

## HIGHLIGHTED TOPIC | *Eccentric Exercise*

# Eccentric Exercise: Many questions unanswered

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LOCOMOTION IS ARGUABLY one of the most ubiquitous and important manifestations of life, equally important to feeding as to escape predators. Evolution came up with three molecular motors to power motion: the actomyosin system Levitsky (11); the microtubule, dynein-based flagellar motors of eukaryotes (13); and the flagellar rotary motors of bacteria (15). All three systems serve propulsion, i.e., they impart kinetic energy to move something with regard to the environment. Thus all three motor systems were primarily “designed” to work concentrically.

With the advent of more complex organisms containing joints, the evolutionary opportunity arose to make locomotion more efficient by storing actomyosin-generated kinetic energy in elastic materials such as abductin, resilin, and elastin (for scallops, see Ref. 3). In a similar vein, sharks use their entire cartilaginous vertebral column as a spring during locomotion (14). Although information on elastic storage of energy in locomotion of aquatic animals is scant, this has extensively been studied in organisms moving over ground (1). During walking, the inverted pendulum mechanism allows for exchanging kinetic with potential energy, whereas during running, potential and kinetic energy is stored as elastic strain energy in tendons and ligaments of the limb to be reused with the next step. In this context, muscles are activated while lengthening or keeping the same length. To our knowledge, the capability to perform negative work (eccentric work) is a unique evolved feature of actomyosin-based muscle systems.

Constant length (isometric) and shortening (concentric) muscle contractions are adequately described on the molecular level by the sliding filament and cross-bridge theory (7, 8). This is not the case for eccentric contractions where the cross-bridge model fails to explain many of the observed phenomena (5). Eccentric contractions have a number of characteristics that set them apart from concentric contractions. Most importantly, with concentric contractions, force decreases with increasing shortening (6). In eccentric contractions, force increases first and then stays constant with increasing lengthening velocity. As a consequence, much larger forces can be generated during active lengthening than during shortening. This exposes muscle and tendon tissues to potentially damaging mechanical stress. Performing concentric and eccentric work on a motor driven ergometer, Bigland-Ritchie and Woods (2) further demonstrated that eccentric work required four times less metabolic energy and only half the electromyographically observed neuronal activation than concentric work. These exciting phenomena set eccentric contractions apart. However, despite their essential role in locomotion, eccentric contractions have remained massively under researched. This

series of mini-reviews describes current thinking both with regard to the fundamental mechanical and neuronal properties of eccentric muscle contractions as well as the application of eccentric contractions in rehabilitation and in sports.

In the first paper of this series of highlighted topics, Herzog (5) looks at the molecular mechanisms that have been invoked to explain force production in actively lengthening muscles. As mentioned above, the sliding filament and cross-bridge theories fail to explain many observations relevant to eccentric muscle contractions. Specifically, Herzog makes the case that “residual force enhancement,” i.e., the persistent increase of force after active muscle lengthening above values that would be expected based on sarcomere length remains unexplained with cross-bridge theory. Herzog discusses competing theories that have been advanced to explain residual force enhancement such as modifications of the cross-bridge kinetics and the “sarcomere length nonuniformity” theories. He suggests that a mechanism based on the active involvement of the cytoskeletal protein titin could explain the disputed experimental findings. Herzog also admits that details of active force regulation during muscle lengthening by actin-titin binding remain unclear and need further research.

Duchateau and Baudry (4) review the evidence pertaining to the neuronal control of eccentric contractions. There is considerable evidence indicating that it is difficult, at least in untrained individuals, to maximally activate muscles in eccentric contractions. This opens the possibility that spinal or cortical mechanisms could constrain motor-unit discharge rate. The evidence that the orderly recruitment pattern of motor units can be reversed in eccentric contractions remains controversial. By contrast, a decreased discharge rate of motor units during eccentric contractions is commonly observed and may constrain muscle activity during active lengthening. Several lines of evidence point to different cortical mechanisms in concentric and eccentric contractions; larger cortical excitability, greater involvement of brain areas, and different modulations of intracortical and interhemispheric coordination have been invoked. On the spinal level, motor-evoked potentials (MEP) are reduced both with transcranial magnetic stimulation (TMS) and electrical stimulation of the cortex (TES) in eccentric compared with concentric contractions. This indicates that a number of different pre- and postsynaptic mechanisms on the level of the motoneuron could be involved. The authors of the review (4) come to the conclusion that despite more information on the neuronal control of eccentric contractions being available today, the exact mechanisms involved on cortical and spinal levels remain unknown.

The potential as well as the use of eccentric contractions in rehabilitation settings is reviewed by LaStayo et al. (10). These authors contend that the major defining properties of eccentric muscle contractions, the potential for high muscle force pro-

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duction and a low energetic cost, make eccentric exercise training uniquely suited as a countermeasure for muscle wastage in many conditions where muscle atrophy is of concern. They also demonstrate that, provided eccentric loads are appropriately dosed and ramped over time, eccentric exercise training can be used safely and effectively in rehabilitation of serious medical conditions, avoiding unwanted muscle damage. The use of eccentric exercise is described in older and frail adults with the aim of fighting sarcopenia and in adults with cardiopulmonary disorders where eccentric exercise allows for achieving training relevant muscle loads at tolerable levels of dyspnea. It is further documented that eccentric exercise has successfully been explored in cancer survivors, in adults with metabolic disorders such as diabetes type 2, and in neurological conditions such as Parkinson's disease in adults and cerebral palsy in children. This research group also reports on their experience with rehabilitation after knee surgery, in particular, replacement surgery for anterior cruciate ligament as well as knee arthroplasty. This review calls for more research in particular with regard to optimizing training regimes in terms of intensity, duration, frequency, and modes of eccentric activity.

Over the last 25 years, eccentric exercise has become a mainstay in the treatment of tendinopathies mainly of the Achilles and the patellar tendon. Kjaer and Heinemeier (9) look critically at the scientific underpinning of the common therapeutic application of eccentric exercise as a first line of treatment for these conditions. They report that tendons are less sensitive than muscles to the difference in type or amount of mechanical load. The beneficial effects of eccentric exercise in overuse injuries of tendons with regard to collagen regulatory factors and fibril alignment is thus currently unexplained on a mechanistic level.

The value of eccentric exercise has often been questioned because of the fact that eccentric contractions in people unaccustomed to this type of exercise can lead to muscle soreness and muscle damage. This is of particular importance in the elderly or in patients with neuromuscular disease. In these cases, any training intervention must be aimed at preventing muscle damage. Lovering and Brooks (12) explore in their mini-review the benefits and risks of eccentric exercise in at-risk populations. They come to the conclusion that exercise (including eccentric components) is generally recommended; however, there are currently no common recommendations for all individuals and guidelines for eccentric exercise are still lacking.

Eccentric muscle contractions are important in practically all sports that involve jumps, running, or throwing as a critical part of the stretch shortening cycle (16). Eccentric exercise training has been shown to be effective in increasing (explosive) muscle strength, muscle cross-sectional area, and muscle fascicle length and can shift the sarcomere operating point toward

longer sarcomere lengths. Judicious use of eccentric training modalities is therefore a promising proposition in the preparation of elite athletes. However, knowledge of the adaptations of the neuromuscular system to eccentric stress remains incomplete.

In conclusion, all six mini-reviews of this highlighted series point to a serious lack of understanding both with regard to the fundamental properties of eccentric exercise as well as its practical applications in rehabilitation and sports. We hope that basic and applied scientists take up the opportunity to do the urgently needed research to bring this field forward.

#### DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

#### AUTHOR CONTRIBUTIONS

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