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Review of the Repeated Bout Effect in Trained and Untrained men

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Abstract High intensity exercise and especially eccentric contractions, produce muscle damage that can be demonstrated by indirect markers such as changes in neuromuscular performance, increased intramuscular proteins in the bloodstream, and delayed onset muscle soreness (DOMS). On the other hand, when exercise sessions are performed repeatedly there is a reduction in the responses of indirect markers of muscle damage, a phenomenon known as the protective effect (repeated bouts effect; RBE). Among the adaptive mechanisms involved in RBE are neural, cellular and mechanical adaptations. However, data related to these adaptations are not yet conclusive. A significant range of studies that evaluated the RBE employed subjects untrained and/or unaccustomed to physical exercise with a few research studies from the trained population, which already have chronic neuromuscular adaptations. Thus, the present review addresses the issue by bringing up to date information about the protective effect both when performed by untrained and trained populations. The data indicate that there is a reduction in the magnitude of indirect markers of muscle damage when the trained population conducts repeated exercise sessions compared to untrained and/or sedentary individuals.Among the adaptive responses involved, the neural theory appears to be the main mechanism involved in mitigating the indirect markers of muscle damage.

Keywords Eccentric Exercise, Muscle Damage, Repeated Bout Effect (RBE)

1. Introduction

Muscle damage resulting from a session high intensity exercise and/or a high volume of eccentric exercise is characterized by disruptions of ultrastructural sarcomeric proteins, changes in the extracellular matrix and basal lamina, degradation of muscle proteins, inflammation, and a release of intramuscular proteins in the bloodstream[1,2,3,4,5,6]. The extent of muscle damage depends on the manipulation of acute variables such as intensity, volume, rest intervals, muscle action, contraction velocity, range of motion, and exercise order[7]. A greater magnitude of effects is observed with exercises that emphasize eccentric muscle actions of high intensity or volume[8].

From a functional perspective and perception, muscle damage can promote changes in neuromuscular performance, delayed onset muscle soreness (DOMS), and increased intramuscular proteins in the bloodstream. These symptoms may be present for several days after a workout involving resistance training[4,9,10]. However, a single session of eccentric exercise can protect skeletal muscle and decrease the magnitude of indirect markers of muscle damage when it is repeated. This phenomenon is known in the literature as the protective effect or the repeated bout effect (RBE)[11,12]. The exact mechanism occurring in the RBE is not fully understood; however, neural, cellular, and mechanical adaptations have been used to explain the possible adaptive mechanism of muscle protection[11,12,13]. Regarding the detection of surrogate markers in untrained men, the presence of the protective effect was retained up to six months following the first session of eccentric isokinetic exercise. However, this effect was decreased by the ninth month and absent after 12 months[14]. Furthermore, as few as two maximal voluntary isometric contractions may confer a protective effect on muscle damage markers after an eccentric exercise bout in untrained men.

These findings are also observed in trained individuals and athletes but with a lower magnitude of symptoms resulting from muscle damage when compared to untrained individuals[10]. However, few studies have examined this effect with trained individuals. Therefore, the present review aims to provide updated information on the protective effect both when performed by untrained and trained populations. We searched and selected articles indexed in PubMed and HighWire with relevance to the theme by using the keywords: muscle damage, RBE, and eccentric exercise.

1.1. Theories and the Adaptive Mechanisms of RBE

RBE refers to the protective effect of a single training

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session with an eccentric component observed in subsequent exercise sessions[11,15,16,17,18,19,20,21]. The RBE is characterized by rapid recovery mechanisms following muscle damage. That is, the is unaffected muscle strength and power, restrictions in range of motion, the sensation of DOMS, and plasma concentrations of cytosolic proteins such as creatine kinase (CK), lactate dehydrogenase (LDH), troponin I, myoglobin and fragments of myosin heavy chain (MHC) are found in high concentrations in the bloodstream post-workout[22,23]. RBE is also characterized by decreased muscle swelling, increased discrete myoglobin (Mb)[5], and lowest levels of blood markers of muscle damage for CK and prostaglandin (PGE)[5,51] Muscle damage after a session of high-intensity eccentric exercise is characterized by specific ultrastructural disruption, protein degradation, inflammation, and increased cytoskeletal proteins in the bloodstream[2,4].

Theories of adjustments related to RBE are being described order neural, cellular and mechanical mechanics, numerous studies have shown a clear and sustained response RBE by all of their theories, however, when presented in isolation there is no consensus among the theories proposed or their actions individual.

According to McHugh, Connolly, Eston and Glein,[11], the first theory of neural adaptation is proposed which is supported by two possible mechanisms. These include increasing the recruitment of slow-twitch motor units and a greater activation in the number of motor units[12].

Changes in motor unit activation between repeated bouts were examined by electromyography (EMG) in humans [24,25]. Theoretically, an increase in the amplitude of the EMG relative to torque production in the repeated session indicates contractile stress redistribution among a large number of fibers. This effect is evident with eccentric strength training[26,27]. Conversely, a decrease in the frequency of the EMG signal during the repeated session theoretically indicates a change in the recruitment of motor units for slow contractions and/or an increase in the synchronization of the motor units. There was no evidence of a change in EMG amplitude between repeated sessions in eccentric exercises with the hamstring muscles[25] and tibialis previous muscles[24]. Warren et al.[24] reported that the median frequency was decreased in the repeated session for the tibialis anterior muscle and this effect was attributed to increased recruitment of slow-twitch motor units. Alternatively, this effect could be attributed to the increased synchronization of the motor units. This effect would be indicative of a neural adaptation to a single bout of eccentric exercise.

Although Warren's[24] results are the first direct evidence of a neural adaptation for a single eccentric exercise session, it is evident that the effect of repeated sessions can occur independent of neural adaptations[28,29]. The RBE has been demonstrated in electrically stimulated eccentric contractio ns in rats performed on the tibialis anterior muscles[28] and in human elbow flexors[29].

Black e McCully[30], evaluated the importance of neural adaptations by comparing the RBE caused by voluntary eccentric contractions and contractions resulting from electrical stimulation. Eighty eccentric contractions were performed with the knee extensors with a separation of 7 weeks between sessions. The RBE was observed after exercise and the magnitude of the electrical stimulation was similar to the observed RBE in the performance of voluntary contractions. This suggests the RBE is not related to changes in muscle recruitment and is potentially related structural changes in the muscle. Corroborating this study, Kamandulis et. al[65] compared the RBE changes in the level of voluntary muscle activation and activation by electrical stimulation (10 sets of 12 maximal voluntary knee extensor contractions[MVC]) with a two-week interval between the first and second session. The results indicate that the RBE following eccentric exercise reduces muscle damage but does not influence the level of voluntary activation.

The second theory is the cellular according to McHugh, Connolly, Eston and Glein,[11], and is supported by three possible mechanisms by a longitudinal addition of sarcomer es, the adaptation to maintain the excitation-contraction (EC) coupling, the adaptation of the inflammatory responses resulting from eccentric contractions[12], increased protein synthesis, increased stress proteins, and removal of fibers susceptible to RBE[32]. Proske & Morgan[8] suggests that the increase in sarcomeres in series is probably indirectly supported by a change of the optimal angle for a longer muscle length which is attached to the RBE. Chen[19] showed that the RBE is induced by the change in the ideal angle for a longer muscle length. However, it cannot be explained by an increased number of sets in the sarcomere RBE.

Morgan[33] demonstrated that muscle damage is irreversible due to the tension during the sarcomere eccentric contractions and, in particular, muscle contractions at lengths on the descending limb of the length of the voltage curve. Numerous animal studies[34,35,36] and voluntary contraction studies in humans[37,38] have shown that the length of the muscle during eccentric contraction is the critical factor in determining the extent of muscle damage. Consequently, large contractions of muscles result in large elongated symptoms of damage.

Morgan[33], based on the theory of muscle damage tension sarcomere provided that the results of the repair process of increasing the number of sarcomeres connected in series and this serves to reduce the voltage during an attack sarcomere repeated thereby limiting the disruption myofibril.

Theoretically, the loss of strength after a session of eccentric exercise could be due to an inability to voluntarily activate motor units secondary to pain or injury. There may also be physical disruptions in the structures that generate power, or a failure to activate intact structures in the generation of force within the muscle fibers (EC coupling)[39,40] that support the voluntary activation of the motor unit. Warren et. al.,[41] suggests that the loss of

strength appears to be the combination of physical damage and a decrease in EC coupling.

The initial damage in eccentric contractions is due to a mechanical disruption of myofibrils. This initial damage triggers a local inflammatory response that leads to an exacerbation of damage before signs of recovery. These events can be referred to as primary and secondary damage. An attenuated inflammatory response to repeated sessions may reflect an adaptation to avoid the proliferation of a mechanical disruption of myofibrils. The reduction of the inflammatory response for a single session of repeated eccentric exercise may simply reflect the fact that there was a disruption mechanical in the series repeated and therefore a lesser degree of stimulation in the inflammatory response.

Mchugh & Pasiakos[42] reports that a single session of eccentric exercise is dependent on the length of the muscles where the eccentric contractions were performed. Ten individuals underwent two sessions of 120 eccentric contractions of knee flexion, separated by two weeks. The results confirm that symptoms of muscle damage are highly dependent on the length of the muscle exercised and demonstrate that the RBE is dependent on the muscle length. Other studies have shown that with even low repetitions (10, 6, or even 2) of maximal eccentric contractions of the elbow flexors are sufficient to confer a protective adaptation to a subsequent session of 24 or 50 maximal contractions. Therefore, the lack of a protective effect can be attributed to the difference in length between the series muscle rather than a lack of symptoms after the initial session.

A third theory is mechanically second McHugh, Connolly, Eston and Glein,[11] and based on the mechanisms of increased stiffness, in both dynamic and passive conditions [12].

The fatigue properties of typical material flexible subjected to a cyclic tensile load has also been described to promote muscle damage,[43] represents a structural failure caused by the accumulated tension and is distinct from the fault caused by applying a voltage that exceeds the tensile strength[43]. A flexible property by and flexible traction experiences plastic deformation before failure, in contrast to a rigid property where no deformation occurs before failure. Skeletal muscle tissue is flexible and its behavior during repeated eccentric contractions is consistent with the elements of fatigue[43]. Another important factor is the intermediate filament where the length-tension curve is determined by overlapping myofilaments that is a function of the sarcomere length[44,45]. During the stretch of the sarcomere, eccentric contractions are highly non-uniform, with some maintaining sarcomere length, while others are stretched beyond the point of filament overlap[46,33] leading to a process known as overflow sarcomere[33]. When a sarcomere is stretched beyond overlapping filaments ("popped") it is placed in increased reliance on passive structures to keep strain series as the number of series shortened sarcomeres. Morgan[33] reported that muscle damage is not a result of the real *popping* (as it was thought to occur in most eccentric contractions), but is thought to be caused by the cyclic stress placed on the supporting passive structures by continued eccentric contractions following 'popping'. Such structures are represented by a presence of the proteins desmin, vimentin, and sinemina[47,48], whose functions are to maintain the structural integrity of the sarcomeres in series and in parallel[47,49].

Transmission of power within skeletal muscle can be increased by the intermediate filament system[49]. Street [50], demonstrated that the intermediate filament system provides a link between damaged areas and to maintain the power output standard. While this may be beneficial in maintaining the strength during the production of eccentric exercise, the final effect may be to raise subsequent damage. When sarcomeres are stretched beyond the myofilaments overlapping the intermediate filament system, this must bear the burden of repeated charges and subsequent contractions will result in mechanical failure of the intermediate filament system.

1.2. Muscle Damage and RBE

The symptoms of muscle damage were determined after a recovery period following the first session with both concentric and eccentric contractions. The mechanism of this effect is still has an uncertain duration. Many authors have investigated the effect after the first session and the period varies from 24 hours up to longer than 6–9 months.

Its benefits are found in short periods of 24 hours[52] and long periods of up to six months. Nosaka et. al[53] and Mair et. al[17] investigated the adaptation to eccentric training that occurred within 4 to 13 days after a training session. Twenty-two male subjects were divided into two groups (Group A had a four-day interval between sessions; Group B had sessions 13 days apart). Each group held a session of eccentric training (7 sets of 10 maximal eccentric contractions of the quadriceps) with the right leg and left leg acting as controls for each other. The level of reported DOMS after the training sessions was analyzed using a numerical scale (scale with 1 = no pain and 10 = maximum pain). The results showed that 24-48 hours after the initial training session, higher levels of pain were reported (7.5 to 8). The pain decreased over the following days. Furthermore, the muscle pain was achieved at lower levels in Group A compared to the first exercise session (5), unlike group B, which had no manifestation of pain. This suggests that after eccentric exercise, even when the recovery period between sessions is not enough (based on the study of 4 days), there is a protective effect identified by a reduction in DOMS after a second session of eccentric training.

Sorichter et. al (1997)[54] using methodology similar to that of Mair et. al (1995) investigated the effect of three frequencies of different exercise sessions during the initial phase of eccentric training. They analyzed muscle strength, muscle soreness, CK, fragments of myosin heavy chain (MHC) type I fibers, and fragments of troponin before and 4 and 7 days after the first training. The same procedure was applied after the second training session. Thirty male subjects, and were divided into three groups (A, B and C).

Group A performed exercise sessions once a day for five days, group B sessions were conducted twice weekly over a two-week period, and group C had sessions three times a week over a three-week period. Results show that markers of injury were mitigated after the last training session, particularly in groups A and B. The RBE also occurred in group C; however, pain levels remained elevated for DOMS after the second training session. This suggests that during the initial phase of eccentric training, one or two days per week are sufficient to maintain the muscle adaptation, while exercise sessions three times per week, can reduce its effects a more extreme. Saka et. al[55] compared in their study, the performance of different muscle groups and reported that the magnitude of muscle damage is greater and the recovery is slower after maximal eccentric exercise of the knee flexors and knee extensors in sedentary men. Chen et al. (2011)[56] suggested that when doing workouts with the arm and leg muscles, muscle damage is more likely in the leg muscles, but knee flexion is more susceptible to muscle damage in relation to knee extension.

2. The Indirect Markers of Muscle Damage and RBE - Individuals Trained x Untrained

Many studies have examined eccentric elbow flexor exercises and its magnitude of attenuating muscle damage that occurs in the second session[4,18,57,58,59,60]. However, other muscle groups such as the knee extensors and flexors corroborate the RBE effects[56,61,62,63]. Among the analyses are neuromuscular markers, biochemical indicators, and subjective scales. These articles will be discussed in the following section.

Starbuck & Eston[64] reported the protective effect of exercise induced elbow flexor muscle damage on the contralateral arm. Fifteen men separated into two groups performed two sets of 60 eccentric contractions (30 degrees per second) with an interval of 2 weeks and were measured for strength, muscle soreness, and arm angle at rest (RAA), at baseline and at 1, 24 and 48 h post-exercise. The degree of strength loss was attenuated ($p < 0.05$) in the ipsilateral arm after the second eccentric exercise session (-22 cf. -3% for sessions 1, 2 and 24 h, respectively). Loss of strength after eccentric exercise was also attenuated ($p < 0.05$) at 24 hours from the contralateral group (-30 cf. from 13% for session 1 and 2, respectively). Muscle soreness (≈ 34 cf. 19 mm) and changes in RAA (≈ 5 cf. 3%) were also lower after the second session of eccentric exercise ($p < 0.05$) but there was no difference in the overall change in these values between groups. Median frequency (MF) was reduced by 31% between sets with no difference between groups. Data support that the RBE is transferred to the untrained limb. A similar reduction in MF between sets for the two groups provides evidence for a neural adaptation. Corroborating these data, Kamandulis et. al,[31] compared the possible changes in the level of muscle activation between sessions 1 and 2 of eccentric exercise performed with an interval of two weeks (i.e., RBE). Ten physically active men who performed 10 sets of 12 maximal voluntary contractions (MVC) of eccentric exercise with the knee extensors during movements performed at a constant speed of 160 degrees per second. Changes in voluntary and electrically-evoked torque in concentric contractions and/or isometric contractions were evaluated at the following times: pre-exercise, 2 min, 1 h, and 24 h after each eccentric exercise. At the same time, points to the voluntary activation were quantified by the superimposed electrical stimulation technique. DOMS and plasma CK activity were determined 48 h after eccentric exercise. The results showed that the decrease in eccentric peak torque was linear throughout the exercise protocol. At the end of series 1 and 2 torque was significantly reduced by 27.7 ± 9.1 (Nm) and 23.4 ± 11.2 (Nm), respectively, with no difference between sets ($p > 0.05$). At 24 hours post-exercise, a lower reduction ($p < 0.05$) in MVC (17.8 ± 5.4%) and electrically-evoked (16.7 ± 4.6%) isometric torque was observed for session 2. In contrast, there was no statistically significant difference in voluntary activation deficits between the two sessions. We conclude that the results indicate that the RBE induced with eccentric exercise appears to reduce muscle damage, but does not influence the level of voluntary activation. In contrast to these data, Falvo et. al.,[65] study supports the hypothesis that RBE is absent in men trained with resistance exercises. A lack of significant differences was observed between groups for all other markers of muscle damage with the exception of the effect observed for the perception of DOMS. In the absence of an RBE for any variable analyzed, it is possible that adjustments associated with the RBE are already present in the strength of resistance-trained men.

Chan, Newton e Nosaka,[66] investigated whether a repeated series of various settings would result in different force production during eccentric exercise and a difference in magnitude of muscle damage after the first and second exercise sessions. Ten untrained men underwent two sessions of eccentric exercise of the elbow flexors in each arm (4 sets in total) with sessions separated by 4 weeks. The results showed that the maximal voluntary contraction strength, range of motion (ROM), cross-sectional area of the biceps, and DOMS changed significantly ($p < 0.05$) after exercise. However, there were no significant differences between the series and 3 x 10 and 10 x 3, the changes in the parameters analyzed following 20 x 3 were similar between the arms, except for range of motion (ROM). No significant differences in changes in all measures, except ROM, were evident when compared to the first and second grades. In conclusion, these results showed that changing the setting of the number of repetitions had little effect on muscle damage. However, Chen & Nosaka,[60] compared the changes in indirect markers of muscle damage after eccentric exercise of the elbow flexors with different eccentric actions. Seventy male athletes were divided into 6 groups (n = 10 per group) based on the number of shares for the first eccentric (ECC1) and second eccentric session (ECC2). Individual groups (30,

50, and 70) underwent only ECC1, and the group repeated the session (30-30, 50-50, 70-70) performed 3 days after ECC2 and ECC1. Another 10 male athletes performed a different number of eccentric actions ECC1 (30) and ECC2 (70) separated by 3 days (30-70). The results showed that there were no significant differences among the four groups studied but the maximal isometric force (MIF) decreased significantly ($p<0.01$) to approximately 60% of pre-exercise levels immediately after ECC1 and recovery of about 70% based on three ECC1 days later for all groups, with no significant difference ($p > 0.01$) between groups. Although there was a small additional reduction ($p<0.05$) immediately after MIF ECC2 groups to 100% (56.1%), 90% (54.5%) and 80% (51.2%), MIF was recovered to the same level as the control group after ECC2 for all groups. The following day also showed decreases in MVC after ECC1 were significantly lower ($p<0.05$) by 30 eccentric actions compared to 50 and 70 eccentric actions. There were no significant differences between groups 50 and 70 ($p = 0.24$) or with groups of 50-50 and 70-70 ($p = 0.26$). Immediately after ECC2, MVC decreased significantly ($p < 0.05$) in groups of 30-30 (5.3%), 30-70 (12.5%), 50-50 (8.2%), and 70-70 (9.1%) and the magnitude of the decrease of the MVC 30-30 for the group was significantly ($p < 0.05$) lower than the other groups. Despite the fall in the post-ECC2 MVC, MVC was recovered to the pre-ECC2 the next day and no significant differences between 30-30 and 30 ($p = 0.31$), 50-50 and 50 ($p = 0.26$), and 70 and 70-70 groups ($p = 0.17$) were evident. Changes in MVC after ECC2 were not significant ($p = 0.91$) between groups of 30-30 and 30-70. This suggests that recovery from eccentric exercise is not delayed by a second session of eccentric exercise regardless of the number of eccentrics actions. In conclusion, the elbow flexors can perform high-intensity eccentric exercise in the early phase of recovery from the initial session and sustain no further initial damage by performing a subsequent session three days after the first. In another study, Chen and Nosaka,[67] reported that the second session of eccentric exercise performed three days after the initial session exacerbated muscle damage and retarded recovery. Fifty-one athletes performed 30 eccentric actions of the elbow flexors using 100% maximal isometric force (MIF) with an elbow joint angle of 90 degrees (ECC1). Three days after ECC1, all subjects except the control group (n = 12) performed the second attack (ECC2) with maximum intensity of 100% (n = 12), 90% (n = 13), or 80 % (n = 14) of ECC1. Changes in all measures for nine days following ECC1 were compared between groups with repeated measures. All measurements changed significantly after ECC1; however, there were no significant differences between groups for any of the measures. These results suggest that it is possible for athletes to complete the second session when the intensity is reduced by 10-20% from the initial session. There were no significant differences between the control group and the other groups. This indicates that the second session of eccentric exercises performed three days after the initial session did not exacerbate muscle damage and slow recovery regardless of the intensity of the second session. It is concluded that the elbow flexors can perform high intensity eccentric exercises during the initial phase of recovery of the initial session and that this does not induce an increase in muscle damage when performing a second meeting three days after the first.

Howatson & Someren,[58], study corroborates Chen & Nosaka,[60], who investigated the first contralateral RBE expressed after a single session of maximal eccentric muscle contractions and secondly, for comparing the magnitude of any protective effects to the ipsilateral control. Sixteen men performed 45 repetitions of maximal eccentric contractions of the elbow flexors. The ipsilateral group (IL, n = 8) repeated the exercise using the same arm and the contralateral group (CL, n = 8) repeated the exercise using the contralateral arm 14 days later. Serum CK, muscle pain, MVC, and range of motion (ROM) were significantly attenuated in the series repeated for IL. CL also showed a significant reduction in the series repeated for CK, muscle pain, and MVC. Despite significant attenuation of the dependent variables in both groups, the change in magnitude was lower in the CL for IL CK, pain, MVC, and ROM. These findings demonstrate an RBE effect exists in the contralateral limb after a single maximal eccentric exercise session; however, the magnitude of protection in the contralateral limb is smaller than that manifested in the ipsilateral limb. The apparent RBE in the contralateral arm observed in this investigation is predominantly mediated by neural mechanisms.

Howatson, Someren e Hortobágyi,[59] hypothesized that an eccentric exercise session with a high or low volume protects against muscle damage after a high volume in the series and subsequent adaptation that would be attributable to neural changes, regardless of the volume of the initial exercise. Sixteen men performed either 45 (ECC45) or 10 (ECC10) maximum eccentric contractions using the elbow flexors. This was followed by a session ECC45 two weeks later. All time-dependent variables showed a significant effect ($p < 0.001$). There was a significant effect ($F1, 4 = 23.1$, $p < 0.001$), indicating a higher CK efflux in session 1 compared with session 2. DOMS was higher in session 1 than in session 2 ($F1, 14 = 14.4$, $p = 0.002$) as observed with a post hoc analysis showing DOMS to be significantly higher in group 1 than for session 45ECC 10ECC 45ECC group and also higher in group 45 and group-ECC 45ECC 10ECC 45ECC in session 2 ($p < 0.001$). Interestingly, the 45ECC-45ECC group showed the greatest reduction in DOMS from session 1 to session 2, corresponding to ~ 70% MVC. Furthermore, the group 45ECC-45ECC showed a 13.2% difference between series 1 (fall of 18.3%) and 2 (5.1% reduction). A significant attenuation of the ROM 2 in the attack was observed ($p = 0.037$). There were no differences among groups at median frequency series 1 and 2 ($p < 0.001$). A session ECC45 maximum eccentric exercise induced more damage than an initial attack ECC10 maximum eccentric exercise; however, both confer protection from subsequent ECC45 maximum eccentric contractions which are attributed, at least in part, to a change

in the content of frequency EMG.

Nosaka et al[14] showed that the initial decreases in maximal isometric strength increases with increasing numbers of eccentric actions 2 (20%) 6 (33%) and 24 (56%). In a study with 34 students, muscle damage can be the result of a loss of strength not only because the fatigue strength was not recovered within 24 h after exercise. It is also possible that there are some differences in adaptive responses to RBE when comparing the different muscle groups and joint movements, something recently described for a single session of eccentric exercise[56]. Starbuck & Eston[64] reported that the degree of strength loss ($p < 0.05$) in the ipsilateral group after the second session of eccentric exercise was -22% cf. -3% for session 1 and 2 at 24 h, respectively. The loss of strength after eccentric exercise was also attenuated ($p < 0.05$) at 24 hours compared to the contralateral group (-30 cf. 1 and 13% for the second session, respectively). Muscle pain (34 cf ≈ 19 mm) and changes in RAA (≈ 5 cf. 3 %) were also lower after the second attack of eccentric exercises ($p < 0.05$), but no difference in the overall change in these values between groups. A similar reduction in MF between sets for the two groups provides evidence for a neural adaptation.

Bloomer et. al[69] demonstrated that an effect of time was observed for CK activity ($p < 0.0001$) together with the peak values 24 hours post-exercise (317 ± 29 U • L^{-1}) relative to pre-exercise (139 ± 29 U • L^{-1}). Creatine kinase activity was significantly higher than the pre–exercise values at 24 and 48 hours post-exercise ($p < 0.05$) confirming other studies. The study by Falvo et. al,[65], supports the hypothesis that RBE is absent in resistance-trained men. This is further supported by the lack of significant differences observed between all groups for other markers of muscle damage with the exception of the effect observed for muscular pain perception. In the absence of any RBE measured variable, it is possible that adaptations associated with RBE are already present in the exercises of resistance force-trained men[70].

Contrasting these studies[71] demonstrated that both CK and DOMS had no significant differences in RBE, with an interval of two days between the first session and the second. Nosaka & Newton[4] showed that nine male students with little or no strength training background performed the same eccentric exercises two days after the initial series. The results showed that it did not affect the recovery of muscle function and activity of CK plasma activity and the development of DOMS. Similarly, Howatson & Someren [58] and Eston et. al[61], reported that the second session of maximal eccentric exercise of the elbow flexors performed three days after the first did not affect changes in indicators of muscle injury. It should be noted that the exercise intensity in these studies was between 50 and 80% of maximum power, and the present study used an eccentric exercise intensity higher for the first (100%) and second session (80-100%). ECC1 resulted in significant reductions in the MIF and ROM, increasing the CIR, the thickness of muscle strength, blood markers of muscle damage (CK, LDH, Mb), and development of DOMS for all groups. These changes were similar to results of previous studies with a similar exercise protocol to this study. It should be noted that the study subjects were athletes and used a high load. Nosaka & Newton[4] investigated concentric and eccentric contractions of the elbow flexors by applying a load of 50% of 1 RM (3 x 10 reps) for both modes of contraction and observed a significant increase in delayed onset muscle pain following eccentric contractions. Nosaka & Newton[4] also showed that submaximal concentric contractions (50% of maximal isometric force) produce changes in surrogate markers of damaged musculature (DOMS and CK). These changes were less pronounced than those found in maximal eccentric contractions, yet the changes were still evident five days after training with this intensity.

Paschalis et. al[71] reported no significant difference between DOMS with high intensity (12 sets of 10 repetitions of maximal eccentric contractions) and low intensity (continuous eccentric contractions at 50% of maximum torque camera) with eccentric exercises of the quadriceps where the total work was the same for the two exercise protocols. These data were also observed by Uchida et. al[72], which confirmed that the intensity of muscle contractions was not an important factor in determining the magnitude of DOMS. Therefore, one may assume that the total volume, rather than the intensity, determines the magnitude of DMT. However, another study by Paddon et. al, [57] used 20 untrained volunteers and found that two days after the first session there was no significant difference between groups ($p > 0.05$). There was a significant reduction of 30% for the average total ECC1, work cam 455 ± 206 J in a range of 324 ± 135 J in six grades. There were no significant changes in total labor or maximum torque during eccentric ECC2.

According to the work of Nosaka et. al,[4], there was a 30% reduction in IEMG and 20% for the MPF during eccentric contractions compared MAX2 with max1, despite the fact that neither IEMG and MPF were not affected during isometric MVCs immediately MAX2 before. Corroborating these findings, Chen[18] reported existence in work levels between EX30 and EX70 groups for MAX2. The group of MAX2 EX70 performed work 32% higher compared to MAX1, while the group performed work EX30 38% lower MAX2. The fact that the group EX70 does not exacerbate symptoms of damage following MAX2 indicates that a protective adaptation.

Nosaka et. al,[4], MIF is less than 60% of pre-exercise and exercise after 5 days. However, showed a faster recovery of MIF over 80% in 5 days after the exercise.

However, when studies are individuals trained in performance, Chen e Nosaka[67] and Falvo et.al[65], reported that the magnitude of change is small without significant differences. Accordingly, Newton et. al.,[8] shares that when comparing the resistance training of men trained and untrained to changes in the most widely used indirect markers of muscle damage after maximum eccentric exercise of the elbow flexors. Fifteen trained men and 15 untrained men were used in this study. All subjects

completed 10 sets of maximum eccentric exercises of six repetition elbow flexors of one arm at a constant speed of 90 degrees per second. Changes in MVC, range of motion, upper arm circumference, plasma CK activity, and DOMS before, immediately after, and 5 days after exercise were compared between groups. The trained group showed significantly ($p < 0.05$) smaller changes in all variables except for DOMS and a faster recovery of muscle function compared with the untrained group. For example, the muscle strength trained group returned to baseline within three days after exercise while the untrained group showed about 40% lower levels than their baseline. These results suggest that trained men are less susceptible to muscle damage induced by maximum eccentric exercise than untrained individuals are. Another approach on RBE was reported by Chen et. al.,[73] who found that little is known about the RBE following more than two sets of eccentric exercise, this study compared responses of muscle damage between four series of eccentric exercises.

Vaczi et.al,[63] reported that sixteen men performed sets of 90 maximal eccentric isokinetic contractions of the knee extensors for 6 consecutive days (B1-B6) and were divided into two groups. One group used a large amplitude motion (120 degrees designated as group L, n = 8), the other group used a small range of movement (60 degrees; group S, n = 8). Peak torque was significantly reduced in both groups, with 25% for the group of large and 14% for the small amplitude motion. However, recent research (Skurvydas et al., 2011) [74] reported that a loss of strength immediately after a session of eccentric exercise with the leg extensor muscles was attenuated by 10% in the second session. Nosaka e et. al[75] and Paschalis et. al ,[71] analyzed the elbow flexors and knee flexors, respectively, for their protocols, while Skurvydas et al.[74] and this study evaluated the knee extensors. Thus, differences may exist in adaptive responses to the RBE when comparing different muscle groups or joint movements, something recently described for a single session of eccentric exercise[56]. Gonzalo et. al,[76] reported the first study to determine the influence of an eccentric training program for young women and RBE. The eccentric training increased the magnitude of muscle pain [70] demonstrated that both DOMS and CK had no significant differences in RBE with an interval of two days between the first and second sessions to corroborate this study. Smith et. al.[70] and Nosaka & Newton[4], showed that performing the same eccentric exercise two days after the initial series does not affect the recovery of muscle function responses of plasma CK and the development of DOMS. Similarly, Paddon-Jones et. al[57] and Chen & Nosaka[67], reported that the second session of maximal eccentric exercise of the elbow flexors performed three days after the first session did not affect changes in indicators of muscle damage. It should be noted that the exercise intensity in these studies was between 50 and 80% of the maximum power, and the present study used the most intense exercises for the first cam (100%) with 80–100% in the second session. ECC1 resulted in significant reductions in MIF and ROM, increasing the CIR, muscle thickness, and the intensity of echo, blood markers of muscle damage (CK, LDH, Mb), and development of DOMS for all groups. These changes were similar to findings from previous studies in an exercise protocol where a similar study was used. Know that the individuals in the study were athletes and used a heavy load. It appears that the long standing time between actions (45 seconds) helped the individuals complete the demanding exercise. The decrease of similar strength immediately after exercise in the present study compared with previous studies that used untrained subjects suggest that exercise was strenuous and unaccustomed even to trained individuals

In another approach to the RBE, Chen, et. al.,[73] reported the results obtained from four exercise sessions over two sets of eccentric exercise. Therefore, fifteen untrained men performed four sessions of 30 maximal isokinetic eccentric contractions of the elbow flexors every 4 weeks. Force maximum voluntary isometric and concentric elbow flexion, range of motion in the elbow joint (ROM), arm circumference, blood markers of muscle damage and muscle soreness were measured before and up to 120 hours after each session. Changes in all the following measures for the second and fourth sessions were significantly lower ($p<0.05$) than those after the first session. The reductions in strength and ROM immediately after the fourth session were significantly lower ($p < 0.05$) than other sections. They concluded that the first session gives greater adaptation, but a new adaptation is induced when the exercise is repeated more than three times. In this line of research on diversity in the responses of RBE, Chen et.al.,[56] reported changes in indirect markers of muscle damage after maximal eccentric exercise, and this would be lower for the knee extensors (KE) and flexor (KF) in comparison with the elbow flexors (EF) and extensors (EE). These data were obtained from a study with 17 sedentary men performing five sets of six maximal isokinetic contractions (90 degrees per second) and eccentric contractions of EF (range of motion, ROM: 90 ° –0 °, 0 = full extension), EE (55 ° –145 °), KF (90 ° –0 °) and KE (30 ° –120 °), with an interval of 4–5 weeks in a counterbalanced order. Regarding the integration of these variables: maximal isometric force and concentric isokinetic best angle, arm circumference, ROM, plasma CK activity, myoglobin concentration, muscle pain, and eco-intensity images from ultrasound B-mode before and for 5 days after exercise, which were compared among the four exercises. All variables changed significantly after EF, EE, and KF exercises, but the exercise did not change the KE ideal angle, arm circumference, and eco-intensity. Compared with KF and KE, EF and EE showed significantly greater changes in all variables with no significant differences between EF and EE. Changes in all variables were significantly higher than for KF or KE. For the same sedentary men, the magnitude of change in the dependent variables after exercise ranged between exercises. The results suggest that the two arm muscles are more susceptible to muscle damage than are the leg muscles, but KF is more susceptible to muscle damage than is KE. The difference in susceptibility of muscle

damage appears to be associated with the use of muscles in daily activities. Corroborating this study, Saka et. al[55] investigated the difference in the magnitude of muscle damage between maximum eccentric exercise of the elbow flexors (EF) and knee extensors (KE). Twelve sedentary male volunteers participated in the study. Range of motion (ROM), peak torque (IPT), DOMS, CK activity, and myoglobin concentration (Mb) were assessed before, immediately after, and at 1, 2, 3, and 7 days after exercise. Total work (TW) during exercise was recorded and corrected by muscle volume (TWC). TWC was higher ($p < 0.01$) for the EF (24[2] joule • cm^{-3}) than for KE (7[0.4] • Joule cm^{-3}). Increased CK at 2, 3, and 7 days ($p < 0.01$) and increased MB in the first, second, third and seventh day were significantly ($p < 0.01$) higher than for KE to EF. The decline in IPT was higher ($p < 0.05$ to 0.01) for EF at all times test compared with KE. The results of this study demonstrate that the magnitude of muscle damage is greater and the recovery is slower after maximal eccentric exercise EF that the KE for sedentary men.

3. Conclusions

The post exercise protective effect has been described to occur in different populations including sedentary individuals, athletes, and individuals with detraining. Such evidence has been observed from the analysis of surrogate markers (neuromuscular performance, subjective perception of DOMS, and increased intramuscular proteins in the bloodstream). However, when individuals are compared, the level relative to trainability of these factors is attenuated regarding both the magnitude and kinetics of the recovery period. However, the vast variability in different forms of protocols employed makes stricter comparisons difficult between various studies.

REFERENCES

[1] Ebbeling, C.B.; Clarkson, P.M "Exercise-induced muscle damage and adaptation." Sports Medicine, v.7, p. 207-234, 1989.

[2] Golden CL, Dudley GA. "Strength after bout of eccentric or concentric actions." Med Sci Sports Exerc, 24 (8): 926-33, 1992.

[3] Sorichter, S., J. Mair, et al. (2001). "Creatine kinase, myosin heavy chains and magnetic resonance imaging after eccentric exercise." J Sports Sci 19(9): 687-91.

[4] Nosaka, K. and M. Newton (2002). "Repeated eccentric exercise bouts do not exacerbate muscle damage and repair." J Strength Cond. Res 16 (1): 117-22.

[5] Kansaki, K, et. al. "The effects of eccentric contraction on myofibrillar proteins in rat skeletal muscle. European Journal Applied Physiology, v. 110, n.5, p 934-952, 2010.

[6] Clarkson, P. M., & Hubal, M. J. "Exercise-induced muscle damage in humans". *Am J Phys Med Rehabil, 81*(11 Suppl), S52-69, 2002.

[7] Brancaccio, P., Lippi, G., & Maffulli, N., "Biochemical markers of muscular damage". *Clin Chem Lab Med, 48*(6), 757-767, 2010.

[8] Bird, SP, Tarpenning, KM, Marino, FE. "Designing resistance training programmes to enhance muscular fitness: a review of the acute programme variables". *Sports Med* 35: 841-851, 2005.

[9] Proske, U., & Morgan, D. L. "Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications". *J Physiol, 537* (Pt 2), 333-345, 2001

[10] Chapman, D., M. Newton, et al. "Greater muscle damage induced by fast versus slow velocity eccentric exercise." Int J Sports Med 27(8): 591-8, 2006

[11] Newton, M. J., Morgan, G. T., Sacco, P., Chapman, D. W., & Nosaka, K. "Comparison of responses to strenuous eccentric exercise of the elbow flexors between resistance-trained and untrained men". *J Strength Cond Res, 22*(2), 597-607, 2008.

[12] McHugh, M. P., Connolly, D. A., Eston, R. G., & Gleim, G. W. "Exercise-induced muscle damage and potential mechanisms for the repeated bout effect". *Sports Med, 27*(3), 157-170, 1999

[13] McHugh, M. P. "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*(2), 88-97, 2003.

[14] Nosaka, K.; Aoki, M. S. "Repeated bout effect: research update and future perspective". Brazilian Journal of Biomotricity, v. 5, n. 1, p. 5-15, 2011.

[15] Nosaka, K., Sakamoto, K., Newton, M., & Sacco, P. "How long does the protective effect on eccentric exercise-induced muscle damage last"? *Med Sci Sports Exerc., 33*(9), 1490-1495,2001.

[16] Clarkson, P. M., K. Nosaka, et al. "Muscle function after exercise-induced muscle damage and rapid adaptation." Med Sci Sports Exerc 24(5): 512-20, 1992

[17] McHugh, M. P. and S. Pasiakos (2004). "The role of exercising muscle length in the protective adaptation to a single bout of eccentric exercise". Eur J Appl Physiol 93(3): 286-93, 2004.

[18] Mair, J., M. Mayr, et al. "Rapid adaptation to eccentric exercise-induced muscle damage. " Int J Sports Med 16(6): 352-6, 1995.

[19] Chen, T. C. "Effects of a second bout of maximal eccentric exercise on muscle damage and electromyographic activity." Eur J Appl Physiol89(2): 115-2, 2003.

[20] Chen T.C, Nosaka K, Sacco P. "Intensity of eccentric exercise, shift of optimum angle, and the magnitude of repeated-bout effect". J Appl Physiol. ; 102:992-9, 2007.

[21] Connolly DAJ, Reed BR, Mchugh MP. "The repeated bout effect: a central or local mechanism?". J Sports Sci Med 3: 80-86, 2002.

[22] Skurvydas, A., M. Brazaitis, et al. "Repeated bout effect is not correlated with intraindividual variability during muscle-damaging exercise." J Strength Cond Res 25(4):

1004-9, 2011.

[23] Brown SJ, Child RB, Day SH, et al. "Exercise-induced skeletal muscle damage and adaptation following repeated bouts of eccentric muscle contractions". J Sports Sci; 15: 215-22, 1997.

[24] Willoughby, D. S., B. McFarlin, et al. "Interleukin-6 expression after repeated bouts of eccentric exercise." Int J Sports Med 24 (1): 15-21,2003.

[25] Warren, G. L., K. M. Hermann, et al. "Decreased EMG median frequency during a second bout of eccentric contractions." Med Sci Sports Exerc 32(4): 820-9, 2000.

[26] McHugh, M. P., Connolly, D. A., Eston, R. G., Gartman, E. J., & Gleim, G. W. "Electromyographic analysis of repeated bouts of eccentric exercise". *J Sports Sci, 19* (3), 163-170, 2001.

[27] Hortobagyi, T., J. Barrier, et al. "Greater initial adaptations to submaximal muscle lengthening than maximal shortening." J Appl Physiol 81(4): 1677-82, 1996.

[28] Hortobagyi, T., J. P. Hill, et al. "Adaptive responses to muscle lengthening and shortening in humans." J Appl Physiol 80(3): 765-72, 1996.

[29] Sacco, P. and Jones, D. A. "The protective effect of damaging eccentric exercise against repeated bouts of exercise in the mouse tibialis anterior muscle." Exp Physiol 77(5): 757-60, 1992.

[30] Nosaka K, Newton M, Sacco P. "Responses of human flexor muscles to electrically stimulated forced lengthening exercise". Acta Physiol Scand. 174:137-45, 2002.

[31] Black, C. D. and K. K. McCully (2008). "Muscle injury after repeated bouts of voluntary and electrically stimulated exercise." Med Sci Sports Exerc 40(9): 1605-15.

[32] S. Kamandulis, A. Skurvydas, M. Brazaitis, L. Škikas, and J.Duchateau, "The repeated bout effect of eccentric exercise is not associated with changes in voluntary activation," *European Journal of Applied Physiology*, vol. 108, no. 6, pp. 1065–1074, 2010.

[33] NOSAKA, K. Exercise-induced muscle damage and delayed onset muscle soreness. In: Cardinale, M.; Newton, R., Nosaka, K. (editors), Strength and Conditioning: Biological Principals and Practical Applications. Chichester, West Sussex, UK: Wiley-Blackwell, p.179-192, 2010.

[34] Morgan DL. "New insights into the behavior of muscle during active lengthening". Biophys J. 57: 209-21, 1990.

[35] Lieber RL, Fridén J. "Muscle damage induced by eccentric contractions of 25% strain". J Appl Physiol. 70 (6): 2498-507, 1991.

[36] Brooks SV, Zerba E, Faulkner JA. "Injury to muscle fibers after single stretches of passive and maximally stimulated muscles in mice". J Physiol. 488 (2): 459-69, 1995.

[37] Hunter KD, Faulkner JA. "Plyometric contraction-induced injury of mouse skeletal muscle: effect of initial length". J Appl Physiol. 82 (1): 278-83, 1997.

[38] Newham, D. J., D. A. Jones, et al. "Muscle fatigue and pain after eccentric contractions at long and short length." Clin Sci (Lond) 74(5): 553-7, 1988.

[39] Child, R. B., J. M. Saxton, et al. "Comparison of eccentric knee extensor muscle actions at two muscle lengths on indices of damage and angle-specific force production in humans." J Sports Sci 16(4): 301-8, 1998.

[40] McHugh, M. P., Connolly, D A J., Eston, R. G., & Gleim, G. W. "Electromyographic analyses of exercise resulting in symptoms of muscle damage". J Sport Sci. 18: 163-172, 2000.

[41] Saxton JM, Donnelly AE. "Length-specific impairment of skeletal muscle contractile function after eccentric muscle actions in man." Clin Sci. 90: 119-25, 1996.

[42] Warren, G. L., C. P. Ingalls, et al. "Excitation-contraction uncoupling: major role in contraction-induced muscle injury." Exerc Sport Sci Rev 29(2): 82-7, 2001.

[43] McHugh M, Pasiakos S., (2004), The role of exercising muscle length in the protective adaptation to a single bout of eccentric exerciseEur J Appl Physiol 93:286–293.

[44] Warren GL, Hayes DA, Lowe DA, et al. "Materials fatigue initiates eccentric contraction-induced injury in rat soleus muscle." J Physiol, 464: 477-89, 1993.

[45] Gordon AM, Huxley AF, Julian FJ. "The variation in isometric tension with sarcomere length in vertebrate muscle fibers." J Physiol , 184: 170-92, 1966.

[46] Huxley AF. "The origin of force in skeletal muscle." Ciba Found Symp, 31: 271-90, 1975.

[47] Flitney FW, Hirst DG. Cross-bridge detachment and sarcomere 'give' during stretch of active frog's muscle. J Physiol , 276: 449-65, 1978.

[48] Fridén J, Lieber RL. "Structural and mechanical basis of exercise-induced injury." Med Sci Sports Exer, 24 (5): 521-30, 1992.

[49] Waterman-Storer CM. The cytoskeleton of skeletal muscle: is it affected by exercise? A brief review. Med Sci Sports Exerc 1991; 23 (11): 1240-9

[50] Patel T J, Lieber R L. "Force transmission in skeletal muscle: from act myosin to external tendons." Exerc Sports Sci Rev, 1997.

[51] Street S F. "Lateral transmission of tension in frog myofibers: a myofibrillar network and transverse cytoskeletal connections are possible transmitters." J Cell Physiol, 114: 346-64, 1983.

[52] Hirose, L.; Nosaka, N.; Newton, M.; Lavender, A.; Kano, M.; Peake, J.,Suzuki, K. "Changes in inflammatory mediators following eccentric exercise of the elbow flexors." Exercise Immunology Review, v. 10, p. 75-90, 2004.

[53] Chen TC, Hsieh SS. "Effects of a 7-day eccentric training period on muscle damage and inflammation." Med Sci Sports Exerc 33:1732-8, 2001

[54] Nosaka, K.; Sakamoto, K.; Newton, M.; Sacco, P. "The repeated bout effect of reduced-load eccentric exercise on elbow flexor muscle damage". European Journal of Applied Physiology, v. 85, p. 34-40, 2001

[55] Sorichter, S., J. Mair, et al. "Muscular adaptation and strength during the early phase of eccentric training: influence of the training frequency." Med Sci Sports Exerc 29(12): 1646-52, 1997.

[56] Saka, T.; Akova, B.; et. al, "Difference in the magnitude of muscle damage between elbow flexors and knee extensors eccentric exercises." Journal of Sports Science and Medicine 8, 107 – 115, 2009.

[57] Chen, T. C., Lin, K. Y., Chen, H. L., Lin, M. J., & Nosaka, K. "Comparison in eccentric exercise-induced muscle damage among four limb muscles." *Eur J Appl Physiol, 111*(2), 211-223,2011.

[58] Paddon-Jones, D., Muthalib, M., & Jenkins, D. "The effects of a repeated bout of eccentric exercise on indices of muscle damage and delayed onset muscle soreness." *J Sci Med Sport, 3*(1), 35-43, 2000.

[59] Howatson, G., &van Someren, K. A. "Evidence of a contralateral repeated bout effect after maximal eccentric contractions." *Eur J Appl Physiol, 101*(2), 207-214,2007.

[60] Howatson, G., Van Someren, K., & Hortobagyi, T. Repeated bout effect after maximal eccentric exercise. *Int J Sports Med, 28*(7), 557-563, 2007.

[61] Chen, T. C. and K. Nosaka, "Effects of number of eccentric muscle actions on first and second bouts of eccentric exercise of the elbow flexors." J Sci Med Sport 9 (1-2): 57-66, 2006.

[62] Eston, R. G., A. B. Lemmey, et al. "Effect of stride length on symptoms of exercise-induced muscle damage during a repeated bout of downhill running." Scand J Med Sci Sports 10(4): 199-204, 2000.

[63] Miyama, M. and K. Nosaka "Protection against muscle damage following fifty drop jumps conferred by ten drop jumps." J Strength Cond Res 21(4): 1087-92, 2007.

[64] Vaczi M, Costa A, Rácz L, Tihanyi J (2009) Effects of consecutive eccentric training at different range of motion on muscle damage and recovery. Acta Physiol Hung 96:459–468

[65] Starbuck, C. and R. G. Eston "Exercise-induced muscle damage and the repeated bout effect: evidence for cross transfer." Eur J Appl Physiol 112 (3): 1005-13, 2012.

[66] Falvo, M. J., Schilling, B. K., Bloomer, R. J., & Smith, W. A. "Repeated bout effect is absent in resistance trained men: an electromyographic analysis." *J Electromyography and Kinesiology, 19*(6), e529-535, 2009.

[67] Chan, R ., Newton, R., & Nosaka, K. "Effects of set repetition configuration in eccentric exercise on muscle damage and the repeated bout effect." Eur J Appl Physiol (2012) 112:2653–2661

[68] Chen, T. C. and K. Nosaka, "Responses of elbow flexors to two strenuous eccentric exercise bouts separated by three days." J Strength Cond Res 20(1): 108-16, 2006.

[69] Falvo, M. J., Schilling, B. K., Bloomer, R. J., Smith, W. A., & Creasy, A. C. "Efficacy of prior eccentric exercise in attenuating impaired exercise performance after muscle injury in resistance trained men." *J Strength Cond Res, 21*(4), 1053-1060, 2007.

[70] Bloomer, R. J., M. J. Falvo, et al. "Prior exercise and antioxidant supplementation: effect on oxidative stress and muscle injury." J Int Soc Sports Nutr 4: 9. 25: 321-63, 2007.

[71] Paschalis, V., Y. Koutedakis, et al. "Equal volumes of high and low intensity of eccentric exercise in relation to muscle damage and performance." J Strength Cond Res 19(1): 184-8, 2005.

[72] Uchida, MC, Nosaka, K, Ugrinowitsch, C, Yamashita, A, Martins, E, Jr., Moriscot, AS, and Aoki, MS. Effect of bench press exercise intensity on muscle soreness and inflammatory mediators. J Sports Sci 27: 499-507, 2009.

[73] Chen, T.C., Chen, H.L., Lin, M.J., Wu, C.J., and Nosaka, K. 2009. Muscle damage responses of the elbow flexors to four maximal eccentric exercise bouts performed every 4 weeks. Eur. J. Appl. Physiol. 106(2): 267–275

[74] Skurvydas, A., Brazaitis, M. and Kamandulis, S. (2011) Repeated bout effect is not correlated with intraindividual variability during muscle-damaging exercise. *The Journal of Strength & Conditioning Research* 25, 1004-1009.

[75] Nosaka K, Sakamoto K. Effect of elbow joint angle on the magnitude of muscle damage to the elbow flexors. Med Sci Sports Exerc 2001; 33:22–29

[76] Fernandez-Gonzalo, R., Bresciani, G., de Souza-Teixeira, F., Hernandez-Murua, J. A., Jimenez-Jimenez, R., Gonzalez-Gallego, J., & de Paz, J. A. (2011). Effects of a 4-week eccentric training program on the repeated bout effect inyoung active women. *Journal of Sports Science and Medicine*, *10*, 692-699.

[77] Smith, L. L., Fulmer, M. G., Holbert, D., McCammon, M. R., Houmard, J. A., Frazer, D. D., et al. "The impact of a repeated bout of eccentric exercise on muscular strength, muscle soreness and creatine kinase." *Br J Sports Med, 28*(4), 267-271, 1994.