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Eccentric Exercise to Enhance Neuromuscular Control

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Context: Neuromuscular alterations are a major causal factor of primary and secondary injuries. Though injury prevention programs have experienced some success, rates of injuries have not declined, and after injury, individuals often return to activity with functionality below clinical recommendations. Considering alternative therapies to the conventional concentric exercise approach, such as one that can target neuromuscular injury risk and postinjury alterations, may provide for more effective injury prevention and rehabilitation protocols.

Evidence Acquisition: Peer-reviewed sources available on the Web of Science and MEDLINE databases from 2000 through 2016 were gathered using searches associated with the keywords *eccentric exercise, injury prevention*, and *neuromuscular control*.

Hypothesis: Eccentric exercise will reduce injury risk by targeting specific neural and morphologic alterations that precipitate neuromuscular dysfunction.

Study Design: Clinical review.

Level of Evidence: Level 4.

Results: Neuromuscular control is influenced by alterations in muscle morphology and neural activity. Eccentric exercise beneficially modifies several underlying factors of muscle morphology (fiber typing, cross-sectional area, working range, and pennation angle), and emerging evidence indicates that eccentric exercise is also beneficial to peripheral and central neural activity (alpha motorneuron recruitment/firing, sarcolemma activity, corticospinal excitability, and brain activation).

Conclusion: There is mounting evidence that eccentric exercise is not only a therapeutic intervention influencing muscle morphology but also targets unique alterations in neuromuscular control, influencing injury risk.

Keywords: injury prevention; neuromuscular; eccentric exercise

Conventional injury prevention and rehabilitation protocols have often focused on targeting muscle strength to reduce injury risk.[41,42,49] Though this approach is well intentioned, emerging evidence indicates that strength alone is not an independent predictor of primary and secondary injuries.[42,44,45,72,84,117] Hence, focusing on strength as a lone therapeutic target does not appear to adequately reduce the risk of injury. Further complicating this situation, common lower extremity injuries such as anterior cruciate ligament (ACL) rupture and ankle sprains can have life-long consequences, as these injuries are known to be a precursor to long-term disability associated with early-onset osteoarthritis.[52,110,116] The extensive health care cost and life-long disability[69,99] of common musculoskeletal injuries highlights the importance of reducing primary and secondary musculoskeletal injury risk.

Emerging evidence indicates that movement patterns that increase the risk of injury occur because of neuromuscular control deficits, which lead to compensatory motor strategies.[38,46,80,84] This lack of motor control or deficit in neuromuscular function has been operationally defined as the neurological mechanisms underlying the unconscious activation of dynamic restraints occurring in preparation for and in

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response to joint motion.[93,94] Clinically, these deficits in neuromuscular control manifest as poor landing mechanics, deficits in postural control, and altered peripheral muscle activation arising from changes in the central nervous system adversely affecting control of the skeletal muscle system.[93,94] Though researchers and clinicians have implemented injury prevention protocols to reduce the incidence of injury by targeting 1 or more of the abovementioned factors of neuromuscular control with some success,[60,113] the role of eccentric exercise as a training modality to mitigate these risk factors and reduce injury rates is often overlooked. The lack of eccentric exercise during injury prevention is likely due, in part, to the outdated notion that eccentric exercise causes muscle injury and soreness.[71,90,91] This negative association between eccentric exercise and injury is likely because of research that uses very high–intensity and volume-lengthening exercises to experimentally induce injury, resulting in a large body of literature that supports the notion that eccentric exercise can be dangerous.[13,27,70,71] Importantly, the muscle strains and subsequent injuries produced in these benchtop experiments have not been reproduced in the clinic, strongly suggesting that eccentric exercise is safe.[14] However, in response to the outdated notion that eccentric exercise produces muscle soreness and injury and is associated with reduced performance,[77,90,91] concentric exercise is often utilized as the clinical default to enhance neuromuscular control. Unfortunately, the concentric exercise approach does not restore neuromuscular function after injury,[63,73,82] and both primary and secondary injury rates remain high.[5,18,74,84] Though the ability of eccentric exercise to remodel muscle morphology is well known,[1,11,12,26,29] and the adoption of eccentric exercise to prevent hamstring strains is gaining traction thanks to programs like FIFA 11+,[85,106] there is also mounting evidence to support its use to enhance neuromuscular control and potentially reduce the incidence of injury. Accordingly, the objectives of this work were to (1) provide clinicians with an updated account of how alterations in neuromuscular control are a leading risk factor for injury and (2) propose a paradigm shift where eccentric exercise is used not only to optimize muscle morphology but also to prevent injury by targeting specific neural adaptations that are associated with poor neuromuscular control (Figure 1).

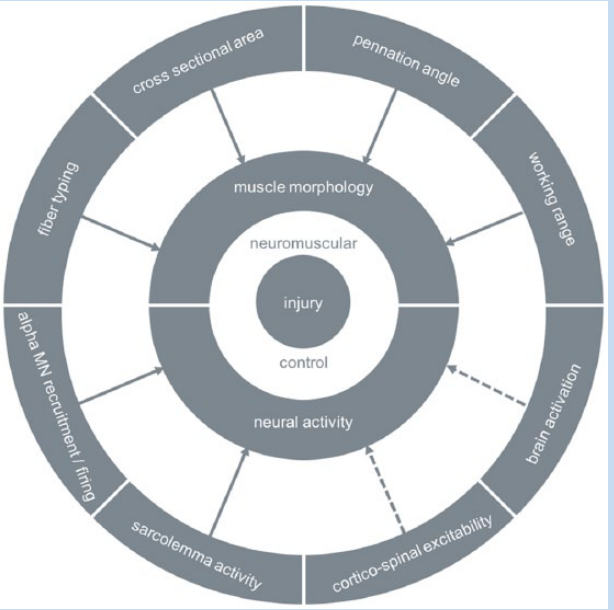

Figure 1. Injury is influenced by neuromuscular control (muscle morphology and neural activity). Eccentric exercise is known to beneficially modify several underlying factors of muscle morphology and neural activity (solid lines), and emerging evidence indicates that eccentric exercise is also beneficial to cortical neural control (dashed lines). Thus, eccentric exercise can be used to optimize neuromuscular control, thereby reducing the risk of injury.

ALTERED NEUROMUSCULAR CONTROL LEADS TO PRIMARY AND SECONDARY INJURIES

Proper neuromuscular control is maintained by an inherently complicated physiological system, and the degree to which alterations in this complex system (alpha-gamma motorneuron coactivation, mechanoreceptors, cortical and spinal mechanisms) contribute to injury is becoming clearer.[79,89] In particular, prospective data sets[45,117] allow researchers to make critical causal links between targetable injury risk factors and primary injury occurrence. Perhaps one of the most striking findings emerging from these studies is that strength alone is not predictive of primary injury.[45,117] Alternatively, improper neuromuscular control appears to be the significant causal risk factor of primary lower extremity injury, as investigators have found that alterations in neuromuscular control can lead to excessive lateral trunk displacement[117] and abnormal knee mechanics (valgus moments) during loading, which are the most predictive risk factors of those who go on to experience ACL injury.[45] Field assessment tools such as the Landing Error Scoring System (LESS) have also shown promise in prospectively predicting primary ACL injury risk in youth soccer players with abnormal landing characteristics[80]; however, evidence thus far has been contradictory, with others demonstrating no relationship between the risk of suffering ACL injury and LESS scores in high school and college athletes.[103] Altered hip and knee mechanics and postural control during loading are the strongest predictive risk factors for individuals who develop patellofemoral pain syndrome.[8] Similarly, in individuals who experience ankle sprains, high postural sway is evident prior to the initial injury,[72] and reduced performance on clinical measures of balance (Star Excursion Balance Test in the anterior direction) has recently been shown to be predictive of future ankle sprains.[32] Though muscle strength is an inherent factor associated with neuromuscular control, a consistent finding among all of the above[8,32,45,72,80,117] is that deficits in balance and landing mechanics are the strongest predictors of

primary injury. Hence, finding therapies capable of optimizing neuromuscular control is vital for those preventing or treating musculoskeletal injury.[49]

The need to identify interventions capable of enhancing neuromuscular control to prevent injury is perhaps most urgently needed after the initial injury during rehabilitation, as patients often return to activity with significant neuromuscular deficits that precipitate secondary injuries.[15,20,84] In the case of patients with ACL reconstruction, altered muscle activation profiles[15,19,21,39,56,57,111] and spinal reflexive excitability[87] persist for months to years after surgery. Knee and ankle joint injuries also adversely affect supraspinal activity, with altered cortical drive to the surrounding musculature[43,57,88,109] and reduced neural efficiency.[6,7] Recent advances in technology have allowed investigators to utilize functional magnetic resonance imaging (fMRI) to better understand the redistribution of activation patterns in the brain that are contributing to prolonged neuromuscular deficits. Notably, investigators recently used fMRI to prospectively assess brain activation in an individual 26 days prior to a second contralateral ACL injury, where alterations in motor planning, sensory processing, and visual motor control potentially predisposed the individual to injury when compared with a healthy matched control.[35]

These chronic neural deficits not only contribute to secondary injury risk[15,47] but prevent effective strengthening,[50] further compounding the risk for early-onset osteoarthritis.[52,110] Unfortunately, the changes in afferent and efferent neural activity after joint injury appear to be resistant to the current standard of care, which is primarily composed of concentrically focused exercises.[50] Data from a recent longitudinal investigation help illustrate this point directly; substantial changes in cortical, spinal, and volitional neural excitability were present after the initial ACL injury, were not rectified with ACL reconstruction, and were still present at return to activity despite 6 months of intensive rehabilitation.[62] Though rising awareness in the rehabilitation community has emphasized the importance of exercises in rehabilitation to target deficits in neuromuscular control,[4,20,78] the rates of traumatic knee joint injuries and ankle injuries have not declined.[5,18,84] Given the mounting data that indicate a direct link between poor neuromuscular control and primary and secondary injuries, alternative interventions capable of targeting the neural mechanisms associated with poor neuromuscular control should be strongly considered when developing an injury prevention protocol.

NEUROMUSCULAR BENEFITS OF ECCENTRIC EXERCISE

Morphological Considerations

A primary advantage of skeletal muscle is that it is a plastic biological material, constantly adapting and remodeling to the demands imposed on it.[67] This constant remodeling provides a therapeutic target that clinicians can exploit, as modifications to the physical stress imposed on muscle provide a means to directly enhance its functionality. Scientists are still unraveling the unique enhancement to muscle functionality from eccentric contractions and how these contractions maintain system stability at the cross-bridge level.[14] In contrast to concentric muscle contractions, where the proposed mechanisms of muscle contractions were scientifically and mathematically derived in 1957 by A. F. Huxley,[51] eccentric muscle contractions have long been considered to be "odd" or "deviating from the norm" (hence the name eccentric). However, without fully understanding the mechanism of muscle contractions, researchers and clinicians have long known that the "repeated bout effect," or the chronic use of eccentric exercise, is capable of beneficially modifying muscle morphology. This has been repeatedly shown in animal and human experiments where the targeted muscle of interest becomes more compliant to strain because of the addition of sarcomeres in series.[14] Arguably the best clinical example of this morphological benefit is the shift of the hamstring torque-angle curve to a longer working length after an eccentric intervention because of the addition of sarcomeres in series, which has implications for reduced injury risk.[11,12] Other notable well-established benefits of eccentric exercise are the ability to promote substantial gains in muscle cross-sectional area,[29] promote optimal fiber length,[12,26] increase pennation angle,[1] and target type II fibers.[40] Again, though the mechanisms involved in the acute morphological benefits of eccentric exercise are still under investigation, new evidence examining eccentric contractions at the cross-bridge level has found that eccentric exercise is capable of directly triggering a signaling complex that regulates tissue growth and adaptation.[92,105] Notably, this signaling complex is only activated when the sarcomere is lengthened by a mechanical force, indicating that only eccentric exercise is capable of engaging this unique mechanism to promote tissue growth.[92] From a clinical perspective, these benchtop experiments provide rationale as to why clinicians see greater acute muscle growth with eccentric exercise as compared with concentric exercise.[59,64,98] Taken together, these data support that both acute and chronic exposure to eccentric exercise appear to be uniquely well suited to remodeling muscle morphology.

Emerging Neural Evidence

New data are emerging that provide a compelling argument for the ability of eccentric exercise to directly influence peripheral and central neural adaptations associated with poor neuromuscular control.[28,66] Investigators have found that eccentric exercise is capable of significantly improving quadriceps electromyographic activity, physiologically indicating that an improvement in central motor drive is causing greater activity at the peripheral-sarcolemma level.[28] Improvement in the recruitment and/or firing rate of alpha motorneurons has also been found in patients with previous ACL reconstruction after just 12 treatments of eccentric exercise to the quadriceps muscle.[66] In patients with spinal cord injuries, volitional muscle activation (central activation ratio) and spinal pathways (Ia alpha motorneuron) are preferentially affected during passive eccentric exercises,[54] suggesting the wide benefit of lengthening contractions to target inhibited central and peripheral nervous

system pathways and promote greater neural activity even in the most extreme of conditions.

NEW TECHNOLOGIES ALLOW FOR NOVEL INSIGHT AND FRAMEWORK

Recently, researchers have started to use neurophysiological testing methods to better understand neuromuscular control associated with musculoskeletal injury. Transcranial magnetic stimulation (TMS), in which a noninvasive magnetic stimulus is applied to the motor cortex, can assess the ability of cortical neurons to activate and transmit impulses to the muscles.[3,31,37,108] Although there is limited research, investigations using TMS have also helped demonstrate that eccentric muscle contractions utilize unique neural mechanisms compared with other modes of muscle contraction.[3,22,37,101,102] In particular, researchers have demonstrated that eccentric contractions utilize greater excitability at the motor cortex compared with both concentric and isometric muscle contractions,[3,37] whereas concentric contractions appear to rely more on spinal-reflexive mechanisms.[3] Greater levels of cortical excitability are used during eccentric contractions as a compensatory strategy to account for inhibition at the spinal level.[22,37] Simply stated, the muscle spindle, which would normally cause a reflexive contraction of the muscle during lengthening, must be inhibited to allow for the eccentric contraction to occur, thereby increasing cortical drive to the muscle.[22] Interestingly, acute inhibition in spinal-reflexive excitability[55,62,81] is present after joint injury and thought to initiate long-term deficits in neuromuscular control.[47] This may explain why traditional, concentrically driven rehabilitation programs are unsuccessful at restoring neuromuscular control in these patients, as concentric exercise attempts to rely on inhibited spinal-reflexive pathways and therefore fails to adequately activate muscles during contraction. Alternatively, eccentric exercise interventions can create immediate gains in muscle strength and activation via selectively targeting central nervous system mechanisms in conjunction with the beneficial morphological adaptations.[3,22,37] Additionally, data suggest that eccentric exercise may have the ability to create neural adaptations at the spinal level, whereas the increase in cortical excitability causes a decrease in presynaptic inhibition over time, leading to improved muscle recruitment and potentially counteracting other inhibitory signals from an injured joint, such as pain and swelling.[24] Therefore, eccentric exercise interventions may be ideally suited for patients with musculoskeletal injury and create an optimal environment for muscle strengthening.[2,37] Furthermore, excitability of the motor cortex is impaired after a variety of musculoskeletal injuries, such as patellar tendinopathy,[95] ACL injury[43,62,115] and reconstruction,[61,62,87] and after ankle sprains and subsequent ankle instability,[9,75,86] which may negatively influence muscle function and movement patterns.[89,114] The ability of eccentric exercise to selectively increase motor cortex excitability as well as create adaptations in spinal level inhibition makes this mode of exercise an attractive addition to current rehabilitation techniques.

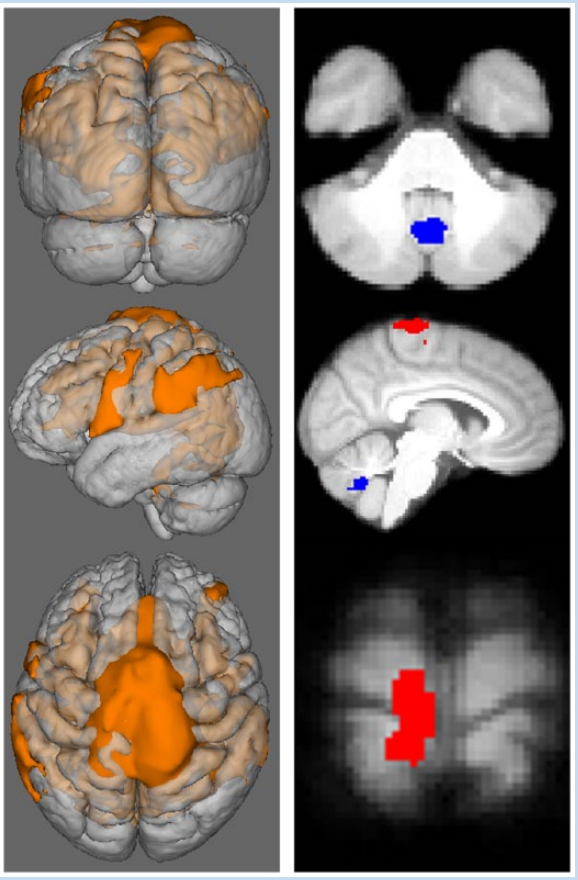

Figure 2. Left: Three-dimensional representation of the whole-brain activation pattern for knee extension-flexion in a cohort of participants who underwent anterior cruciate ligament (ACL) reconstruction (n = 15).[36] Right: Two-dimensional images pinpointing areas of increased activation in red-orange and decreased activation in blue during knee extension-flexion in those with ACL reconstruction relative to matched controls. Note the increase in motor cortex activation (lower right) and decrease in cerebellum activation (upper right).

This unique neural recruitment pattern and neuroplasticity associated with eccentric contractions may have the ability to address injury-induced neural changes and improve motor control.[33-35,58] In fact, new data suggest that the delivery of eccentric exercise, relative to concentric, may attenuate deficits in neuromuscular control induced by injury by not only improving cortical excitability but also by targeting specific motor control pathways in the brain.[25,58] To support this notion, in preliminary work using fMRI, real-time functional motor network reorganization is seen during eccentric quadriceps contractions after ACL reconstruction that addresses the primary maladaptive plasticity seen after injury (Figures 2[36] and 3, preliminary data). Specifically, when patients with ACL reconstruction who have undergone the traditional concentric

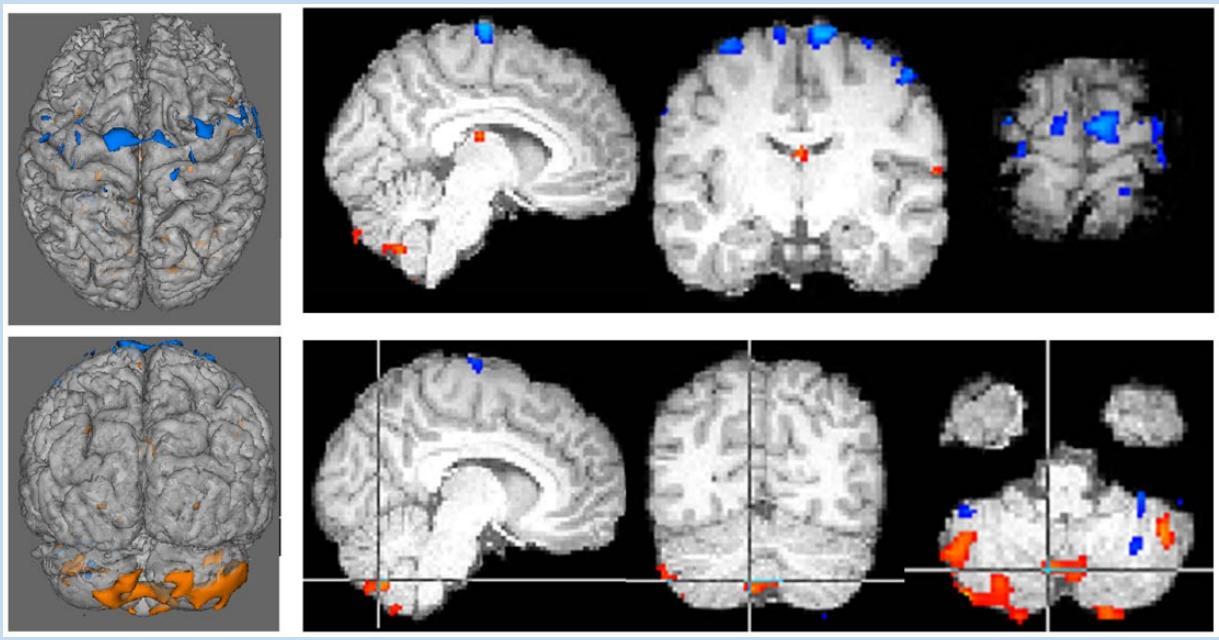

Figure 3. Left: Three-dimensional representation of the contrast between eccentric-concentric quadriceps contractions in those with anterior cruciate ligament (ACL) reconstruction relative to matched controls (n = 2). Right: Two-dimensional images pinpointing areas of increased activation in red-orange and decreased activation in blue during eccentric quadriceps contraction relative to concentric contraction. The activation pattern for eccentric contractions in the 2 ACL-reconstructed participants may uniquely reverse the activation pattern for knee movement that is present after injury. These data are from ongoing work and are unpublished.

bias rehabilitation scheme engage in knee movement exercises, they increased activation of the primary motor cortex (units are in BOLD [blood oxygen level–dependent signal, a correlate of neural activity] mean region increase, 2.18% ± 0.7%) and decreased activation of the cerebellum (BOLD mean region decrease, 0.39% ± 0.13%) relative to healthy matched controls (Figure 2). This altered cortical-cerebellar state after ACL reconstruction[36] may provide a partial mechanism for the increased cocontraction,[112] reflex inhibition,[62,104] and adaptive reactive stabilizing activation of the quadriceps and hamstring musculature after injury, as the cerebellum plays a key role in sensory-motor integration and precision force control.[68] Furthermore, this neural activation pattern associated with concentric rehabilitation appears to be suboptimal, as ACL-reconstructed individuals have poorer quadriceps muscle control and functional performance as well as decreased activity levels despite combined surgical and rehabilitative interventions.[63] Although not fully understood, it is possible that this altered cortical-cerebellar state after ACL reconstruction may be due to the extensive unilateral concentric muscle strengthening utilized during rehabilitation and the use of conscious cortical mechanisms to maintain knee stability (ie, the patient uses an internal focus of control, focusing on the knee joint and quadriceps musculature to engage in movement).[76] Interestingly, by engaging in eccentric muscle contractions as compared with concentric, increased cerebellar activation is seen (BOLD mean region increase, 2.4% ± 1.15%) and decreased cortical activation (primary motor cortex activation; BOLD mean region decrease, 2.0% ± 1.21%) (Figure 3, preliminary data). Thus, eccentric contractions may be able to reverse this altered cortical-subcortical state, promoting a neural activation pattern that is more like that of healthy controls, providing a compelling mechanism for therapeutic intervention. Importantly, the cerebellum plays a key role as a processing unit for optimal motor coordination[96]; thus, exercises that can facilitate its activation may be able to improve neuromuscular control more globally. Concentric contractions depend on spinal mechanisms for regulation of muscle force via the muscle spindle regulation of contractile properties, whereas in eccentric contractions, spinal mechanisms are inhibited to allow muscle lengthening without reflexive contractions.[3,23] This depressed muscle spindle feedback to the brain during eccentric contractions may further increase the need for heighted feed-forward control and accurate sensory predictions of the cerebellum to regulate motor output.[68,107] Hence, by engaging in eccentric contractions, clinicians may be able to reduce primary and secondary injury risk by selectively targeting brain centers (eg, cerebellum) that reduce motor coordination error.

NOVEL ECCENTRIC INTERVENTIONS FOR IMPROVING NEUROMUSCULAR CONTROL

In scenarios where eccentric exercise of the involved limb is contraindicated (eg, acute postoperative stages), clinicians can also consider using eccentric cross-exercise. Cross-exercise is the ability for exercise of 1 limb to cause an increase in strength of the contralateral, nonexercised limb.[100] This mode of exercise is capable of enhancing neuromuscular control by selectively targeting neural pathways that are associated with altered movement patterns.[28] Compared with concentric cross-exercise, eccentric cross-exercise provides greater immediate and sustained gains in strength and electromyographic activity in the untrained limbs of healthy individuals.[48] The cross-exercise strength gains that are produced in the nonexercised limb occur as a result of enhanced cortical (TMS) and spinal neural activity.[16,118] At the cortical level, the benefits of cross-exercise result from increased interhemispheric brain activity.[17,28,118] Spinal reflexive pathways involving reduced reciprocal inhibition (Hoffmann reflex) contribute to improved strength in the nonexercised limb.[97,118] Similar to exercising the involved limb, in healthy adults, an eccentric cross-exercise training protocol is capable of improving alpha motorneuron recruitment and/or firing rate in the nonexercised leg (central activation ratio).[65] After eccentric cross-exercise, relative to concentric cross-exercise, a reduced intracortical inhibition silent period and improved corticospinal excitability (measured via TMS) were noted, further supporting eccentric cross-exercise uniquely moderating neural pathways associated with neuromuscular control.[53]

THEORETICAL MODEL FOR HOW ECCENTRIC EXERCISE CAN PREVENT INJURY

Alterations in neuromuscular control that lead to injury may not be overcome by conventional injury prevention/rehabilitation programs. Alterations in muscle morphology and neural activity are the 2 primary factors that regulate neuromuscular control. Hence, to optimize neuromuscular control, clinicians should focus on finding therapies capable of targeting these underlying factors of muscle function. A number of recent published works have looked to develop novel eccentric exercise protocols that are able to optimize neuromuscular function in injury prevention and rehabilitation protocols. To beneficially modify quadriceps neuromuscular control, we point readers to eccentric exercise and cross-exercise protocols.[10,30,66,83] Modifying neuromuscular properties of the hamstring muscles may benefit from the use of Nordic hamstring curls.[11] Although it is well known that eccentric exercise is capable of promoting beneficial changes in muscle morphology, emerging evidence suggests that eccentric exercise is also capable of beneficially modifying peripheral and central neural activity. Based on the available evidence, we have proposed a paradigm shift where eccentric exercise is not considered harmful and should be incorporated into injury prevention protocols to target specific neural and morphological factors that are associated with poor neuromuscular control, which can be utilized to prevent injury (see Figure 1). This theory is developed from current data suggesting that eccentric exercise is beneficial to both muscle morphology and neural activity, which are underlying factors of muscle performance that have been linked to injury risk. However, based on this review, the reader should be aware that there is a general lack of evidence in the implementation of eccentric exercise programs for the purpose of preventing musculoskeletal injury. Although the evidence summarized in this theoretical model demonstrates that eccentric exercise is beneficial to neuromuscular control, there remains a gap in the literature on whether this improvement in muscle function translates to beneficial injury prevention strategies. Future research should look to include eccentric-based exercise programs when assessing the efficacy of injury prevention programs to directly elucidate the beneficial aspect of eccentric exercise on injury prevention.

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