early work has begun to investigate the clinical relevance of epidural spinal cord stimulation to enhance locomotor activity (Herman et al., 2002; Minassian et al., 2005; 2007a; Huang et al., 2006; Harkema et al., 2011) and other functional movements (Harkema et al., 2011) in spinal cord injured people.

Transcutaneous lumbar spinal cord stimulation

Transcutaneous lumbar spinal cord stimulation uses commercially available, self-adhesive skin electrodes placed over the lower back and abdomen (Figure 2; Minassian et al., 2007b; Hofstoetter et al., 2008).

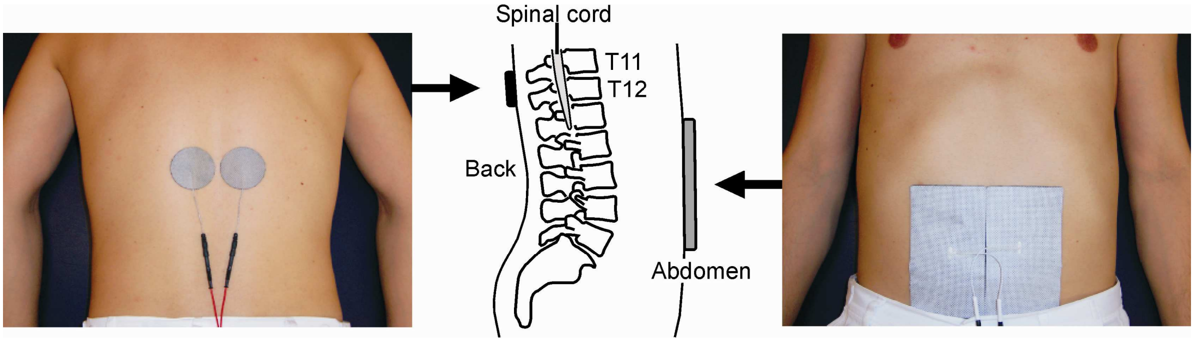

Figure 2: Electrode placement for transcutaneous lumbar spinal cord stimulation. Stimulation electrodes are a pair of round electrodes with diameters of 5 cm placed on each side of the spine. This paraspinal electrode pair is positioned between the T11-T12 vertebrae to stimulate the lumbar spinal cord. Reference electrodes are a pair of large rectangular electrodes (8 cm x 13 cm) covering the lower abdomen. The two electrodes of each pair are connected to function as a single electrode.

The stimulation activates sensory fibers within the lumbar and upper sacral posterior roots. The specific, localized depolarizations of these posterior root fibers in spite of the distant stimulation are made feasible by the tissue heterogeneity of the volume conductor in-between the electrodes and by the neuroanatomy of the terminal spinal cord (Ladenbauer et al., 2010, Danner et al., 2011; Szava et al., 2011).

The direct, electrical stimulation of large-diameter afferents is reflected by the elicitation of so-called posterior root-muscle reflexes (PRM reflexes) in many lower limb muscles, when single pulses are applied (Figure 3). Neural structures within the spinal cord are not directly electrically stimulated, but transsynaptically activated by the posterior root-stimulation.

The reliable stimulation of sensory nerve fibers of multiple posterior roots is essential for the application of transcutaneous spinal cord stimulation in human electrophysiological studies (delivering single or few pulses to elicit PRM reflexes) and as a neuromodulation technique (with continuous stimulation).

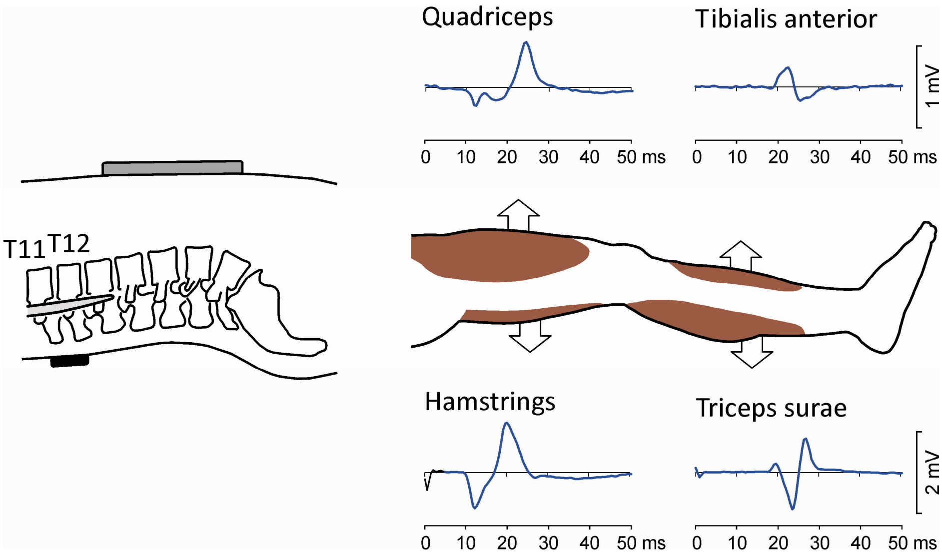

Figure 3: A single stimulus-pulse applied transcutaneously to the lumbar spinal cord evokes brief contractions (twitches) of effectively all lower limb muscles of left and right side. The electromyographic activities of these so-called posterior root-muscle reflexes (PRM reflexes; Minassian et al., 2007b) are displayed here for thigh and leg muscle groups in a subject with intact nervous system. The reflex-nature of the responses can be demonstrated by the prolonged period of excitability changes of PRM reflexes of up to 10 seconds following a prior stimulus applied to the lumbosacral spinal cord (Minassian et al., 2009). Another characteristic of the PRM reflex is its attenuation when vibration is applied to the Achilles tendon (Minassian et al., 2007b), the patellar tendon, or the tendons of the hamstrings. Symmetric, biphasic rectangular pulses (1 ms +1 ms width) delivered by a constant-voltage stimulator were empirically found to require rather low stimulus intensities to elicit PRM reflexes (28.6-34.3 V, impedance 700-900 Ω; Minassian et al., 2007b; Hofstoetter et al., 2008; Ladenbauer, 2010).

There is an increasing number of human neurophysiological studies applying transcutaneous spinal cord stimulation to elicit short-latency reflexes in the lower limb muscles of individuals with intact nervous system or spinal cord injury (Courtine et al., 2007; Hofstoetter et al., 2008; Kitano & Koceja 2009; Dy et al., 2010).

The potential of this non-invasive method in controlling spinal spasticity and augmenting mobility in spinal cord injured persons is currently being investigated (Minassian et al., 2010). Figure 4 shows an example of how transcutaneous stimulation of the lumbar spinal cord can modify active treadmill-stepping of an incomplete spinal cord injured person.

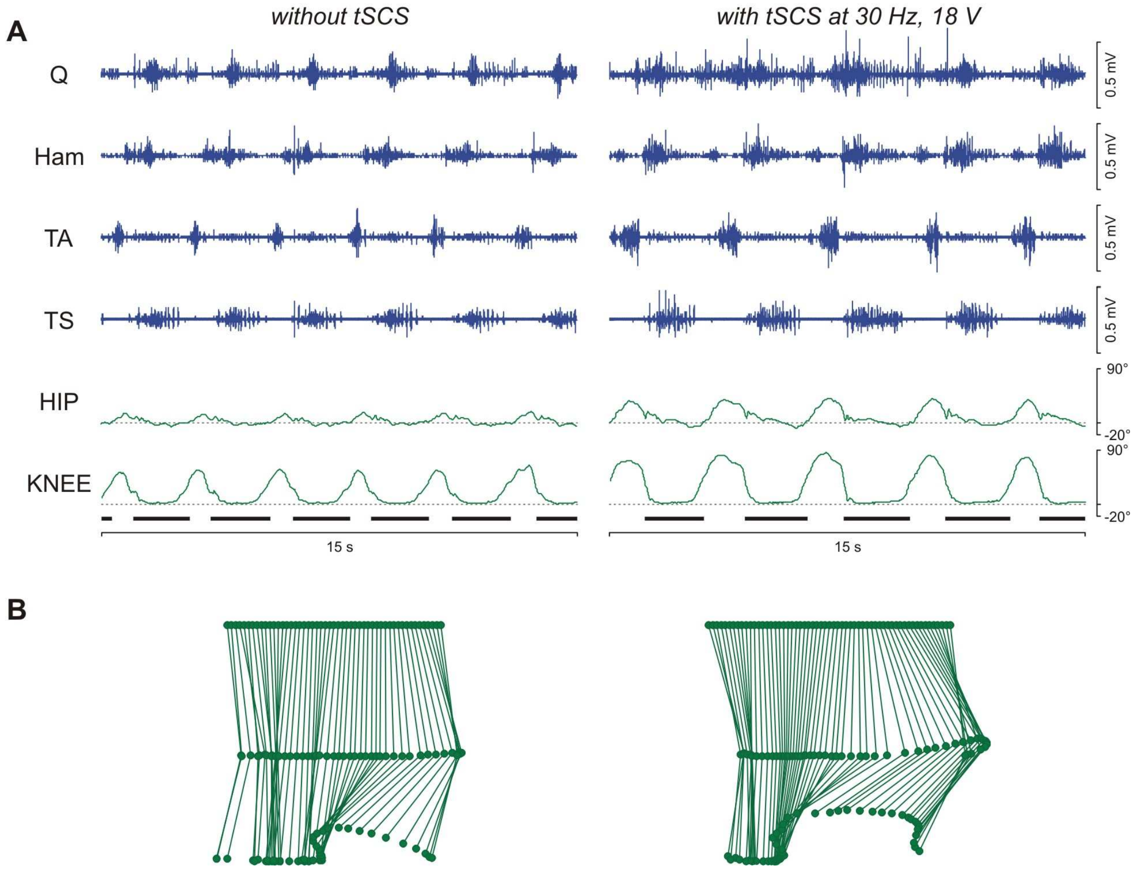

Figure 4: Active treadmill stepping at 1.6 km/h of an incomplete spinal cord injured person without (left column) and during (right column) the application of continuous transcutaneous lumbar spinal cord stimulation. A. Electromyographic activities of right quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS) and electro-goniometer recordings of hip and knee angles. Horizontal bars mark stance phases. B. Stick figures calculated from the hip and knee angle recordings as shown in A. Manual assistance and body weight support were not required. Stimulation was applied over the T11-T12 spinous processes at 30 Hz and an intensity generating paraesthesiae in the lower limb dermatomes during continuous stimulation without eliciting PRM reflexes. The subject was a female aged 28 with an incomplete spinal cord injury at T8/9 level following a vascular event, classified as AIS D, in a chronic, stable condition (10 years post-injury). She had preserved stretch and cutaneomuscular reflexes below the level of the lesion, and motor scores ranged from 3-5 in the right and 2-4 in the left lower limb muscles. She could walk over ground with two crutches, without braces and physical assistance (WISCI II-scale of 16) but was not a community or homebound functional ambulator.

Transcutaneous lumbar spinal cord stimulation can become a promising new evaluation and intervention approach meeting the principles of restorative neurology, i.e. for the assessment of mechanisms responsible for neurological deficits as well as for the improvement of impaired nervous system function through modification of altered neural control.

References

Barolat G, Singh-Sahni K, Staas WE Jr, Shatin D, Ketcik B, Allen K. Epidural spinal cord stimulation in the management of spasms in spinal cord injury: a prospective study. Stereotact Funct Neurosurg. 1995; 64:153-64.

Courtine G, Harkema SJ, Dy CJ, Gerasimenko YP, Dyhre-Poulsen P. Modulation of multisegmental monosynaptic responses in a variety of leg muscles during walking ad running in humans. J Physiol. 2007; 582: 1125-1139.

Danner SM, Hofstoetter US, Ladenbauer J, Rattay F, Minassian K. Can the human lumbar posterior columns be stimulated by transcutaneous spinal cord stimulation? A modeling study. Artif Organs. 2011; 35: 257-62.

Dimitrijevic MM, Dimitrijevic MR, Illis LS, Nakajima K, Sharkey PC, Sherwood AM. Spinal cord stimulation for the control of spasticity in patients with chronic spinal cord injury: I. Clinical observations. Cent Nerv Syst Trauma. 1986a; 3: 129-144.

Dimitrijevic MR, Illis LS, Nakajima K, Sharkey PC, Sherwood AM. Spinal cord stimulation for the control of spasticity in patients with chronic spinal cord injury: II. Neurophysiologic observations. Cent Nerv Syst Trauma. 1986b; 3: 145-152.

Dimitrijevic MR, Gerasimenko Y, Pinter MM. Evidence for a spinal central pattern generator in humans. Ann N Y Acad Sci. 1998; 860: 360-376.

Dy CJ, Gerasimenko YP, Edgerton VR, Dyhre-Poulsen P, Courtine G, Harkema SJ. Phase-dependent modulation of percutaneously elicited multisegmental muscle responses after spinal cord injury. J Neurophysiol. 2010; 103: 2808-2820.

Gerasimenko YP, Makarovskii AN, Nikitin OA. Control of locomotor activity in humans and animals in the absence of supraspinal influences. Neurosci Behav Physiol. 2002; 32: 417-423.

Harkema S, Gerasimenko Y, Hodes J, Burdick J, Angeli C, Chen Y, Ferreira C, Willhite A, Rejc E, Grossman RG, Edgerton VR. Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a case study. Lancet. 2011; 377: 1938-47.

Herman R, He J, D'Luzansky S, Willis W, Dilli S. Spinal cord stimulation facilitates functional walking in a chronic, incomplete spinal cord injured. Spinal Cord. 2002; 40: 65-68.

Hofstoetter US, Minassian K, Hofer C, Mayr W, Rattay F, Dimitrijevic MR. Modification of reflex responses to lumbar posterior root stimulation by motor tasks in healthy subjects. Artif Organs. 2008; 32: 644-648.

Huang H, He J, Herman R, Carhart MR. Modulation effects of epidural spinal cord stimulation on muscle activities during walking. IEEE Trans Neural Syst Rehabil Eng. 2006; 14: 14-23.

Jilge B, Minassian K, Rattay F, Pinter MM, Gerstenbrand F, Binder H, Dimitrijevic MR. Initiating extension of the lower limbs in subjects with complete spinal cord injury by epidural lumbar cord stimulation. Exp Brain Res. 2004; 154: 308-326.

Ladenbauer J, Minassian K, Hofstoetter US, Dimitrijevic MR, Rattay F. Stimulation of the human lumbar spinal cord with implanted and surface electrodes: a computer simulation study. IEEE Trans Neural Syst Rehabil Eng. 2010; 18: 637-45.

Kitano K, Koceja DM. Spinal reflex in human lower leg muscles evoked by transcutaneous spinal cord stimulation. J Neurosci Methods. 2009; 180: 111-115.

Minassian K, Hofstoetter US, Tansey K, Rattay F, Mayr W, Dimitrijevic M. Transcutaneous stimulation of the human lumbar spinal cord: Facilitating locomotor output in spinal cord injury. Soc Neurosci Abstr. 286, 2010.

Minassian K, Hofstoetter US, Rattay F, Mayr W, Dimitrijevic MR. Posterior root-muscle reflexes and the H reflex in humans: Electrophysiological comparison. Program No. 658.12. 2009 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2009. Online.

Minassian K, Persy I, Rattay F, Pinter MM, Kern H, Dimitrijevic MR. Human lumbar cord circuitries can be activated by extrinsic tonic input to generate locomotor-like activity. Hum Mov Sci. 2007a; 26: 275-295.

Minassian K, Persy I, Rattay F, Dimitrijevic MR, Hofer C, Kern H. Posterior root-muscle reflexes elicited by transcutaneous stimulation of the human lumbosacral cord. Muscle Nerve. 2007b; 35: 327-336.

Minassian K, Persy I, Rattay F, Dimitrijevic MR. Peripheral and central afferent input to the lumbar cord. Biocybernetics and Biomedical Engineering 2005; 25: 11-29.

Minassian K, Jilge B, Rattay F, Pinter MM, Binder H, Gerstenbrand F, Dimitrijevic MR. Stepping-like movements in humans with complete spinal cord injury induced by epidural stimulation of the lumbar cord: electromyographic study of compound muscle action potentials. Spinal Cord. 2004; 42: 401-416.

Pinter MM, Gerstenbrand F, Dimitrijevic MR. Epidural electrical stimulation of posterior structures of the human lumbosacral cord: 3. Control of spasticity. Spinal Cord. 2000; 38: 524-31.

Richardson RR, McLone DG. Percutaneous epidural neurostimulation for paraplegic spasticity. Surg Neurol. 1978; 9:153-5.

Száva Z, Danner SM, Minassian K. Transcutaneous electrical spinal cord stimulation: Biophysics of a new rehabilitation method after spinal cord injury. VDM Verlag Dr. Müller (22. April 2011), ISBN-10: 3639341546, ISBN-13: 978-3639341546.