

Is Postexercise Muscle Soreness a Valid Indicator of Muscular Adaptations?

Brad J. Schoenfeld, MSc, CSCS, CSPS¹ and Bret Contreras, MA, CSCS²

¹Department of Health Science, Lehman College, Bronx, NY; and ²School of Sport and Recreation, Auckland University of Technology, Auckland, New Zealand

ABSTRACT

DELAYED ONSET MUSCLE SORENESS (DOMS) IS A COMMON SIDE EFFECT OF PHYSICAL ACTIVITY, PARTICULARLY OF A VIGOROUS NATURE. MANY EXERCISERS WHO REGULARLY PERFORM RESISTANCE TRAINING CONSIDER DOMS TO BE ONE OF THE BEST INDICATORS OF TRAINING EFFECTIVENESS, WITH SOME RELYING UPON THIS SOURCE AS A PRIMARY GAUGE. THIS ARTICLE DISCUSSES THE RELEVANCE OF USING DOMS TO ASSESS WORKOUT QUALITY.

INTRODUCTION

Delayed onset muscle soreness (DOMS) is a common occurrence in response to unfamiliar or vigorous physical activity. It has been noted observationally that many individuals who regularly perform resistance training consider DOMS to be one of the best indicators of training effectiveness, with some relying upon this source as a primary gauge (37). In fact, there is a long-held belief that DOMS is a necessary precursor to muscle remodeling (13).

Current theory suggests that DOMS is related to muscle damage from unfamiliar or unaccustomed exercise (48). Although the exact mechanisms are

not well understood, DOMS appears to be a product of inflammation caused by microscopic tears in the connective tissue elements that sensitize nociceptors and thereby heighten the sensation of pain (28,42). Histamines, bradykinins, prostaglandins, and other noxious chemicals are believed to mediate discomfort by acting on type III and type IV nerve afferents that transduce pain signals from muscle to the central nervous system (6). These substances increase vascular permeability and attract neutrophils to the site of insult. Neutrophils, in turn, generate reactive oxygen species (ROS), which can impose further damage to the sarcolemma (8). Biochemical changes resultant to a structural disruption of the extracellular matrix (ECM) also have been implicated to play a causative role (53). It has been proposed that damage to myofibers facilitates the escape and entrance of intracellular and extracellular proteins, whereas disturbance of the ECM promotes the inflammatory response (53). In combination, these factors are thought to magnify the extent of soreness. In addition, DOMS can be exacerbated by edema, whereby swelling exerts increased osmotic pressure within muscle fibers that serve to further sensitize nociceptors (6,28).

DOMS is most pronounced when exercise training provides a novel stimulus to the musculoskeletal system (4). Although both concentric and eccentric training can induce DOMS, studies show that lengthening actions have the most profound effect on its manifestation (7). As a general rule, soreness becomes evident about 6–8 hours after an intense exercise bout and peaks at approximately 48 hours postexercise (42). However, the precise time course and extent of DOMS is highly variable and can last for many days depending on factors, such as exercise intensity, training status, and genetics. The prevailing body of literature does not support sex-related differences in the expression of DOMS (11,45).

THEORETICAL BASIS FOR USING DOMS AS A GAUGE FOR MUSCULAR ADAPTATIONS

The first step in determining whether DOMS provides a valid gauge of muscle development is to establish whether the theory has biological plausibility. Plausibility can possibly be inferred from the correlation between DOMS and exercise-induced muscle damage (EIMD). It has been

KEY WORDS:

DOMS; delayed onset muscle soreness; workout quality; muscle damage; EIMD

posited that structural changes associated with EIMD influence gene expression, resulting in a strengthening of the tissue that helps protect the muscle against further injury (1,44). When considering the mechanisms of muscle hypertrophy, there is a sound theoretical basis suggesting that such damage is in fact associated with the accretion of contractile proteins (48). What follows is an overview of the evidence supporting a hypertrophic role for EIMD. An in-depth discussion of the topic is beyond the scope of this article, and interested readers are referred to the recent review by Schoenfeld (48).

It is hypothesized that the acute inflammatory response to damage is a primary mediator of hypertrophic adaptations. Macrophages, in particular, are believed to promote remodeling pursuant to damaging exercise (60), and some researchers have hypothesized that these phagocytic cells are required for muscle growth (23). Current theory suggests that macrophages mediate hypertrophy through the secretion of cytokines synthesized within skeletal muscle (also known as myokines). Myokines have been shown to possess anabolic properties, exerting their effects in an autocrine/paracrine fashion to bring about unique effects on skeletal muscle adaptation (36,43,51). It should be noted that some research has shown that myokine production may be largely independent of damage to muscle tissue (62). This may be a function of the specific myokine response because numerous myokines have been identified with each displaying unique responses to exercise training (40). Neutrophils, another phagocytic leukocyte, also may play a role in inflammatory-mediated post-exercise hypertrophy, conceivably by signaling other inflammatory cells necessary for muscle regeneration. One such possibility is ROS (65), which can function as key cellular signaling molecules in exercise-induced adaptive gene expression (14,20,21,59). Studies show that ROS promote growth in both smooth muscle and cardiac muscle (55), and it has been suggested that they

induce similar hypertrophic effects on skeletal muscle (56).

Muscle damage also may mediate hypertrophy by facilitating activation of satellite cells (i.e., muscle stem cells). When stimulated by mechanical stress, satellite cells generate precursor cells (myoblasts) that proliferate and ultimately fuse to existing cells, providing the necessary agents for remodeling of muscle tissue (63,67). In addition, under certain conditions, satellite cells are able to donate their nuclei to the existing muscle fibers, enhancing their capacity for protein synthesis (2,34). Evidence substantiates that satellite cell activity is upregulated in response to EIMD (12,46,49). This is consistent with the survival mechanisms of the muscle cell where damaged fibers must quickly obtain additional myonuclei to facilitate tissue repair. Activation of satellite cells provides these needed myonuclei and co-expressing various myogenic regulatory factors, such as Myf5, MyoD, myogenin, and MRF4, which are involved in muscle reparation and growth (10). To this end, studies indicate that a person's ability to expand the satellite cell pool is a critical factor in maximizing muscle growth (41). It should be noted, however, that satellite cells are responsive to both muscle damaging and nondamaging exercises (40), and it is not clear whether their activity is enhanced by EIMD in a manner that promotes meaningful differences in muscle hypertrophy.

Cell swelling is another potential mechanism by which muscle damage may promote hypertrophic adaptations. EIMD is accompanied by an accumulation of fluid and plasma proteins within the fiber, often to an extent whereby this buildup exceeds the capacity of lymphatic drainage (16,31,42). This results in tissue edema, with significant swelling persisting in trained subjects for at least 48 hours after an exercise bout (19). Cellular swelling is theorized to regulate cell function (17), stimulating anabolism via increasing protein synthesis and decreasing protein breakdown (15,33,54). Although the exact mechanisms remain poorly understood, it appears that

membrane-bound, integrin-associated volume sensors are involved in the process (27). These osmosensors activate intracellular protein kinase transduction pathways, possibly mediated by autocrine effects of growth factors (5). The effects of cell swelling subsequent to EIMD have not as yet been directly investigated, however, and it therefore remains unclear whether the associated edema promotes similar anabolic and anti-catabolic effects to those reported in the literature.

Despite the sound theoretical rationale, direct research showing a cause-effect relationship between EIMD and hypertrophy is currently lacking. It has been shown that muscle damage is not obligatory for hypertrophic adaptations (3,13,25). Thus, any anabolic effects resulting from damaging exercise would be additive rather than constitutive. Furthermore, it is important to note that excessive damage has a decidedly negative effect on exercise performance and recovery. By definition, severe EIMD decreases force-producing capacity by 50% or more (40). Such functional decrements will necessarily impair an individual's ability to train at a high level, which in turn would be detrimental to muscle growth. Moreover, although training in the early recovery phase of EIMD does not seem to exacerbate muscle damage, it may interfere with the recuperative process (24,38). Studies indicate that regeneration of muscle tissue in those with severe EIMD can exceed 3 weeks, with full recovery taking up to 47 days when force production deficits reach 70% (47). In extreme cases, EIMD can result in rhabdomyolysis (40), a potentially serious condition that may lead to acute renal failure (61).

When taking all factors into account, it can be postulated that EIMD may enhance hypertrophic adaptations, although this theory is far from conclusive. The hormesis theory states that biological systems' response to stressors follows an inverted U-shaped curve (44). This is consistent with Selye's (50) concept of the general adaptation syndrome and would

suggest that if EIMD does indeed promote muscle development, optimum benefits would be realized from mild to moderate damage. However, an optimal degree of damage for maximizing muscle growth, assuming one does in fact exist, remains to be determined.

IS THERE A CAUSAL LINK BETWEEN DOMS AND MUSCLE HYPERTROPHY?

Given that DOMS is related to EIMD and assuming EIMD is indeed a mediator of hypertrophy, the question then becomes whether these events can be linked to conclude that DOMS is a valid indicator of growth. Although it is tempting to draw such a relationship, evidence suggests reason for skepticism. First, it remains debatable as to whether DOMS is an accurate gauge of muscle damage. There is little doubt that DOMS is a by-product of EIMD (6,40). However, studies show that soreness, as reported on a visual analog scale, is poorly correlated with both the time course and the magnitude of accepted markers of EIMD, including maximal isometric strength, range of motion, upper arm circumference, and plasma creatine kinase levels (39). Magnetic resonance imaging changes consistent with edema also do not correlate well with the time course of DOMS, with soreness peaking long before swelling manifests (6). So although DOMS may provide a general indication that some degree of damage to muscle tissue has occurred, it cannot be used as a definitive measure of the phenomenon.

What is more, humans can experience DOMS without presenting local signs of inflammation (40). In a study of subjects who performed different forms of unaccustomed eccentric exercise (including downhill treadmill running, eccentric cycling, downstairs running), Yu et al. (66) found no significant evidence of inflammatory markers postexercise despite the presence of severe DOMS. Other studies have reported similar findings after the performance of submaximal, eccentrically based exercise (29,30). These results provide reason for caution when attempting to

use DOMS as a gauge of muscular adaptations given the theorized role of the acute inflammatory response in tissue remodeling subsequent to EIMD. It also deserves mention that noneccentric aerobic endurance exercise can cause extensive muscle soreness. Studies show the presence of DOMS after marathon running and long-duration cycling (57). These types of exercise are not generally associated with significant hypertrophic adaptations, indicating that soreness alone is not necessarily suggestive of growth.

Moreover, DOMS displays a great deal of interindividual variability (58). This variability persists even in highly experienced lifters, with some consistently reporting perceived soreness after a workout, whereas others experiencing little, if any, postexercise muscular tenderness. Anecdotally, many bodybuilders claim that certain muscles are more prone to soreness than others. They report that some muscles almost never experience DOMS, whereas other muscles almost always experience DOMS after training. Recent research supports these assertions (52). Because the bodybuilders possess marked hypertrophy of the muscles that are and are not prone to DOMS, it casts doubt on the supposition that soreness is mandatory for muscle development. Moreover, genetic differences in central and peripheral adjustments and variations in receptor types and in the ability to modulate pain at multiple levels in the nervous system have been proposed to explain these discrepant responses (35). Yet, there is no evidence that muscle development is attenuated in those who fail to get sore postexercise.

Resistance exercises and activities that place peak tension at longer muscle lengths have been shown to produce more soreness than exercises that place peak tension at shorter muscle lengths (22). Whether these alterations affect the magnitude of hypertrophic adaptations has yet to be studied, but it has been postulated that torque-angle curves in resistance training might augment hypertrophy through varying mechanisms (9). It is therefore conceivable that

exercises that stress a muscle maximally at a short muscle length can promote hypertrophic gains without inducing much, if any, soreness.

Training status has an effect on the extent of DOMS. Soreness tends to dissipate when a muscle group is subjected to subsequent bouts of the same exercise stimulus. This is consistent with the "repeated bout effect," where regimented exercise training attenuates the extent of muscle damage (32). Even lighter loads protect muscles from experiencing DOMS during subsequent bouts of exercise (26). Therefore, training a muscle group on a frequent basis would reduce soreness, yet could still deliver impressive hypertrophic results. A number of explanations have been provided to explain the repeated bout effect, including a strengthening of connective tissue, increased efficiency in the recruitment of motor units, greater motor unit synchronization, a more even distribution of the workload among fibers, and/or a greater contribution of synergistic muscles (3,57).

In addition to reducing joint torque and muscle force, DOMS may negatively affect subsequent workouts in other ways and therefore impede strength and hypertrophic gains. Pain associated with DOMS has been shown to impair movement patterns, albeit in individuals with high pain-related fear (64). Altered exercise kinematics arising from DOMS-related discomfort can reduce activation of the target musculature and potentially lead to injury. Moreover, some researchers have speculated that DOMS could reduce the motivation levels involved in subsequent training, reducing exercise adherence (18). Therefore, excessive DOMS should not be actively pursued because it ultimately interferes with progress.

PRACTICAL APPLICATIONS

In conclusion, there are several takeaway points for the strength coach or personal trainer as to the validity of using DOMS as a measure of workout quality. Because muscle damage is theorized to mediate hypertrophic adaptations (48), there is

some justification to actively seek muscle damage during a training session if maximal hypertrophy is the desired goal. Given that DOMS is a gross indicator of EIMD, soreness can provide a modicum of insight as to whether damage has taken place postexercise. So although common strategies to minimize DOMS, such as increasing training frequency, adhering to the same exercise selection, performing concentric-only exercises, and performing solely exercises that stress short muscle lengths, can help maintain short-term athletic performance, they may ultimately compromise hypertrophic adaptations by blunting EIMD.

On the other hand, caution must be used in drawing qualitative conclusions given the poor correlation between DOMS and the time course and extent of EIMD. Some muscles appear to be more prone to DOMS than others, and there seems to be a genetic component that causes certain individuals to experience persistent soreness, whereas others rarely get sore at all. In addition, high levels of soreness should be regarded as detrimental because it is a sign that the lifter has exceeded the capacity for the muscle to efficiently repair itself. Moreover, excessive soreness can impede the ability to train optimally and decrease motivation to train. Thus, the applicability of DOMS in assessing workout quality is inherently limited, and it therefore should not be used as a definitive gauge of results.

Conflicts of Interest and Source of Funding: The authors report no conflicts of interest and no source of funding.



Brad J. Schoenfeld is a lecturer in exercise science at Lehman College in the Bronx, NY, and is currently completing his doctoral work at Rocky

Mountain University.



Bret Contreras is currently pursuing his PhD in Sports Science at the AUT University in Auckland, New Zealand.

REFERENCES

1. Barash IA, Mathew L, Ryan AF, Chen J, and Lieber RL. Rapid muscle-specific gene expression changes after a single bout of eccentric contractions in the mouse. *Am J Physiol Cell Physiol* 286: C355–C364, 2004.
2. Barton-Davis ER, Shoturma DI, and Sweeney HL. Contribution of satellite cells to IGF-I induced hypertrophy of skeletal muscle. *Acta Physiol Scand* 167: 301–305, 1999.
3. Brentano MA and Martins Krueel LF. A review on strength exercise-induced muscle damage: Applications, adaptation mechanisms and limitations. *J Sports Med Phys Fitness* 51: 1–10, 2011.
4. Byrnes WC and Clarkson PM. Delayed onset muscle soreness and training. *Clin Sports Med* 5: 605–614, 1986.
5. Clarke MS and Feedback DL. Mechanical load induces sarcoplasmic wounding and FGF release in differentiated human skeletal muscle cultures. *FASEB J* 10: 502–509, 1996.
6. Clarkson PM and Hubal MJ. Exercise-induced muscle damage in humans. *Am J Phys Med Rehabil* 81: 52–69, 2002.
7. Cleak MJ and Eston RG. Muscle soreness, swelling, stiffness and strength loss after intense eccentric exercise. *Br J Sports Med* 26: 267–272, 1992.
8. Connolly DA, Sayers SP, and McHugh MP. Treatment and prevention of delayed onset muscle soreness. *J Strength Cond Res* 17: 197–208, 2003.
9. Contreras B, Cronin J, Schoenfeld BJ, N R, and Sonmez GT. Are all hip extension exercises created equal? *Strength Cond J* 35: 17–22, 2013.
10. Cornelison DD and Wold BJ. Single-cell analysis of regulatory gene expression in quiescent and activated mouse skeletal muscle satellite cells. *Dev Biol* 191: 270–283, 1997.
11. Dannecker EA, Hausenblas HA, Kaminski TW, and Robinson ME. Sex differences in delayed onset muscle pain. *Clin J Pain* 21: 120–126, 2005.
12. Dhawan J and Rando TA. Stem cells in postnatal myogenesis: Molecular mechanisms of satellite cell quiescence, activation and replenishment. *Trends Cell Biol* 15: 666–673, 2005.
13. Flann KL, LaStayo PC, McClain DA, Hazel M, and Lindstedt SL. Muscle damage and muscle remodeling: No pain, no gain? *J Exp Biol* 214: 674–679, 2011.
14. Gomez-Cabrera MC, Domenech E, and Vina J. Moderate exercise is an antioxidant: Upregulation of antioxidant genes by training. *Free Radic Biol Med* 44: 126–131, 2008.
15. Grant AC, Gow IF, Zammit VA, and Shennan DB. Regulation of protein synthesis in lactating rat mammary tissue by cell volume. *Biochim Biophys Acta* 1475: 39–46, 2000.
16. Guyton A. *Textbook of Medical Physiology*. Philadelphia, PA: WB Saunders, 1986. pp. 366–368.
17. Haussinger D. The role of cellular hydration in the regulation of cell function. *Biochem J* 313(Pt 3): 697–710, 1996.
18. Howatson G, Hough P, Pattison J, Hill JA, Blagrove R, Glaister M, and Thompson KG. Trekking poles reduce exercise-induced muscle injury during mountain walking. *Med Sci Sports Exerc* 43: 140–145, 2011.
19. Howatson G and Milak A. Exercise-induced muscle damage following a bout of sport specific repeated sprints. *J Strength Cond Res* 23: 2419–2424, 2009.
20. Jackson MJ. Free radicals generated by contracting muscle: By-products of metabolism or key regulators of muscle function? *Free Radic Biol Med* 44: 132–141, 2008.
21. Ji LL, Gomez-Cabrera MC, and Vina J. Exercise and hormesis: Activation of cellular antioxidant signaling pathway. *Ann N Y Acad Sci* 1067: 425–435, 2006.
22. Jones DA, Newham DJ, and Torgan C. Mechanical influences on long-lasting human muscle fatigue and delayed-onset pain. *J Physiol* 412: 415–427, 1989.
23. Koh TJ and Pizza FX. Do inflammatory cells influence skeletal muscle hypertrophy? *Front Biosci (Elite Ed)* 1: 60–71, 2009.
24. Krentz JR and Farthing JP. Neural and morphological changes in response to a 20-day intense eccentric training protocol. *Eur J Appl Physiol* 110: 333–340, 2010.
25. LaStayo P, McDonagh P, Lipovic D, Napoles P, Bartholomew A, Esser K, and Lindstedt S. Elderly patients and high force resistance exercise—a descriptive report: Can an anabolic, muscle growth response

- occur without muscle damage or inflammation? *J Geriatr Phys Ther* 30: 128–134, 2007.
26. Lavender AP and Nosaka K. A light load eccentric exercise confers protection against a subsequent bout of more demanding eccentric exercise. *J Sci Med Sport* 11: 291–298, 2008.
 27. Low SY, Rennie MJ, and Taylor PM. Signaling elements involved in amino acid transport responses to altered muscle cell volume. *FASEB J* 11: 1111–1117, 1997.
 28. Malm C. Exercise-induced muscle damage and inflammation: Fact or fiction? *Acta Physiol Scand* 171: 233–239, 2001.
 29. Malm C, Nyberg P, Engstrom M, Sjodin B, Lenkei R, Ekblom B, and Lundberg I. Immunological changes in human skeletal muscle and blood after eccentric exercise and multiple biopsies. *J Physiol* 529(Pt 1): 243–262, 2000.
 30. Malm C, Sjodin TL, Sjoberg B, Lenkei R, Renstrom P, Lundberg IE, and Ekblom B. Leukocytes, cytokines, growth factors and hormones in human skeletal muscle and blood after uphill or downhill running. *J Physiol* 556: 983–1000, 2004.
 31. McGinley C, Shafat A, and Donnelly AE. Does antioxidant vitamin supplementation protect against muscle damage? *Sports Med* 39: 1011–1032, 2009.
 32. McHugh MP. Recent advances in the understanding of the repeated bout effect: The protective effect against muscle damage from a single bout of eccentric exercise. *Scand J Med Sci Sports* 13: 88–97, 2003.
 33. Millar ID, Barber MC, Lomax MA, Travers MT, and Shennan DB. Mammary protein synthesis is acutely regulated by the cellular hydration state. *Biochem Biophys Res Commun* 230: 351–355, 1997.
 34. Moss FP and Leblond CP. Satellite cells as the source of nuclei in muscles of growing rats. *Anat Rec* 170: 421–435, 1971.
 35. Nicol C, Kuitunen S, Kyrolainen H, Avela J, and Komi PV. Effects of long- and short-term fatiguing stretch-shortening cycle exercises on reflex EMG and force of the tendon-muscle complex. *Eur J Appl Physiol* 90: 470–479, 2003.
 36. Nielsen AR and Pedersen BK. The biological roles of exercise-induced cytokines: IL-6, IL-8, and IL-15. *Appl Physiol Nutr Metab* 32: 833–839, 2007.
 37. Nosaka K. Exercise-induced muscle damage and delayed onset muscle soreness (DOMS). In: *Strength and Conditioning: Biological Principles and Practical Applications*. Cardinale M, Newton R, and Nosaka K, eds. West Sussex, United Kingdom: John Wiley and Sons, 2011. pp. 187.
 38. Nosaka K, Lavender A, Newton M, and Sacco P. Muscle damage in resistance training: Is muscle damage necessary for strength gain and muscle hypertrophy? *Int J Sport Health Sci* 1: 1–8, 2003.
 39. Nosaka K, Newton M, and Sacco P. Delayed-onset muscle soreness does not reflect the magnitude of eccentric exercise-induced muscle damage. *Scand J Med Sci Sports* 12: 337–346, 2002.
 40. Paulsen G, Mikkelsen UR, Raastad T, and Peake JM. Leucocytes, cytokines and satellite cells: What role do they play in muscle damage and regeneration following eccentric exercise? *Exerc Immunol Rev* 18: 42–97, 2012.
 41. Petrella JK, Kim J, Mayhew DL, Cross JM, and Bamman MM. Potent myofiber hypertrophy during resistance training in humans is associated with satellite cell-mediated myonuclear addition: A cluster analysis. *J Appl Physiol* 104: 1736–1742, 2008.
 42. Proske U and Morgan DL. Muscle damage from eccentric exercise: Mechanism, mechanical signs, adaptation and clinical applications. *J Physiol* 537: 333–345, 2001.
 43. Quinn LS. Interleukin-15: A muscle-derived cytokine regulating fat-to-lean body composition. *J Anim Sci* 86: E75–E83, 2008.
 44. Radak Z, Chung HY, Koltai E, Taylor AW, and Goto S. Exercise, oxidative stress and hormesis. *Ageing Res Rev* 7: 34–42, 2008.
 45. Rinard J, Clarkson PM, Smith LL, and Grossman M. Response of males and females to high-force eccentric exercise. *J Sports Sci* 18: 229–236, 2000.
 46. Russell B, Dix DJ, Haller DL, and Jacobs-El J. Repair of injured skeletal muscle: A molecular approach. *Med Sci Sports Exerc* 24: 189–196, 1992.
 47. Sayers SP and Clarkson PM. Force recovery after eccentric exercise in males and females. *Eur J Appl Physiol* 84: 122–126, 2001.
 48. Schoenfeld BJ. Does exercise-induced muscle damage play a role in skeletal muscle hypertrophy? *J Strength Cond Res* 26: 1441–1453, 2012.
 49. Schultz E, Jaryszak DL, and Valliere CR. Response of satellite cells to focal skeletal muscle injury. *Muscle Nerve* 8: 217–222, 1985.
 50. Selye H. Stress and the general adaptation syndrome. *Br Med J* 1: 1383–1392, 1950.
 51. Serrano AL, Baeza-Raja B, Perdiguero E, Jardi M, and Munoz-Canoves P. Interleukin-6 is an essential regulator of satellite cell-mediated skeletal muscle hypertrophy. *Cell Metab* 7: 33–44, 2008.
 52. Sikorski EM, Wilson JM, Lowery RP, Joy JM, Laurent CM, Wilson SM-C, Hesson D, Naimo MA, Averbuch B, and Gilchrist P. Changes in perceived recovery status scale following high volume, muscle damaging resistance exercise. *J Strength Cond Res* 27: 2079–2085, 2013.
 53. Stauber WT, Clarkson PM, Fritz VK, and Evans WJ. Extracellular matrix disruption and pain after eccentric muscle action. *J Appl Physiol* 69: 868–874, 1990.
 54. Stoll BA and Scretto G. Prenatal influences and breast cancer. *Lancet* 340: 1478, 1992.
 55. Suzuki YJ and Ford GD. Redox regulation of signal transduction in cardiac and smooth muscle. *J Mol Cell Cardiol* 31: 345–353, 1999.
 56. Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, and Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. *J Appl Physiol* 88: 61–65, 2000.
 57. Tee JC, Bosch AN, and Lambert MI. Metabolic consequences of exercise-induced muscle damage. *Sports Med* 37: 827–836, 2007.
 58. Tegeder I, Meier S, Burian M, Schmidt H, Geisslinger G, and Lotsch J. Peripheral opioid analgesia in experimental human pain models. *Brain* 126: 1092–1102, 2003.
 59. Thannickal VJ and Fanburg BL. Reactive oxygen species in cell signaling. *Am J Physiol Lung Cell Mol Physiol* 279: L1005–L1028, 2000.
 60. Tidball JG. Inflammatory processes in muscle injury and repair. *Am J Physiol Regul Integr Comp Physiol* 288: 345–353, 2005.
 61. Tietjen DP and Guzzi LM. Exertional rhabdomyolysis and acute renal failure following the Army Physical Fitness Test. *Mil Med* 154: 23–25, 1989.

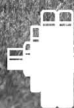
62. Toft AD, Jensen LB, Bruunsgaard H, Ibfelt T, Halkjaer-Kristensen J, Febbraio M, and Pedersen BK. Cytokine response to eccentric exercise in young and elderly humans. *Am J Physiol Cell Physiol* 283: 289–295, 2002.
63. Toigo M and Boutellier U. New fundamental resistance exercise determinants of molecular and cellular muscle adaptations. *Eur J Appl Physiol* 97: 643–663, 2006.
64. Trost Z, France CR, Sullivan MJ, and Thomas JS. Pain-related fear predicts reduced spinal motion following experimental back injury. *Pain* 153: 1015–1021, 2012.
65. Uchiyama S, Tsukamoto H, Yoshimura S, and Tamaki T. Relationship between oxidative stress in muscle tissue and weight-lifting-induced muscle damage. *Pflugers Arch* 452: 109–116, 2006.
66. Yu JG, Malm C, and Thornell LE. Eccentric contractions leading to DOMS do not cause loss of desmin nor fibre necrosis in human muscle. *Histochem Cell Biol* 118: 29–34, 2002.
67. Zammit PS. All muscle satellite cells are equal, but are some more equal than others? *J Cell Sci* 121: 2975–2982, 2008.

DISCOVER

WHAT NSCA MEMBERSHIP CAN DO FOR YOU



Visit **NSCA.com** to see membership tiers and pricing.



NSCA[™]
NATIONAL STRENGTH AND
CONDITIONING ASSOCIATION

everyone stronger
NSCA.com