

FES TRAINING OF DENERVATED MUSCLES IN HUMAN

H. Kern^{*}, C. Hofer^{*}, M. Mödlin, C. Forstner, D. Raschka-Högler, W. Mayr^{**}, H. Stöhr^{***}

^{*}Ludwig Boltzmann Institute of Electrostimulation and Physical Rehabilitation,
Department of Physical Medicine, Wilhelminenspital Wien, Austria

^{**}Department of Biomedical Engineering and Physics, University of Vienna, Austria

^{***}Department of Biomedical Research, University of Vienna, Austria

SUMMARY

Prior clinical work showed that electrical stimulation therapy with exponential current is able to slow down atrophy and maintaining the muscle during non permanent flaccid paralysis. But exponential currents are not sufficient for long-term therapy of denervated degenerated muscles (DDM).

We initiated a European research project investigating the rehabilitation strategies in human but also studying the underlying basic scientific knowledge of muscle regeneration from satellite cells or myoblast activity in animal experiments.

The necessary stimulation parameters used in the prior studies that are sufficient for long-term treatment of DDM are forbidden by current EU regulations. In spite of this fact we were able to show that stimulation training of denervated degenerated muscles is possible. At beginning of training only single muscle twitches can be elicited by biphasic pulses with durations of 120 – 150ms. Later with an improved structural and metabolic muscle state the tetanic contraction of the muscle with special stimulation parameters (pulse duration of 30 – 50ms, stimulation frequency of 16 – 25Hz, pulse amplitudes of up to 250mA) can be achieved /14/. Since there are no nerve endings for conduction of stimuli large size anatomically shaped electrodes are used for stimulation. The electrodes made of soft conducting rubber are applied with a wet sponge cloth or gel directly to the skin. This ensures an evenly contraction of the whole muscle.

PRIOR RESEARCH

In the last 15 years we examined the possibility of training denervated human muscles by means of functional electrical stimulation (FES) in complete denervated paraplegics.

In patients with complete conus cauda lesion (Frankel A) was examined if by using appropriate electrical stimulation muscular degeneration could be prevented and already degenerated muscles could be improved to an extent that tetanic contractions and functional movements could be triggered using FES. These patients started training with electrical stimulation within the first 2 years after the lesion. Tetanic muscle contractions with knee extension moments of about 20Nm could be obtained after one and a half year.

Muscle training was begun in the sitting position with single twitches (biphasic rectangular pulse, average pulse width 120 ms). Later on training with tetanic contraction cycles (on: 2 seconds, off: 2-4 seconds) was performed. Initially without weight until nearly complete knee extension was achieved and later with weight cuffs 0,5 – 1 kg on the ankle (8 – 12 repetitions, 4 - 6 series, once a day).

Improvement in muscle force (+60%) and muscle cross-section area (about 35%) within 1 year of tetanic muscle training was documented by means of torque measurement and computer tomography respectively.

As knee stabilization in the standing position requires relatively low muscle force and

standing up is supported by the upper body, standing training can be started early on. In our patients FES started 1 – 2 years after lesion (complete conus cauda). Standing training could be carried out 9 – 12 months after commencement of FES.

CLINICAL PROBLEMS OF FES OF DDM IN HUMAN

The prior study showed that denervated muscle can be treated with electrical stimulation, but at the same time highlighted problems that remain unsolved:

1. Maximum time span between injury and onset of stimulation training where successful restoration of DDM is still achievable
2. Slow increasing contraction force
3. Daily time expenditure for training is very high
4. High variation in developed contraction force (knee extension torque varies 20-25%) due missing warning signal in case of overstraining the muscle like pain or co-contraction that are reducing the knee extension torque
5. Muscle endurance is very low despite daily training of up to 2 x 30min.

Maximum time span elapsed after denervation

Stimulation therapy for denervated musculature should start within 5 years after denervation. After 5 years degeneration of muscle with connective tissue and fat is progressed so far that restoration of muscle tissue is hardly achievable. But to date 2 patients with a complete conus cauda lesion started stimulation after about 25 years and 1 patient with a plexus lesion started stimulation after 12 years are participating in our program.

The underlying mechanism of regeneration of denervated degenerated muscle and the factors triggering this mechanisms are at present unknown. Especially if there is a spontaneous regeneration of myoblasts (autonomous regeneration) or an electrically induced activity of satellite cells is to be answered still.

Long time span for hyperplasia and hypertrophy

If training with FES is commenced late after injury and the muscle is already degenerated, restoration of muscle takes at least two years. Within this period about 1 – 2 (4) Mio. new muscle fibers have to be built. That equals a synthesis rate of minimal 1000 new fibers per day over a period of 3 years.

This explains the slow increasing muscle force and combined with it the slow functional improvement of the muscle.

Intramuscular structural changes are much bigger than measurable gain of muscle force because of connective tissue and fat as well as broken sarcomeres have to be transformed and rebuilt.

Daily training time expenditure

Due to the fact of missing nerves and thus no distribution of the stimulation pulses each muscle or muscle group respectively has to be trained individually. Treatment of multiple muscles is impossible because of technical limitations regarding the maximum stimulation current. Connective tissue and fat acting as an electrical shunt are reducing the difference of electrical potential that is needed to excite the muscle cell membrane. The decreased membrane resting potential and the reduced metabolism of the muscle fiber seem to be the reason for the long pulse duration and the slow twitch character and fatigue of the muscle.

High variations in developed knee extension torque

In spite of continuous FES training with constant pulse parameters and treatment protocols we observed variations of up to 25% in developed knee extension torque.

Different co-activation of the hamstrings by the electrical field distributed over the whole thigh could be one of the effects causing this variations. Another reason for this effect could be a local overstrain of the muscle that is not prevented because of missing warning signals like pain. An accompanying monitoring of CPK acting as an indicator for muscle overstrain would be desirable in the future. We did not perform in our outpatients this monitoring of CPK because of its short half-life period and the necessary frequent measurements.

Endurance of muscle is very low

In the experimental work already done the concentration of aerobic muscle enzymes recovered up to the normal range. Nevertheless muscle endurance during standing exercises with switching stimulation alternating left and right (simulation of gait) was not very high. With this intermitting stimulation (1s on- 1s off-time) sufficient blood circulation was ensured, but the stimulated musculature fatigued very fast.

This behavior might be caused by the long diffusion distance between the capillaries and the muscle fibers because of the intrafibrillary located mitochondria in electrically trained muscles. Contrary to voluntary trained muscle where the mitochondria are subsarcolemmal located. These observations and the hypothesis regarding the long diffusion distance are to be proved in the proposed European project. Additionally should be examined if the site of mitochondria formation could be influenced by FES in animal experiments.

REFERENCES

- /1/ Boonstra A.M., Va Weerden T.W., Eisma W.H., Pahlplatz V.B.M. and Oosterhuis H.J.G.H.: The effect of low-frequency electrical stimulation on denervation atrophy in man. *Scand J Rehab Med* 19: 127-134, 1987.
- /2/ Carraro U, Catani C, Belluco S, Cantini M, Marchioro L: Slow-like electrostimulation switches on slow myosin in denervated fast muscle. *Exp Neurol* 94: 537-553, 1986.
- /3/ Carraro U, Catani C, Saggin L, Zrunek M, Szabolcs M, Gruber H, Streinzer W., Mayr W, Thoma H: Isomyosin changes after functional electrostimulation of denervated sheep muscle. *Muscle Nerve* 11: 1016-1028, 1988.
- /4/ Duchateau J., Hainaut K.: Effects of immobilization on contractile properties, recruitment and firing rates of human motor units. *J.Physiol.*442: 55-65, 1990.
- /5/ Galvani A.: De viribus electricitatis in motu musculari; *Commentarius de Bononiensi Scientarium et Artium Instituto adque Academia Commentarii* 7: 363, 1791.
- /6/ Gordon T., Stein R.B., Martin T.: Physiological and histochemical changes in human muscle produced by electrical stimulation after spinal cord injury, *J Neurol Sci* 98, Suppl. 141, 1990.
- /7/ Greve J.M., Muszkat R., Schmidt B., Chiovatto J., Barros T.E., Batisttella L.R.: Functional electrical stimulation (FES): muscle histochemical analysis. *Paraplegia* 31: 764-770, 1993.
- /8/ Holle J., Frey M., Gruber H., Kern H., Stöhr H., Thoma H.: Functional electrostimulation of paraplegics (experimental investigations and first clinical experience with an implantable stimulation device). *J. Orthopedics* 7: 1145-1155, 1984.
- /9/ Kern H.: Functional Electrical Stimulation in Paraplegic Spastic Patients. *Artificial Organs* 21(3):195-196, 1997.

- /10/ Kern H., Kainz A., Lechner J., Tausch F., Mayr W., Franke H., Schmutterer R., Schwanda G., Stöhr H., Kumpan W., Schurawitzky J., Mostbeck A., Gruber H.: Auswirkung elektrisch induzierter Bewegungstherapie. *Z.Phys.Med.Baln.Med.Klim.* 15: 317-318, 1986.
- /11/ Kern H., Frey M., Holle J., Schwanda G., Stöhr H., Thoma H.: Funktionelle Elektrostimulation querschnittgelähmter Patienten 1 Jahr praktische Anwendung, Erfolge der Patienten und Erfahrungen. *Z.f. Orthopädie* 1: 123, 1-12, 1985.
- /12/ Kern H.: Elektrostimulation im Sport und Rehabilitation, Dissertation, Universität Wien, 1994.
- /13/ Kern H.: Funktionelle Elektrostimulation paraplegischer Patienten. *Österr. Z. Phys. Med.* 5, Heft 1 Supplementum, 1995.
- /14/ Kern H., Hofer C., Strohhofer M., Mayr W., Richter W., Stöhr H.: Standing up with denervated muscles in humans using functional electrical stimulation. *Artif Organs.*, 23(5):447-52, 1999.
- /15/ Lake D.A.: Neuromuscular Electrical Stimulation. An Overview and its Application in the Treatment of Sports Injuries. *Sports Medicine* 13(5): 320-336, 1992.
- /16/ Lomo T., Westgaard R.H., Engebretsen L.: Different stimulation patterns affect contractile properties of denervated rat soleus muscles. In: Pette D. (ed) *Plasticity of muscle*. De Gruyter, Berlin, pp. 297-309, 1980.
- /17/ Neumayer C., Happak W., Kern H., Gruber H.: Hypertrophy and Transformation of Muscle Fibers in Paraplegic Patients. *Artificial Organs* 21(3): 188-190, 1997.
- /18/ Nix W.A.: The plasticity of motor units in regard to electrically imposed activity patterns- electrical stimulation and its possible clinical application. *Fortschr.Neurol.Psychiat.* 57: 94-106, 1989.
- /19/ Reichmann H., Hoppeler H., Mathieu-Costello L., Von Bergen F., Pette D.: Biochemical and ultrastructural changes of skeletal muscle mitochondria after chronic electrical stimulation in rabbits. *Pflügers Arch* 404: 1-9, 1985.
- /20/ Salmons S., Henriksson J.: The adaptative response of skeletal muscle to increased use. *Muscle and Nerve* 4: 94-105, 1981.
- /21/ Salmons S, Jarvis JC, Mayne CN, Chi MM, Manchester JK, McDougal DB Jr, Lowry OH: Changes in ATP, phosphocreatine, and 16 metabolites in muscle stimulated up to 96 hours. *Am J Physiol*, 271(4 Pt 1):C1167-71, 1996.
- /22/ Schubert W.: Funktionelles Training schlaff gelähmter Muskulatur. *Biomed. Technik* 30, 115, 1985.
- /23/ Zrunek M, Bigenzahn W, Mayr W, Unger E, Feldner-Busztin H. A laryngeal pacemaker for inspiration controlled direct electrical stimulation of denervated posterior cricoarytaenoid muscle in sheep. *Eur Arch Otorhinolaryngol* 1991;248(8):445-8.

AUTHOR'S ADDRESS

Univ. Doz. Dr. Dr.

Helmut Kern

Ludwig Boltzmann Institute of Electrostimulation and Physical Rehabilitation,

Department of Physical Medicine and Rehabilitation,

Wilhelminenspital Wien

Montleartstrasse 37

A-1171 Wien

helmut.kern@phys.wil.magwien.gv.at