ETIOLOGY OF ECCENTRIC EXERCISE INDUCED MUSCLE DAMAGE AND REPEATED BOUT EFFECT

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Review paper

Abstract

Eccentric exercise (ECC) is characterized with muscle damage and ability of muscle to adapt to the damage coming after. This adaption referred to "repeated bout effect (RBE)" whereby making the muscle less prone to future damage. Typical signs of this protective effect are a faster recovery, less inflammatory response and less development of delayed onset muscle soreness following different neural, mechanical and cellular adaptations in sequence. However, the duration of protective effect varies across muscle group as it has been shown when a single bout of 30-min of downhill running (-10 degrees slope) reaped after 6 weeks, generated the same of muscle soreness and serum creatine kinase (CK), and myoglobin in subjects. Debate exists concerning to avoid of RBE to maintain all aspects of muscle damage coming after a second bout of the same eccentric exercise for related clinical properties that it may produce. Nonetheless, in reality reduced indicators of muscle damage is a possible event but not always guaranteed although putative repair and regeneration phase following eccentric muscle damage take place as yet they are temporary. In this respect, researchers use of an eccentric term with an assumption that blood flow or glaucous availability increases as it results micro - damage in musculoskeletal system *that could be exploited to enhance blood volume in hypertensive individual or glucose availability* in *diabetes patients. Thus even though, muscle damage following a bout of eccentric exercise elevates pain and inhibits short-term recovery of muscle function, it may result in a positive healing process in body as it previously has been proven ''no pain, no gain''.*

***Key Words:** **e**ccentric exercise, **m**uscle damage, muscle adaption*

Etiology of Eccentric exercise Induced Muscle Damage

Muscle damage is caused by an unaccustomed eccentric activity, has been a recurring theme in physiology form the beginning of 20th century (Hough, 1902). In normal daily routine an eccentric exercise (ECC) is used in the landing phases of movements such as walking, running at downhill, stair descents, landing from a jump, lowering heavy pieces and many other ordinary movements (Isner-Horobeti et al., 2013). Characterised eccentric activity is an elongation of the muscle during simultaneous contraction (Stauber, 1989). Important features of eccentric muscle action, which largely account for the extent of damage experienced in this form of contraction, are the higher forces exerted and the lower motor unit activation for a given force ratio when compared to concentric or isometric muscle contractions (Eston et al., 2003). Moreover, eccentric actions result in greater skeletal muscle damage because of cross-bridges stretching and mechanical detachment of cross-bridges with greater force versus concentric or an isometric actions that can develop by seven days (Enoka, 1996; Cheung et al., 2003). Histological evidence has shown that, damage after eccentric contraction is disrupted sarcomere in myofibrils and more specifically in Z-lines (Friden and Lieber, 1992). This appears to be particularly focussed among the Type II muscle fibres, which have the narrowest and weakest Z lines (Eston et al., 2003). Initially, eccentric muscle actions result in a distribution of sarcomere lengths. According to the 'popping sarcomere' hypothesis, (Morgan, 1990; Proske and Morgan, 2001) stretch induced

muscle damage results from very non-uniform lengthening of sarcomeres when active muscle is stretched beyond optimum length. Lengths beyond optimum have been equated with the descending limb of the length, where the longest sarcomeres will be the weakest beyond myofilament overlap. During repeated eccentric contractions, the sarcomeres from the weaker to the stronger are progressively over-extended (''popped'') to a point of no myofilament overlap up until rising passive tension compensates for falling active tension (Morgan & Proske, 2004). Upon the muscle relaxation phase, the myofilaments of overstretched sarcomeres may fail to reconnect, resulting in disrupted sarcomeres. This ultrastructural disruption can spread to adjacent areas of the muscle, and can ultimately lead to damage to the membranes of the sarcoplasmic reticulum or sarcolemma, (Proske & Allen, 2005; Newham et al., 1983), "shearing" of transverse tubules (t-tubules) (Takekura et al., 2001) and Z-lines "streaming" (Friden et al., 1981). Simultaneously, excitation – contraction (E-C) coupling is disrupted, and Ca^{2+} moves freely into the sarcoplasm where it activates proteolytic pathways related to muscle fibre degradation and regeneration (Proske and Allen, 2005), impairs muscle function and strength (Ingalls et al., 1999). This process appears to produce common symptoms associated with muscle damage, delayed - onset muscle soreness (DOMS), and increases in muscle protein and proteolytic enzyme such as creatine kinase (CK), myoglobin (Mb) and lactate

dehydrogenase (LDH) in circulation (Clarkson et al., 1986; Lu et al., 1992), which represent as secondary symptoms of damaged muscle after plasma membrane damage. Subsequently, the breakdown of myocellular components elevates accumulation of inflammatory pain mediators including histamine, bradykinins and prostaglandins in the damaged muscle (Sayers and Hubal, 2008) within the activation of type III and IV pain receptors (O'Conner and Cook, 1999). This is followed by an influx of protein-rich fluid into the muscle via the increased permeability of small blood vessels following eccentric exercise (Smith, 1991). Ultimately, an exerted osmotic pressure (Friden et al., 1986) and oedema result from an accumulation of proteins and transudate in the interstitial space (Arnheim, 1989; Page, 1995). Research confirms that interstitial fluid accumulates transitory and osmotic cellular metabolites as the speed of their removal is too slow in comparison to the pace of their delivery from cells and plasma (Havas et al., 1997; Sorichter et al., 1995). The fluid surplus infiltrates lymphatic vessels and goes further to the blood and continues to its constant interchange (Havas et al., 1997). The flow of lymph is aided by skeletal muscle contractions, negative pressure inside the chest during inspiration, a suctorial effect produced by fast blood flow in veins and the regular twitch of large lymphatic vessels (Lindena et al., 1984). This inflammatory response that leads to the muscle vasodilatation causes a transfer of fluid to the affected muscles for removal of damaged contractile proteins and cellular debris (Pyne,1994) which may change the pattern of local blood flow after eccentric actions (Ahmadi et al., 2008) .

Underlying Mechanisms of Repeated Bout Effect

Systemic markers of muscle damage are limited in terms of sensitivity and reliability (McKune et al., 2012) as a single bout of eccentric exercise protects against muscle damage from subsequent eccentric bouts (McHugh, 2003). This adaption referred to "repeated bout effect (RBE)" whereby making the muscle less prone to future damage. Typical signs of this protective effect are a faster recovery, less inflammatory response and less development of delayed onset muscle soreness (Clarkson et al., 1992). The potential mechanisms underlying for this protection of repeated bout effect have been categorized into three broad as neural, mechanical and cellular adaptations (McHugh et al., 1999). The neural adaptation points to a change in motor unit recruitment during the repeated bout in which limits the extent of damage (Warren et al., 2000). This alteration includes increasing the recruitment of slow-twitch motor units (type I fibers) and a greater synchrony in the number of motor units following the second bout of eccentric exercise. This change in motor unit activation could limit the subsequent myofibrillar damage (McHugh, 2003; McHugh et al., 1999). Corroborating this idea, Hortobagyi and colleagues (1998) reported no significant changes in force,

creatine kinase (CK) level and soreness after second bout of eccentric contractions but still myofibrillar disruption in quadriceps muscle. These results indicate that the rapid force recovery following eccentric exercise is mediated at least in part by neural factors and that this recovery may occur independently of cell disruption. Mechanical adaption serves to protect against eccentric muscle damage in mechanical properties in musculoskeletal system. It follows with an increased stiffness in passive or dynamic muscle condition. The increased stiffness referred to elastic properties or extensibility in muscles which continues after eccentric contractions (McHugh, 2003). This protective effect contributes to adaption in the cytoskeleton proteins proteins (i.e., desmin, vimentin, and sinemina) whose functions are to maintain the structural integrity of the sarcomeres in parallel (Flitney and Hirst, 1978; Waterman-Storer, 1991). Yu and Thornell (2002) suggested that the increased staining of actin and desmin following biopsies from soleus muscle in healthy male reflects an increased synthesis of these proteins as part of an adaptation process after unaccustomed eccentric exercise.

Other adaptions include an increased intramuscular connective tissue due to regeneration properties following a damaging bout of eccentric activity which allow for a better dissipation of the mechanical stress in myofibrillar during repetitive eccentric mode and thus limit the eccentric induced muscle damage. To endure this point after a prolonged period of immobilization Lapier and colleagues (1995) demonstrated that an increase in muscle connective tissue content in rat's extensors digitroum longus muscles decreased the injury response to subsequent a damaging bout eccentric muscle actions. Cellular adaptation according to McHugh, Connolly, Eston and Gleim (1999) is supported by three possible mechanisms in the contractile machinery including longitudinal addition of sarcomeres, adaptation to maintain excitation – contraction (E–C) coupling and adaptation in inflammatory response. Morgan and Allen (1999) suggested that addition of sarcomeres in series, resulting in shorter average sarcomere length and possibly also of more uniform length and thereby limiting myofibrillar destruction. Subsequently, the sequence of impairment excitation – contraction (E–C) coupling may prevent (McHugh, 2003).

These attenuated ultrastructural disruption alter inflammatory response to decrease in serum CK activity after the second exercise bout. In agreement to this, Stupka and colleagues (2001) have shown that cellular adaptations to eccentric knee extension exercise are associated with attenuated serum CK activity and, potentially, an increase in the activity of the ubiquitin proteosome proteolytic pathway. Protective effect conferred by repeated bout effect can last up as early 24 hours (Meneghel et al., 2013) up to 6 months apart depend upon the exercise mode, intensity, duration, muscles involved, and rest intervals (Nosaka et al., 2001).

The repeated bout effect has been found to increase with the number of eccentric bouts performed, although the greatest relative effects are achieved after the first bout (Chen et al., 2009) paradoxically, the initial bout of eccentric exercise does not have to cause appreciable damage in order to confer a protective adaption (Brown et al., 1997). After all, it is plausible that the extent of the "repeated bout effect" is related to the intensity of muscle damage (Rowlands et al., 2001). In this regard, Nosaka and colleagues (1991) suggested that the greater the muscle damage induced in an initial bout of eccentric exercise, the greater the resulting adaptations and protection against a subsequent bout of eccentric exercise.

Prophylactic Effect of Repeated Bout Effect

Physiological adaptations of muscle damage after second bout in response to eccentric contraction depends on exercise intensities in which are determined by relative exercise program (Féasson et al., 2002). Decreases in muscle soreness level, and plasma creatine kinase (CK), myoglobin (Mb) and lactate dehydrogenase (LDH), analgesic and faster recovery time have occurred following diverse ECC exercise modalities however they are temporary as one element of related damaged muscle diminishes yet other elements still is remained. Byrnes et al. (1985) for example stated that when a single bout of 30-min of downhill running (-10 degrees slope) reaped after 6 weeks, generated the same of muscle soreness and serum (CK), and Mb in subjects. Hortobagyi et al. (1998) also reported while one hundred eccentric knee extensions impaired neuromuscular function and disturbed myofibrillar array, the same bout repeated one week later did not alter neuromuscular performance, but did cause myofibrillar disruption. It is unlikely thus to thoroughgoing adaption in terms of "repeated bout effect" from induced muscle damage. Debate exists concerning to avoid of RBE to maintain all aspects of muscle damage coming after a second bout of the same eccentric exercise for related clinical properties that it may produce. Nonetheless, in reality reduced indicators of muscle damage is a possible event but not always guaranteed although putative repair and regeneration phase following eccentric muscle damage take place as yet they are temporary (Byrnes et al., 1985; Hortobagyi et al., 1998). This can be a favorable condition for individual in whom engaged with ECC in their way of life. For instance, Selkow et al. (2013) has been shown circulatory responses were altered after eccentric exercise induced muscle damage where blood volume and flow both significantly increased after exercise bout that lead to an enhancement for hypertensive in which blood flow is blunted in their vessel.

Elsewhere, Paschalis et al. (2011) have found improved blood lipid profile as health risk factors after bouts of eccentric exercise that could be exploited to enhance glucose delivery and uptake by skeletal muscle in which prove to be of benefit in the diabetic patient. Thus even though, muscle damage following an eccentric exercise elevates pain and inhibits short-term recovery of muscle function, it may result in a positive healing process in body (Connolly et al., 2003) as it previously has been proven ''no pain, no gain'' (Lee, et al., 2001).

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ETIOLOGIJA MIŠIĆNOG OŠTEĆENJA INDUCIRANA EKSCENTRIČNIM VJEŽBANJEM I U PONOVLJENIM PRODULJENIM UČINCIMA

Sažetak

Ekscentrične vježbe (ECC) karakterizira oštećenje mišića i sposobnost mišića da se prilagodi na štetu koja dolazi poslije. Ova adaptacija iz "ponovljenog efekta (RBE)", pri čemu je mišić manje sklon budućem oštećenju. Tipični znakovi ovog zaštitnog učinka su brži oporavak, manje upalni odgovor i manji razvoj odgođenog početka boli mišića jer slijedi drugačije živčane, mehaničke i stanične prilagodbe u nizu. Međutim, trajanje zaštitnog učinka varira diljem mišićne skupine kao što pokazuje npr. aktivnost od 30-min trčanja u spustu (10 stupnjeva nagiba) ostvareno nakon 6 tjedana, desila se ista mišićna bola i serum kreatin kinaze (CK), i mioglobina kod subjekata. Razmišljanja i rasprava postoje da bi se izbjeglo RBE i zadržali svi aspekti oštećenja mišića koji dolaze nakon druge aktivnosti istih ekscentričnih vježbi koje je moguće proizvesti. Ipak, u stvarnosti smanjeni pokazatelji oštećenja mišića su mogući događaji, ali ne uvijek zajamčeni, iako navodno popravak i faza regeneracije sljedećeg ekscentričnog oštećenja mišića će se privremeno održati. U tom smislu, istraživači koriste izraz 'ekscentrično' s pretpostavkom da je protok krvi ili povećava dostupnost tekućina kako rezultira mikro-oštećenjima mišićno-koštanog sustava što povećava volumen krvi kod hipertenzivnih ili dostupnosti glukoze kod dijabetičnih bolesnika. Dakle, iako oštećenja mišića nakon nastupa ekscentrične vježbe povećava bol i sprječava kratkoročni oporavak funkcije mišića, može rezultirati u pozitivnom procesu ozdravljenja u tijelu, kao što je ranije pokazano ''na pain – no gain''.

Ključne riječi: *ekscentrična vježba, oštećenje mišića, mišićna adaptacija*

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