

Effective spinal cord stimulation (SCS) for evoking stepping movement of paralyzed human lower limbs: study of posterior root muscle reflex responses

K. Minassian¹, B. Gilge¹, F. Rattay¹, M.M. Pinter²
F. Gerstenbrand³, H. Binder³, M.R. Dimitrijevic⁴

1. TU-BioMed, Vienna University of Technology, Austria

2. Maria-Theresien-Schloessel Neurological Hospital, Vienna, Austria

3. Ludwig Boltzmann Institute for Restorative Neurology and Neuromodulation, Vienna, Austria

4. Baylor College of Medicine, Houston, TX, USA

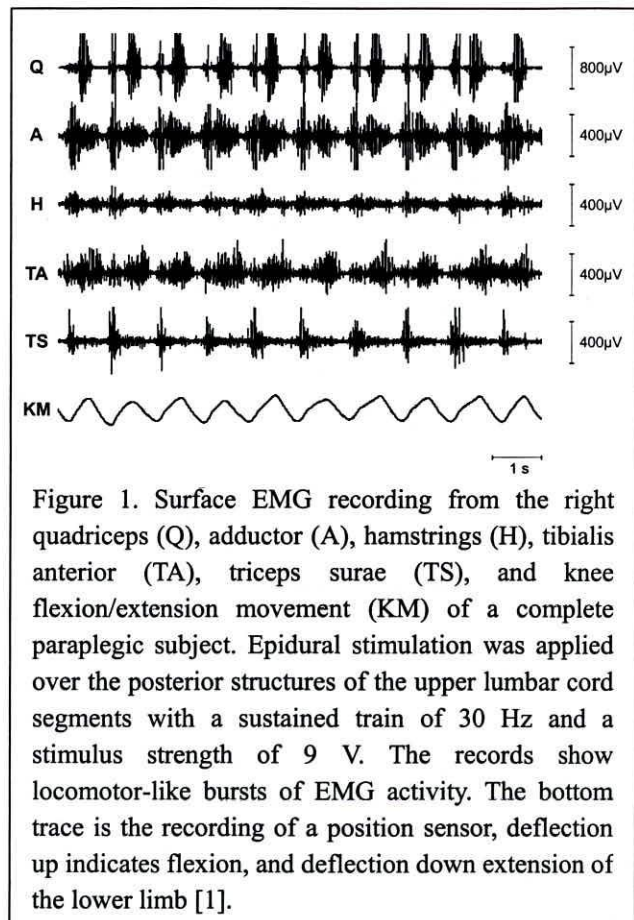
e9225637@student.tuwien.ac.at

Abstract

In this study we examined EMG responses of lower limb muscles to repetitive electrical stimulation of the human lumbar cord isolated from brain control. We found that the muscle activity elicited at low frequencies (2 Hz) are monosynaptic posterior root muscle reflexes. A sustained train of stimuli at higher frequencies (16 Hz or more) establishes longer spinal reflex pathways involving interneuronal networks, the monosynaptic EMG response is progressively replaced by a second response with longer but also constant latency. When the frequency is further increased to 30-50 Hz, a locomotor-like EMG activity can be induced, and the amplitude and occurrence of the second response progressively augments. During the bursting phases of rhythmical EMG activity the amplitude of the first monosynaptic response is completely suppressed. Our study suggests, that the driving input from brain structures can be replaced artificially by a non-patterned input via the posterior roots and interpreted by the lumbar interneuronal network to respond with a patterned, rhythmical activity.

1. Introduction

The basic motor pattern for stepping is generated by neuronal circuits contained entirely within the lumbosacral spinal cord. This interneuronal network is activated by descending tonic signals from the brain. In complete spinal cord injured people, with the cord transected at cervical or



thoracic level, the spinal cord segments that innervate the lower limb muscles are isolated from brain control. It has been shown that a sustained train of electrical stimuli at 30-50 Hz, applied epidurally to posterior structures of the

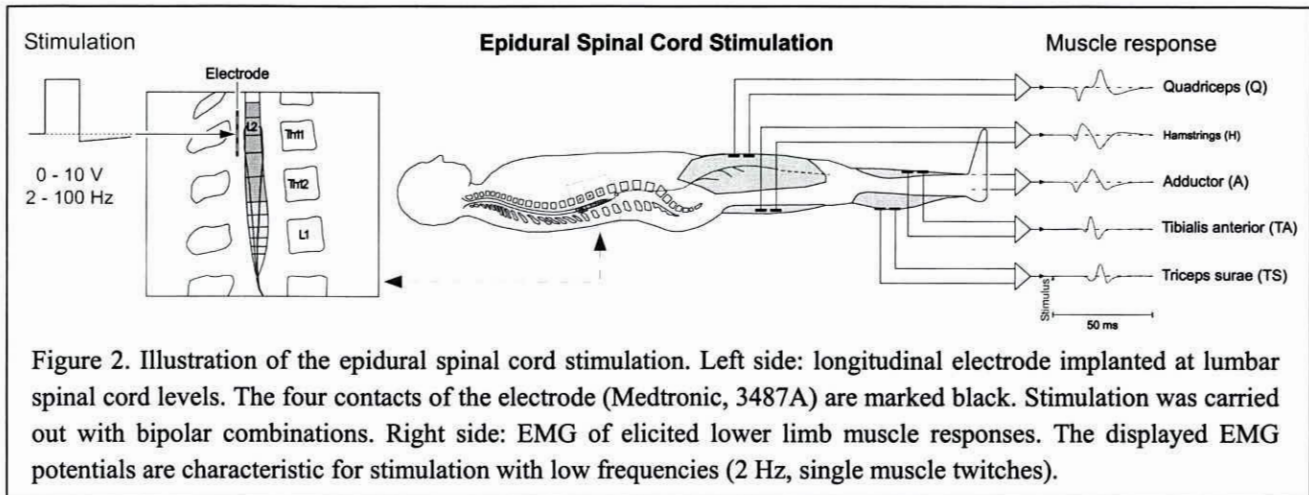


Figure 2. Illustration of the epidural spinal cord stimulation. Left side: longitudinal electrode implanted at lumbar spinal cord levels. The four contacts of the electrode (Medtronic, 3487A) are marked black. Stimulation was carried out with bipolar combinations. Right side: EMG of elicited lower limb muscle responses. The displayed EMG potentials are characteristic for stimulation with low frequencies (2 Hz, single muscle twitches).

human lumbar cord can elicit locomotor-like stepping movements in people with posttraumatic sustained spinal cord injury (SCI) above the lumbar cord [1]. This finding demonstrates, that the absent descending driving input from brain structures can be replaced externally by a tonic electrical activity generated by the epidural electrode. The lumbar interneuronal networks are capable of interpreting the non-patterned input and respond with a patterned, rhythmical activity.

The subjects with SCI included in this study have epidural electrodes implanted at Th11/Th12 vertebral levels to control a severe form of spasticity. The bipolar electrode is oriented rostrocaudally and placed over the posterior median aspect of the spinal cord. Electrical stimulation at this level of the spinal cord can induce muscle responses of the lower limbs. The electromyographic activity of these muscles were recorded with surface electrodes placed over the bellies of quadriceps (Q), hamstrings (H) (=semitendinosus, semimembranosus, and biceps femoris), tibialis anterior (TA), and triceps surae (TS) muscles (Fig. 2). We examined elicited EMG responses to repetitive stimulation with amplitudes of 0-10 V and frequencies of 2-100 Hz. At low frequencies of 2 Hz every stimulation pulse (with appropriate stimulation strength) induces a single muscle twitch. The latencies of these responses are very short and correspond to the central and efferent delay of H-reflex latencies. Consecutive muscle twitches have a constant latency, the shape of their EMG potentials does not change. Our findings suggest that the responses are the result of depolarization of the large myelinated primary muscle afferents in the dorsal roots which have mono- (oligo-)

synaptic projections to corresponding motoneurons. This proposition is further confirmed by our computer simulations of the potential distribution in the spinal cord and surrounding structures generated by an implanted bipolar electrode (based on the model presented in [2]), and by the analysis of the refractoriness of the observed muscle responses. For stimulation with the same voltage but higher stimulation frequencies (16 Hz or more) the same neural structures are directly affected by the electrical field, but the sustained artificial input via the posterior roots is capable of activating spinal interneuronal networks and establishing a longer spinal reflex organization. Figure 3 demonstrates, how the short-latency response ("early response") is more and more suppressed at higher stimulation frequencies and a new response with longer latency ("late response"), that is presumably polysynaptic, is built up.

2. Summary and Conclusions

The prolongation of the reflex pathway can be especially observed during the bursting periods of rhythmical activity. While the clear cut early response is only present at stimulation frequencies lower than 16 Hz, a late response with the early twitch completely suppressed denotes the other extreme. In reality the processing of the peripheral afferent input is very dynamic, but chances for processing via more complex interneuronal systems are bigger during rhythmical motor unit discharges than during tonic one. In spite of the dynamics of each response during a bursting phase, they all have a rather constant latency. Averaged EMG-signals of single responses within

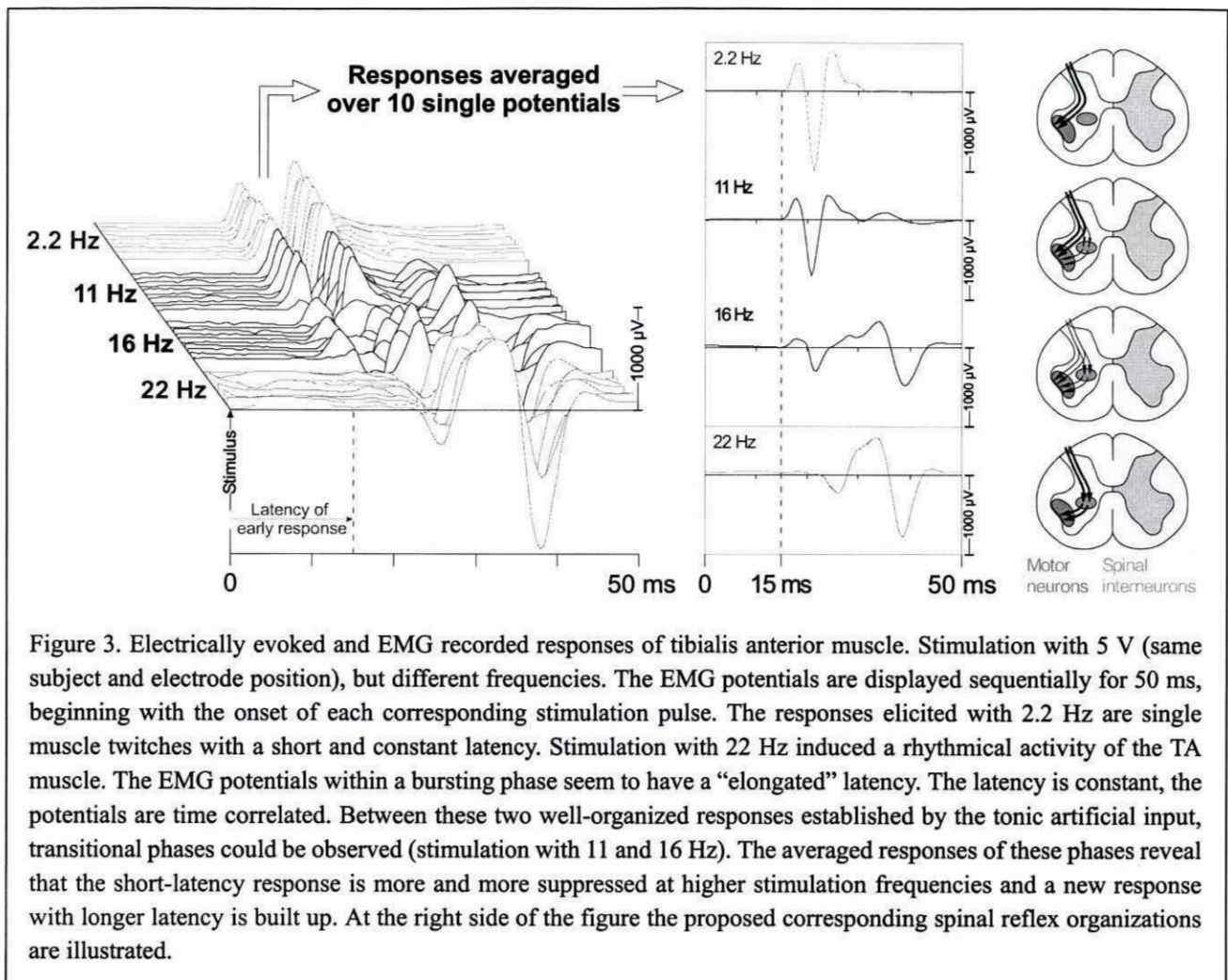


Figure 3. Electrically evoked and EMG recorded responses of tibialis anterior muscle. Stimulation with 5 V (same subject and electrode position), but different frequencies. The EMG potentials are displayed sequentially for 50 ms, beginning with the onset of each corresponding stimulation pulse. The responses elicited with 2.2 Hz are single muscle twitches with a short and constant latency. Stimulation with 22 Hz induced a rhythmical activity of the TA muscle. The EMG potentials within a bursting phase seem to have a “elongated” latency. The latency is constant, the potentials are time correlated. Between these two well-organized responses established by the tonic artificial input, transitional phases could be observed (stimulation with 11 and 16 Hz). The averaged responses of these phases reveal that the short-latency response is more and more suppressed at higher stimulation frequencies and a new response with longer latency is built up. At the right side of the figure the proposed corresponding spinal reflex organizations are illustrated.

a bursting phase have well-defined peaks and valleys indicating that consecutive responses are time correlated. This information indicates that the time-locked late responses are due to a previously set up neuronal organization once a bursting activity is established.

Acknowledgment

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¹ TU-BioMed, Vienna University of Technology, Austria

² Neurological Rehabilitation Center Rosenhügel, Vienna, Austria

³ Ludwig Boltzmann Institute for Restorative Neurology and Neuromodulation, Vienna, Austria

⁴ Baylor College of Medicine, Houston, TX, USA

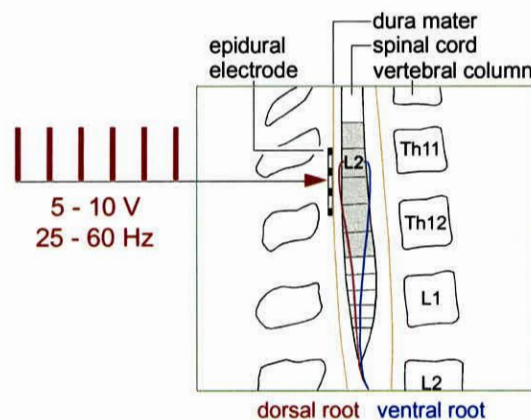
OBSERVATION

Non-patterned electrical stimulation of the posterior structures of the lumbar spinal cord in subjects with complete spinal cord injury can induce patterned, locomotor-like activity.

RESEARCH QUESTION

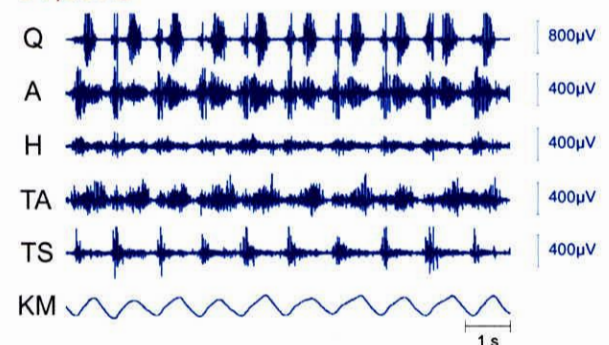
What is the nature of the basic electrophysiological element of the induced rhythmic response?

epidural spinal cord stimulation



EMG of induced muscle responses

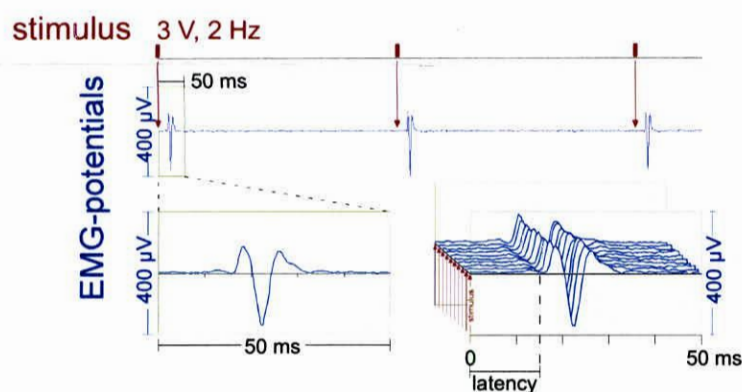
9V, 30 Hz



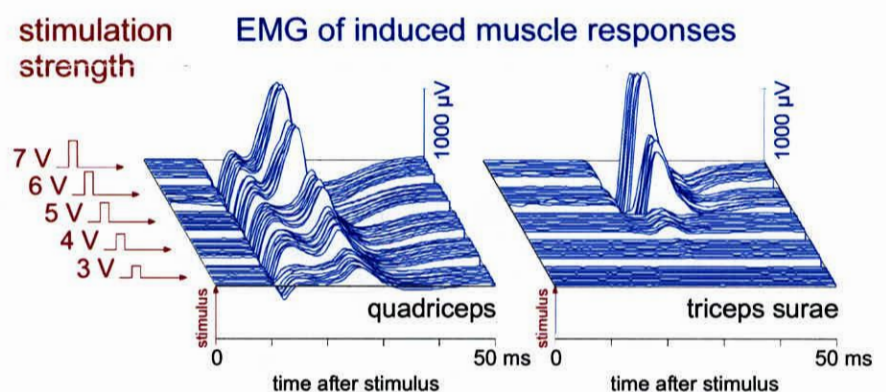
EMG of quadriceps (Q), adductor (A) hamstrings (H), tibialis anterior (TA), and triceps surae (TS). KM: recording of a position sensor, deflection up = flexion, deflection down = extension of the lower limb.

RESULTS

Stimulation with 2 Hz: short latency reflex responses

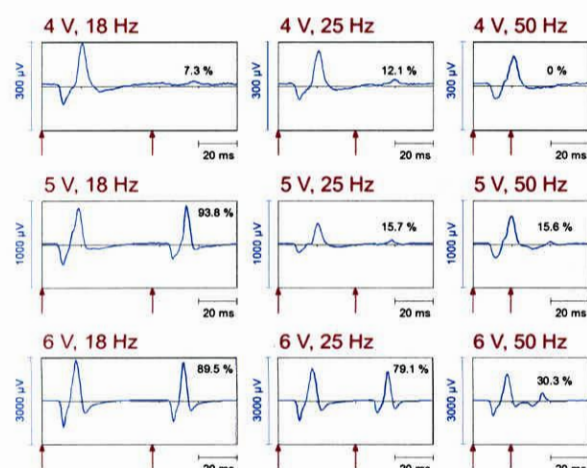


EMG-potentials of induced single muscle contractions of tibialis anterior: short and constant response latencies.

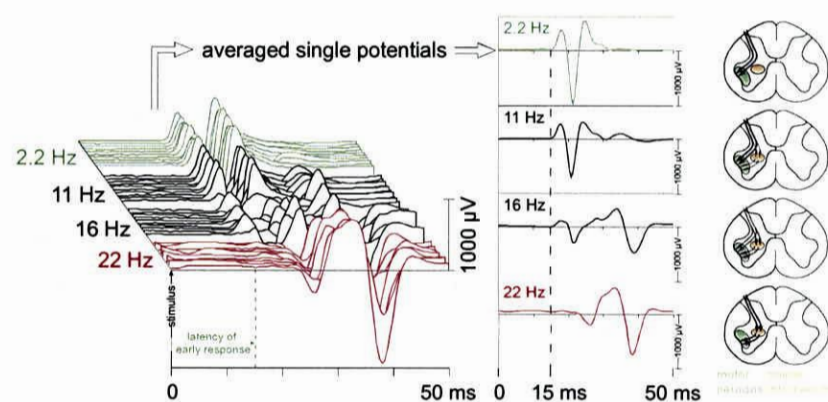


Increasing the stimulus strength results in stronger responses of activated muscles (Q) and recruitment of additional muscles (TS) innervated by different cord segments.

Stimulation with > 10 Hz: central effects



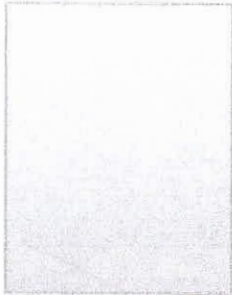
Relative refractory period of two stimuli



TA responses to sustained stimulation with different frequencies: the short-latency response is more and more suppressed at higher stimulation frequencies and a new response with longer latency is built up. Right side: proposed corresponding spinal reflex organizations.

CONCLUSIONS


Epidural SCS at low frequency (2 Hz) induces muscle responses with short and constant latency. We propose that these responses arise from direct excitation of large muscle afferents in the posterior roots with subsequent monosynaptic activation of motoneurons = Posterior Root Muscle Reflex Responses. Moreover, stimulation with 10 Hz or more can additionally activate interneurons transsynaptically. We can conclude that interneuronal networks capable of generating basic motor patterns for stepping can be activated by tonic afferent input via the lumbar dorsal roots.



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