Effects of Spinal Cord Electrical Stimulation in Patients with Vertebrospinal Pathology

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Until now, no scientific neurophysiologic methods of diagnostics and treatment of vertebrospinal pathologies were developed. Previous study showed that electrical stimulation of lumbar segments of the spinal cord in animals with complete spinal cord transection induced a well-coordinated weight-bearing locomotion. The present comparative study of motor activity triggered by electrical epidural stimulation of one or two segments of the spinal cord in spinal patients showed that stimulation of lumbar (L2-L4) or sacral (S2) segments facilitated generation of motor patterns of muscle activity. Combination of electrical stimulation with locomotor training resulted in the appearance of stepping patterns characteristic of normal walking and tonic activity of the muscles needed for body balance maintenance.

Key Words: *spinal cord; electrical stimulation; vertebrospinal pathology; surface EMG; locomotor training*

Considerable attention is now focused on rehabilitation of locomotor function in patients with spinal cord lesions, which evidently results from wide prevalence of the spine cord pathologies. At present, there are virtually no scientifically based methods of diagnostics and rehabilitation of motor functions of the spinal cord. Previous studies showed that electrical stimulation of the lumbar intumescence could induce stepping pattern of EMG-activity in leg muscles [8] and initiate locomotor-like movement of patient's light-loaded legs [6]. Recently we have demonstrated that electrical stimulation of the spinal cord (ESSC) can be efficiently used in the treatment and social rehabilitation of spinal patients [3]. ESSC promotes structural and functional recovery of the spinal cord and peripheral neuromuscular apparatus resulting in shortening of the rehabilitation period. Moreover, ESSC promotes regress of neuropathological symptoms, improves patient's quality of life, and promotes their social adaptation [4]. Experimental studies on rats with completely transected spinal cord showed that simultaneous electrical stimulation of spinal segments L2 and S1 induced a well-coordinated locomotor activity with correct foot positioning and pronounced support phase during walking [2].

Our aim was to compare motor activity evoked in the leg muscles during mono- and bipolar electrical stimulation of various spinal cord segments in spinal patients with motor abnormalities.

MATERIALS AND METHODS

The study was carried out at the Department of Spinal Surgery No. 6, Phthisiopulmonology Research Institute (St. Petersburg), in October-December 2009. Hospitalized patients (n=4) with signs of progressive vertebrogenous myelopathy were examined (Table 1). The degree of neurological abnormalities and their evolution were assessed according to ASIA standards (American Spinal Injury Association, 1988). The study strictly adhered to the deontological and ethical

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regulations of Russian Federation. During the study, original medical technique myelopathy treatment was used (FS-2007/139-u, 2007). For ESSC, 2-4 electrodes (Cooner Wire Co., w363A) were implanted to the dorsal surface of the dura mater in various regions of the spinal cord [4]. Location of the electrodes was established according to methodical guidelines of RF Ministry of Health No. 96/269 (1998) in dependence on the degree of injury to the spinal cord.

Therapeutic ESSC (stimulation frequency of 1-12 Hz) was carried out 2 times for 30 min in addition to the routine pharmacotherapy. The vertical postural and locomotor training were carried out with 2 patients. Patient TP was trained in a treadmill with a body-supporting facility (a driven-gait orthosis) [5] for 30 days two times daily prior to ESSC session. During this training, the endurable walking time and maximum walking velocity were recorded. Patient TA was trained in a verticalizer, which maintained vertical posture with foot support. The training sessions were carried out daily for 30-60 min for 35 days before implanting the electrodes.

During the treatment course, spinal cord reflexes were tested electrophysiologically. In addition, ESSC-induced leg motor activity was recorded with the same epidural electrodes used for electric stimulation (Table 1). Two types of ESSC were used in the study. The first type of ESSC used monopolar stimulation via each of the implanted electrodes and the indifferent electrode placed on the skin in the paravertebral region. The second type of ESSC employed bipolar stimulation of two segments via two implanted electrodes. ESSC-induced responses of the leg muscles were recorded in supine position with EMG electrodes positioned on *m. biceps*, *m. quadriceps*, *m. gastrocnemius*, and *m. tibialis* of the leg that demonstrated greater motor responses. Diagnostic ESSC and EMG recording were performed using original 4-channel EMGST-1 software-hardware complex. The testing procedure consisted of two stages: first, the minimum (threshold) stimulus amplitude induced the motor response was chosen, and then 1.5-2-fold greater stimuli were used to recorder the evoked motor responses (EMG) with ANDEX software. EMG was analyzed to reveal late responses (latency >10 msec, signs of walking movements [1]) burst EMG activity characteristic of walking, and tonic activity of extensor muscles maintaining vertical posture and body balance under normal conditions.

RESULTS

In all examined patients, different responses to bipolar stimulation of two spinal segments and to monopolar stimulation of a single segment were revealed. These differences were related to both changes in ESSC threshold and in the structure of evoked EMG. The thresholds of ESSC are shown in Table 2. In virtually all cases of bipolar stimulation, the thresholds of muscle responses were significantly lower than the thresholds determined with monopolar stimulation of a single segment. A decrease of the threshold was observed on days 6-14 after the start of ESSC. The thresholds did not depend on stimulation frequency.

The structure of EMG responses was different in patients with plegia and paresis of the low extremities (Fig. 1). In plegic patients, bipolar stimulation induced only the early responses in *m. quadriceps*, while in *m. gastrocnemius* it evoked both the early and late responses (Fig. 1, *a*). Similar stimulation in a female patient with paresis induced the step-like movements accompanied with burst-like EMG

TABLE 1. Examined Patients

Patient ID	Age (years)	Sex	Diagnosis	Location of the skin electrodes
K.S./1270	22	Female	The consequences of combined injury, dislocation fracture of segment Th7 of 22.08.09, myelopathy, low paraplegia. ASIA-A-B. The post-operative conditions of 2009	Th5, **L2**, L4, **S2**
S.A./1895	50	Male	The consequences of C5-7 spondylitis, myelopathy, ASIA-A-B. The post-operative conditions of 2009	C5, **L4**, L5, S2
T.P./1151	58	Female	The consequences of Th8-L1 tubercular spondylitis, myelopathy, low deep spastic paraparesis. ASIA-B. The post-operative conditions of the spinal column	**L2**, **S2**
T.A./1868	38	Female	The consequences of L1 vertebral body fracture, myelopathy. ASIA-B-C. The post-operative conditions of 2008	**L5**, **S2**

Note. The bold type indicates the segments subjected to diagnostic ESSC.

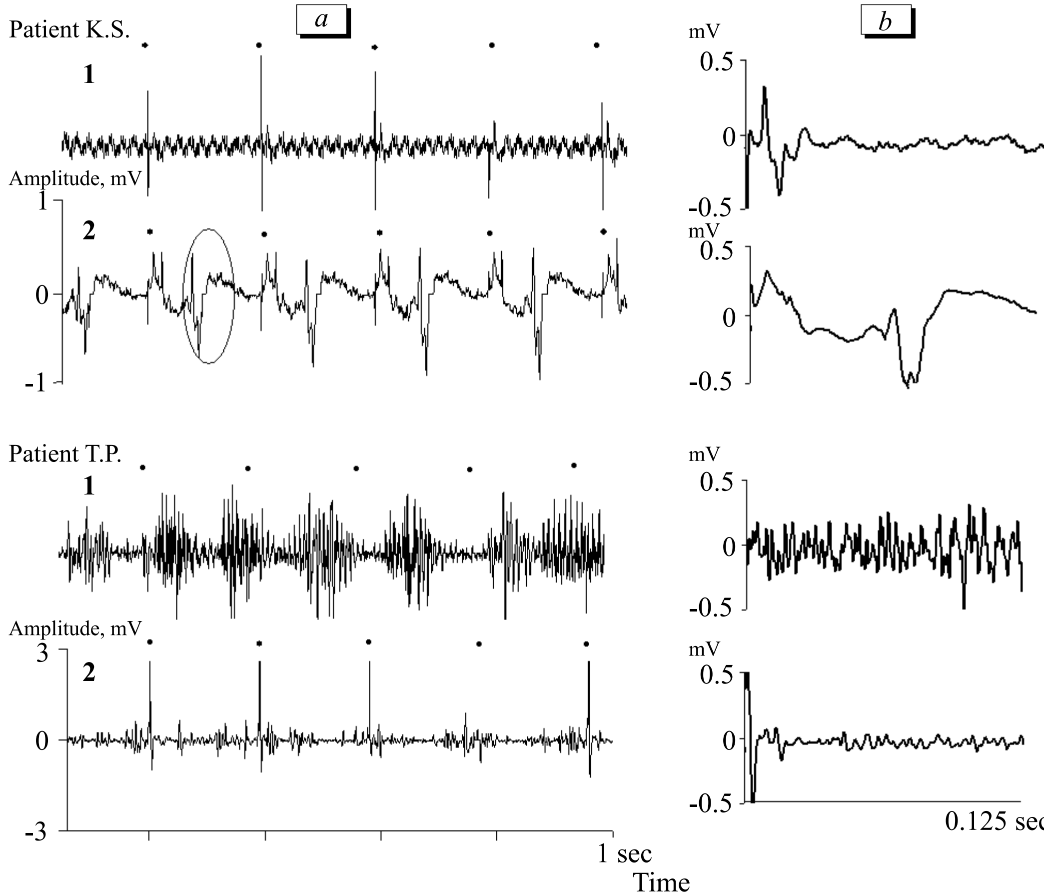

Fig. 1. EMG-patterns (*a*) in *m. quadriceps rect*. (*1*) and *m. gastrocnemius lat*. (*2*) with corresponding averaged responses (*b*, *n*=25) evoked by bipolar ESSC of L2 and S2 segments at 5 Hz in female patients K.S. and T.P. on the fourth and third therapy week, respectively. The late response is encircled. Here and in Figs. 2 and 3: the points are the stimulation marks.

activity in *m. quadriceps*, while *m. gastrocnemius* demonstrated a clear-cut early component followed by a burst of EMG activity (Fig. 1, *b*). EMG bursts did not depend on stimuli as was clearly seem after averaging of the responses. During monopolar ESSC, the plegic patients also demonstrated only the early or single late responses, while in the patients with paresis, pronounced burst activity was observed, but this effect was less pronounced than in bipolar ESSC (Fig. 2).

Changes in stimulation frequency and duration of therapeutic ESSC affected the pattern of EMG activity (Table 2, Fig. 2). In patient T.P., burst-like activity appeared in 3 weeks after the onset of any type of ESSC and remained stable to the end of ESSC therapy. In patient T.A., single EMG bursts were observed during monopolar ESSC at 2 and 5 Hz despite plegic conditions (Table 2). In patients K.S. and S.A., burst-like activity appeared sporadically in 2-4 weeks after the onset of therapeutic ESSC and was observed only during bipolar stimulation (Table 2). Analysis of EMG responses of flexors and extensors revealed no reciprocity in the responses of these muscles, *i.e.* there were no walking movements. This can be explained by the use of therapeutic frequency range (below 12 Hz) in this examination, which is far lower than the frequency needed to induce walking movements in patients with complete vertebral fracture (30-40 Hz) [8]. Tonic muscle activity was recorded only in patients T.P. and T.A. and predominantly during stimulation at 12 Hz. Tonic and burst-like EMG activities in patients T.P. and T.A. were probably related to motor training. In patient T.A., this training was performed before ESSC therapy. In this case, burst-like activity was observed immediately after implantation of electrodes. In patient T.P., motor training started simultaneously with therapeutic ESSC. In this case, stable burst-like activity was observed in 3 weeks after the start of ESSC and motor training. This complex therapy resulted in pronounced improvement of motor functions reflected in facilitation of evoking the late responses and burst-like EMG activity (Fig. 3). In this case, the endurable time of the training procedure increased 5-fold to the end of the therapy course. Moreover, the walking velocity increased from 0.3-0.4 m/sec at the beginning of the therapy to 1.6 m/sec to the end of it.

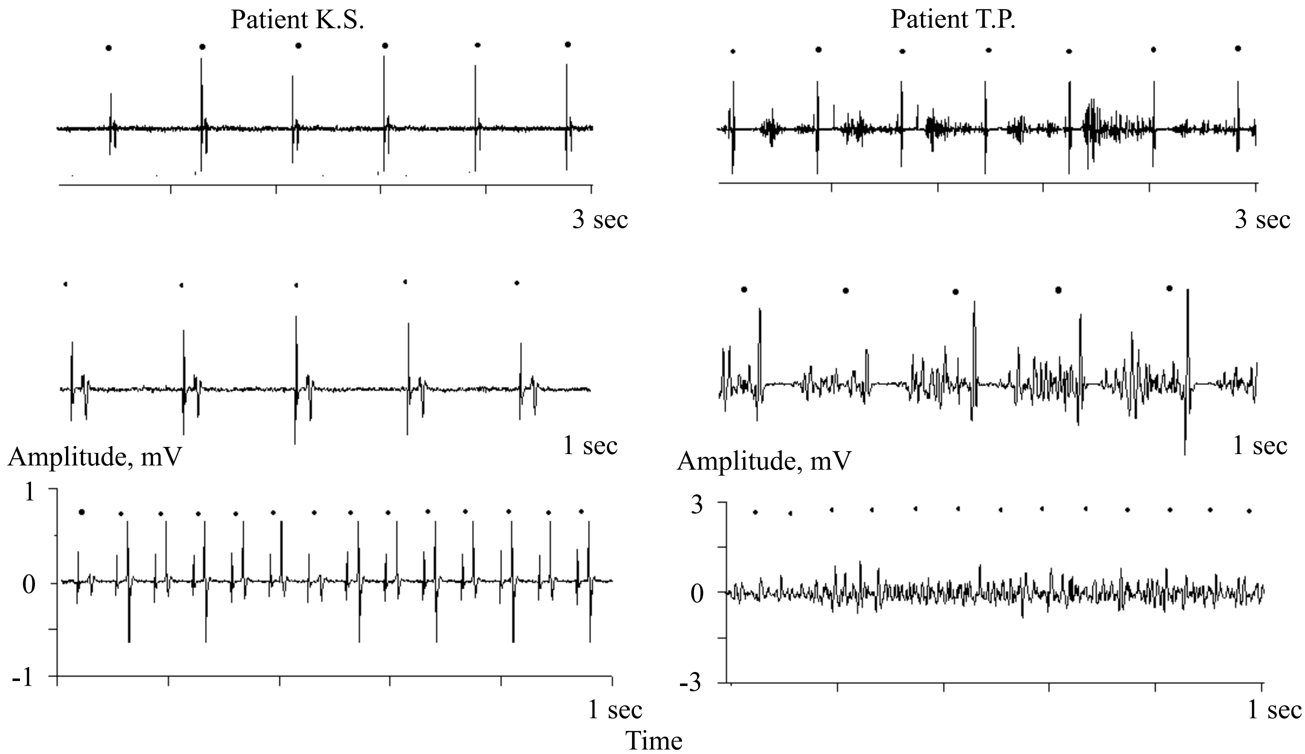

Fig. 2. EMG-patterns in *m. gastrocnemius lat.* during monopolar ESSC of segment S2 at 2 Hz (upper traces), 5 Hz (middle traces), and 12 Hz (bottom traces).

The effect of stimulation of the leg proprioceptors during motor training on reconditioning of locomotion in the animals with complete vertebral fracture was widely examined. The experiments with rats showed that motor training in treadmill restored locomotion [10]. When it was supplemented with ESSC applied to two segments below the vertebral fracture and injection of serotonin-stimulation agents, the coordinated walking movements of the extremities were observed, which provided the full support to the body weight [7]. Reconditioning of locomotor function of the spinal cord correlated with restoration of the late polysynaptic components [9].

This study showed that the ESSC effect on the motor activity of the leg muscles in patients with vertebrospinal pathology depended on the degree of motor disturbances. In patients with incomplete spinal cord injury, burst-like EMG activity (a sign of stepping movements) was evoked far easier than in the patients with complete vertebral fracture. In many cases, bipolar stimulation of two segments of the spinal cord was more efficient than the monopolar stimulation. The experiments with different stimulation frequency showed that ESSC applied at 2 or 5 Hz induced burst-like activity of leg muscles, while stimulation at 12 Hz produced tonic EMG activity. Vertical posture training combined with walking elements and ESSC induced regular motor patterns in EMG characteristic of the normal walking and triggered the tonic activity needed to maintain the posture and balance of the body.

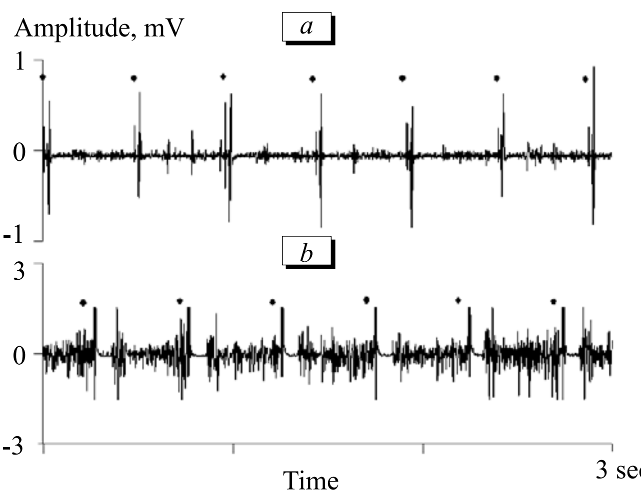

Fig. 3. Alterations in EMG-patterns evoked in *m. tibialis ant.* in female patient T.P. recorded in 2 weeks (*a*) and in 4 weeks (*b*) after the onset of rehabilitation therapy with ESSC (2 Hz) and locomotor training.

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TABLE 2. Changes in ESSC Thresholds[1] and EMG Patterns in Low Extremities over the Entire Observation Period during ESSC Applied to One or Two Segments of Spinal Cord

Patient ID	Examination period after ESSC onset	Frequency, Hz	ESSC via bottom electrode[2]	ESSC via top electrode[2]	Bipolar SCES[2]
K.S.	Primary	1	3[1]/-	4/-	1/-
	1 week	1	3/+	4/-	1/++
	4 week	2	3/+	2/+	1.2/b
		5	3/+	1.8/+	1.2/++
		12	1.6/+	2.4/+	1/++
S.A.	Primary	1	8/-	3/-	1/-
	1 week	1	1.7/-	1/-	1/-
	2 week	2	11/-	3.5/-	1.5/++
		5	7.5/+	2.5/+	1/b
		12	10/+	4/+	4/b
T.A.	Primary	2	8.3/b	2.7/t	1.7/+
		5	5/b	5/+	1.7/++
		12	6.7/t	1.3/t	1/t
T.P.	Primary	1	1.2/-	1.6/-	1/-
	3 day	1	2/+	12.5/+	1/+
	2 week	2	1.5/++	1.3/+	1/++
	3 week	2	3/b	3.5/b	1/b
		5	1.5/b	3/b	1/b
		12	1.3/+	2.3/b	1/b
	4 week	2	1/b	1.5/b	1.3/b
		5	1/b	1.3/b	1.2/b
		12	1/b	1/b	1/b
M±*m*			3.88±3.19*	2.96±2.41**	1.26±0.65

Note. [1]The thresholds are normalized relatively the lowest value documented over the entire observation period for every patient. [2]Positions of top and bottom electrodes are shown in Table 1. The symbols indicate the following: "–", absence of late components in the responses; "+", rare and small late responses; "++", regular and pronounced late responses; "*b*", pronounced burst-like activity; "*t*", the responses could not be resolved due to enhanced tonic activity. *$p<0.0002$, **$p<0.002$ for comparison of ESSC thresholds in evoking movements during monopolar and bipolar stimulation (Student's test).

REFERENCES

1. Yu. P. Gerasimenko, I. A. Lavrov, I. N. Bogacheva, *et al*., *Ross. Fiziol. Zh.*, **89**, No. 9, 1046-1057 (2003).
2. Yu. P. Gerasimenko, P. E. Musienko, T. R. Moshonkina, and A. N. Makarovski, *A Method to Model and Train Patients with Chronic Lesion to Spinal Cord. Patent of RF*, No. 115819, Bull. No. 30, October 27, 2009.
3. A. N. Makarovski, A. E. Garbuz, Yu. P. Gerasimenko, A. D. Mitusov, *Traumatol. Orthoped. Russ*., No. 6, 16-20 (1995).
4. A. N. Makarovski, A. E. Garbuz, Yu. T. Shapkov, and Yu. P. Gerasimenko, *Apparatus for Diagnostics and Electric Stimulation of Spinal Cord Structures. Inventor's certificate of USSR*, *No. 1832515*, October 13, 1992.
5. Yu. P. Gerasimenko, A. N. Makarovski, and A. M. Nazarov, *Automated Driven-Gait Training Orthosis to Rehabilitate Leg Locomotion. Patent of RF*, *No. 56178*, Bull. No. 25, September 10, 2006.
6. E. Yu. Shapkova, A. Yu. Mushkin, and V. A. Gutorko, *A Method to Treat Patients with Chronic Lesion to Spinal Cord. Patent of RF*, *No. 2204423,* Bull. No. 20, May 20, 2003.
7. G. Courtine, Y. Gerasimenko, R. van den Brand, *et al., Nat. Neurosci.*, **12**, No. 10, 1333-1342 (2009).
8. M. R. Dimitrijevic, Gerasimenko Y., and M. M. Pinter, *Ann. New York Acad. Sci*., **860**, 360-376 (1998).
9. I. Lavrov, C. J. Dy, A. J. Fong, *et al., J. Neurosci.*, **28**, No. 23, 6022-6029 (2008).
10. T. Moshonkina, V. Avelev, Y. Gerasimenko, *et al., Ind. J. Physiol. Pharmacol*., **46**, No. 4, 499-503 (2002).