

Optimization of Musculoskeletal Rehabilitation through Inclusion of Individual Factors of Cellular Plasticity

Optimierung der muskuloskelettalen Rehabilitation durch Einbezug individueller Faktoren der zellulären Plastizität

Injuries to the locomotor apparatus are a special therapeutic challenge. Affected persons are subjected after injury and several weeks of limited work capacity of the supportive and muscle tissues to a negative modelling of the muscle and tendon tissues involved.

This leads to a loss of strength and endurance through deconditioning of the neuromuscular systems. Due to the longer-lasting reduction of mobility and work capacity, persons who do not undergo therapy are also at risk that their health will suffer gradually via systemic influences of metabolic and psychological factors (1). Based on reports of annually ca. 1,900 Euros per person, measures to maintain musculoskeletal health account for a not negligible medico-economic substrate.

Degeneration of the Inactive Locomotor Apparatus

Load-controlled measures as part of a medical training therapy accompanied by controlled physical exercise are the method of choice for reestablishing the functional relationships after primary, possibly surgical, treatment of a musculoskeletal injury. This is justified by the dependence of the protein metabolism of musculoskeletal tissue on the effect of physiological stimuli. The phenomenon is manifest especially in the load-regulated cellular plasticity of skeletal muscles and the associated tendons (4). It can be assumed that a missing or greatly reduced mechanical and metabolic stress explains the observed decrease in muscle strength and endurance in the recuperation phase after musculoskeletal injury (4, 5, 8). The data confirm that mechanical relief elicits recognizable molecular and anatomical changes in the affected musculature within only a few days (4). We point out here the loss of cellular structures of the myofibrils, capillaries and mitochondria, which are involved in strength production and energy supply in the skeletal muscle. When immobility lasts from two to six weeks, a 30% decrease can be measured in the muscle mass. In extreme cases of non-reconstructed tendon rupture, this may convert to critical degeneration of the cellular composition due to irreversible steatosis and muscle shortening (5, 8). It can be assumed that appropriate rehabilitation can hinder or reverse the degeneration of the musculoskeletal tissue by stimulation of growth and differentiation processes (5).

Physiological Parameters of Rehabilitation

The challenge for successful rehabilitation lies in the lack of knowledge about the time course of deconditioning after an injury, or respectively the dose-effect relationship and specificity of the selected exercise therapy. Rehabilitation these days is performed based on experience and unweighted recommendations about volume and intensity, possibly with a heuristic approach (2).

Physical parameters of the active mechanical and metabolic stimuli during a muscle contraction, for example the tension time and changes in metabolite concentrations, control the effect of exercise therapy at the skeletal muscle level through gene-mediated effects on protein metabolism (3, 4). Practice-relevant deductions for the extent of muscular adaptation can be drawn from the elevation of the synthesis rate of myofibrillar proteins, respectively mitochondrial proteins, following strength or endurance training. Here it must be remembered that the specificity of adaptation only becomes established after repeated stimulus effect. Despite principal knowledge of the role of contractile factors for the maintenance of protein synthesis in immobilized skeletal muscle, this is only inadequately - or inconsistently - taken into account in general medical training therapy after musculoskeletal injury. Based on assumptions of intentionally high intensity and volume of muscular contractions during training by ambitious athletes, it can be assumed that untrained patients are generally treated too conservatively, or with a too-low dose or too late to stop the "disintegration" of the muscle structure following injury.

Constitutional Factors

The anticipated biological parameters introduced are probably related to the variability of reconditioning of the musculoskeletal system within a medical training therapy. Despite plausible clinical and medicine-economical relevance, attempts at explanation of this observation have received little attention thus far.

As it happens, the composition of musculoskeletal tissue, in addition to developmental-historical influences, is characterized largely by the interaction of conditional and constitutional factors. Constitutional factors have decisive influence on the outcome of a training intervention. Human studies show that there is a natural variability of cellular and functional adaptation of the skeletal muscle >

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after comparable training stimuli, which is determined by both the training status and by genetic factors. Natural sequence variations in certain genes (so-called gene polymorphisms) determine the extent of improvement in aerobic capacity through endurance training and are associated with the character of the phenotype of athletes (7). Results by our team show that the I-allele of the genes for the angiotensin-converting enzyme (ACE) influences the middle cross section of the muscle fiber, the maximal aerobic performance and the effect size of structural changes in volume density of the mitochondria and capillary length in skeletal muscle after endurance training (10, 11). The item discriminability of anatomical parameters in the skeletal muscle has been found to be one order of magnitude greater than that of systemic effects (10, 11).

Analogous to this, myogenic effects can be assumed for certain polymorphisms in the genes for actinin-3 (R577X) and myostatin (K153R), especially for muscle fiber injury after high load. On the other hand, it has been shown that certain metabolic parameters, such as capillarization and the lipid content in certain genotypes, in so-called "Non-responders", have little or no muscular response to endurance training (11). Genetic differences are considered as factors of post-operative rehabilitation and gene-based algorithms have been suggested for training monitoring; but they are not considered adequately proven (9).

Compensation of a Genetic Handicap

Results of a preliminary study show that the blood-pressure regulating angiotensin system in the skeletal muscle reacts differently in untrained and endurance-trained subjects among carriers of the ACE I-allele (10). This observation indicates that

endurance training repeated over several years can compensate an ACE-I/D genotype based individual genetic "handicap" via epigenetic processes. Presumably this is related to the improved microcirculation in the skeletal muscle of trained persons under exercise, due to the increased functional capillarization (10). Aspects of this load-dependent mechanism are also expressed at the systemic level through a differing preference for hypertrophy of the skeletal muscle, respectively the myocardium, in carriers of the ACE I allele (10).

Conclusion

The inclusion of individual genetic and further constitutional factors of muscle plasticity could be a valuable complement for the optimization of therapy success of muscular rehabilitation. Further research based on the measuring of evidence-based physiological and genetic characteristics is indicated to establish and validate the individual relationship between the type and dose of exercise stimulus and its effect in general. It should be taken into account that the individual biological parameters may possibly be only locally discriminant and a molecular "handicap" can be compensated at the systemic level. ■

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