Effect of eccentric and concentric contraction mode on myogenic regulatory factors expression in human vastus lateralis muscle

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Abstract
Skeletal muscle contractions are caused to release myokines by muscle fiber. This study investigated the myogenic regulatory factors, as MHC I, IIA, IIX, Myo-D, MRF4, Murf, Atrogin-1, Decorin, Myonection, and IL-15 mRNA expression in the response of eccentric vs concentric contraction. Eighteen healthy men were randomly divided into two eccentric and concentric groups, each of 9 persons. Isokinetic contraction protocols included maximal single-leg eccentric or concentric knee extension tasks at 60°/s with the dominant leg. Contractions consisted of a maximum of 12 sets of 10 reps, and the rest time between each set was 30 s. The baseline biopsy was performed 4 weeks before the study, and post-test biopsies were taken immediately after exercise protocols from the vastus lateralis muscle. The gene expression levels were evaluated using Real-Time PCR methods. The eccentric group showed a significantly lower RPE score than the concentric group (P ≤ 0.05). A significant difference in MyoD, MRF4, Myonection, and Decorin mRNA, were observed following eccentric or concentric contractions (P ≤ 0.05). The MHC I, MHC IIA, IL-15 mRNA has been changed significantly compared to the pre-exercise in the concentric group (P ≤ 0.05). While only MHC IIX and Atrogin-1 mRNA changed significantly in the eccentric group (P ≤ 0.05). Additionally, the results showed a significant difference in MyoD, MRF4, IL-15, and Decorin at the follow-up values between eccentric or concentric groups (P ≤ 0.05). Our findings highlight the growing importance of elucidating the different responses of muscle growth factors associated with a myogenic activity such as MHC IIA, Decorin, IL-15, Myonectin, Decorin, MuRF1, and MHC IIX mRNA in following various types of exercise.

Keywords Eccentric contraction · Concentric contraction · Gene expression · Myogenic regulatory factors

Introduction
Skeletal muscle is a highly adaptable and malleable tissue that participates in voluntary contraction according to command and responds to environmental and physiological challenges (Frontera and Ochala 2015; Lee and Jun 2019). Increasing data suggest that skeletal muscle in response to exercise training, synthesizes a range of secreted factors, known as myokines, that may play a significant role in muscle development and regeneration (Henriksen et al. 2012; Molanouri Shamsi et al. 2015). In this regard, previous research has established functions of myogenic regulatory factors (MRFs) to differentiate and grow muscle (Berkes and Tapscott 2005; Wei and Paterson 2001). MRFs (Myo-D, myogenin, MRF-4, myf5) have a significant role in synthesizing muscle protein through sarcomeric factors such as tropomyosin, troponin-c, myosin heavy and light chains (Bergstrom et al. 2002). Previously studies found that stretching stimulation induced the myocyte growth and differentiation and changed muscle of myosin heavy chains (MHC) isoforms level (Kurokawa et al. 2007; Sakiyama et al. 2005). Also, MRF-4, Myo-D, and myogenin genes were substantially increased following a single resistance exercise (Wilborn et al. 2009; Yang et al. 2005). Therefore, it indicates that the MRFs family are susceptible to single bouts of resistance training and could be implicated in myogenesis and hypertrophy’s modulation.
Nevertheless, several experiments have found no impact on myf5 (Yang et al. 2005) and MRF-4 (Kim et al. 2005) mRNA in the response of resistance exercise. In comparison, skeletal muscle protein synthesis is mostly related to the myosin contractile protein (McCall et al. 1999). In this regard, MHC isoforms are the most abundant muscle protein, making MHC an essential modulator of muscle fiber’s functional diversity (Wilborn et al. 2009). In animals and humans, intense resistance exercise improved the MHC isoforms mRNA (Caiozzo et al. 1996; Wilborn et al. 2009; Willoughby and Nelson 2002). Consequently, it seems that muscle contraction intensity has a remarkable role in MHC expression. It has been shown that during differentiation of myoblast, IL-15 mRNA expression is increased (Lee and Jun 2019). Several studies found that exercise training could be aggregated IL-15 in skeletal muscles (Brunelli et al. 2015; Tamura et al. 2011). Besides, IL-15 has anabolic effects on skeletal muscles by increasing insulin sensitivity (Barra et al. 2012; Quinn et al. 2011). However, chronic injection of IL-15 causes atrophy (Pistilli and Alway 2008) and hypertrophy in animals model (Quinn et al. 2002, 1995). Myonectin is another myokine released into the bloodstream through muscle contraction and facilitates the uptake of fatty acids into cells through enhanced fatty acid transfer genes (Seldin et al. 2012; Seldin and Wong 2012). Accordingly, the expression of myonectin is upregulated by voluntary exercise in the muscles and blood (Seldin et al. 2012). Hence, myonectin can improve muscle mass by increasing and decreasing protein synthesis and protein breakdown, respectively. Decorin, identified as a myokine, plays a critical role in the cell–matrix crosstalk modulation (Brandan et al. 1991; Henningsen et al. 2010). Moreover, Decorin promotes hypertrophy of muscle fibres by prohibiting myostatin (Guiraud et al. 2012; Kanzleiter et al. 2014; Miura et al. 2006). Although overexpression of decorin enhances the expression of MyoD and follistatin, it reduces MuRF1 and atrogin-1 (Marshall et al. 2008). Resistance training has already been shown to improve the systematic appearance of decoration (Kanzleiter et al. 2014; Mitchell et al. 2013).

On the other hand, skeletal muscle protein balance is controlled by both breakdown and synthesis of muscle protein (Masiero et al. 2009; Sandri 2013). The special muscle protein ligases, atrogin-1 and muscle ring finger-1 (MuRF1), were considered proteolysis enzymes for ubiquitin-mediated (Gumucio and Mendias 2013; Mendias et al. 2011) that were considerably increased by forkhead transcription factors (FoxO) (Yang et al. 2005). In this regard, the lack of Atrogin-1 and MuRF1 inhibits muscle atrophy in mice (Bodine et al. 2001; Gomes et al. 2001), are identified as primary mediators of degradation and atrophy muscle protein (Foletta et al. 2011). Similarly, MuRF1 and atrogin-1 mRNA are improved by resistance exercise that induces muscle hypertrophy (Léger et al. 2006). Besides, the mode of exercise contraction regulated the MuRF1 and atrogin-1 values differently. In that way, after single-bout of eccentric and concentric contraction, the mRNA level of atrogin-1 expression is de-regulated 3–12 h after exercise (Coffey et al. 2006; Louis et al. 2007; Mascher et al. 2008), whereas increasing of MuRF1 levels have been found 1–4 h after exercise (Louis et al. 2007; Mascher et al. 2008; Yang et al. 2006). In another study, atrogin-1 downregulation and MuRF1 upregulation have been shown by isolated eccentric and concentric contraction, respectively (Kostek et al. 2007; Nedergaard et al. 2007).

Concentric contraction involves the dynamic shortening of sarcomeres, while eccentric contraction involves the lengthening of sarcomeres (Taghibeikzadehbadr et al. 2020). There is some evidence that eccentric contraction produces significantly muscle force, neuromuscular adaptations, increased anabolic signalling and gene expression, and a more rapid protein synthetic response than concentric contraction (Farthing and Chilibeck 2003; Franchi et al. 2017; Maeo et al. 2018; Roig et al. 2009). Morais et al. showed excessive concentric training increases gastrocnemius glycogen content in C57BL/6 mice (Morais et al. 2018). However, chronic concentric and eccentric exercise protocols do not lead to sarcomerogenesis in mouse skeletal muscle (Morais et al. 2020). Nevertheless, some studies (Blazevich et al. 2007; Cadore et al. 2014; Schoenfeld et al. 2017) have indicated the same increases in strength and muscle hypertrophy after eccentric and concentric contraction, specifically in similar intensity or volume of exercises. On the other hand, excessive eccentric exercise inhibits hypertrophy (Da Rocha et al. 2016), endoplasmic reticulum stress (Pereira et al. 2016a, b), and impairs the insulin signal transduction (Pereira et al. 2016a, b) in mice skeletal muscle. Given the gaps in our knowledge base, the different effects of eccentric and concentric contraction on hypertrophy and strength gains are controversial. From all the above, it can be conducted that the signalling pathways of these two contractions are likely to result in structural, physiological, and molecular differences in skeletal muscle (Isner-Horobeti et al. 2014). Hence, the response of MHC I, IIA, IIX, Myo-D, MRF4, Murf, Atrogin-1, Decorin, Myonectin, and IL-15 mRNA expression has been investigated following eccentric and concentric exercise in human vastus lateralis muscle.

**Materials and procedure**

**Participants**

Eighteen healthy men were recruited to this study and randomly divided into eccentric (n = 9) and concentric (n = 9) groups. The experimental protocol consisted of two sessions (familiarization and isokinetic test) described below.
Subjects were not involved in resistance training and lower body musculoskeletal conditions for at least six months before beginning the study. All procedures were approved by the University of Tehran ethical committee (Ethic No: IR.UT.SPORT.REC.1397.029) (Table 1).

**Familiarization**

A week before each resistance exercise, the knee extension Maximal Voluntary Isometric Action (MVIA) of the dominant leg was determined using a standard dynamometer (Biodex, Shirley, NY USA). Leg dominance was identified by asking the individuals the preferred leg to kick a ball (van Melick et al. 2017). Before testing the MVIA, all subjects performed a general warm-up consisting of 10-min cycling without load at the range of 60–80 rpm on the stationary cycle before the MVIA test. Subsequently, each participant briefly familiarised the isokinetic dynamometer, involving 5–10 submaximal contractions (25% of MVIA) with the dominant leg.

For MVIA, the knee was positioned at a 60° knee extension (full extension—0°). Three trials (5 s for each trial) were conducted, with intervals of 3 min between them. Additional trials were performed if the participants did not achieve at least two trials with similar results. Participants were strongly encouraged during the task.

After MVIA tests, individuals were familiarized with the maximal eccentric and concentric leg extension force was measured. Following a five-minute warm-up on a cycle ergometer, participants received detailed instructions on the eccentric and concentric leg extension exercises and performed ten repetitions of each exercise at maximal effort. The maximum force of the knee extensors for eccentric and concentric leg extension was performed with the dominant leg at 60°/s.

**Isokinetic test**

The experimental protocol was conducted on a separate day (7 days apart from the familiarization session). Before the isokinetic test, each individual performed a general warm-up consisting of five-minute cycling without load and a specific warm-up using the Biodex isokinetic device at 25% of MVIA (5 concentric or eccentric contractions, according to the group randomization, with intervals of 30 s between each set). The participants then performed one of the isokinetic protocols below with the dominant leg.

**Eccentric protocol**

Each contraction was performed at 60°/s. Individuals performed 12 sets of 10 repetitions with 30 s of rest between each set, for a total of 120 contractions. Movement at the shoulders, hips, and thigh (exercised leg) were restrained with straps to isolate the knee extensors during the protocols and secure the participant to the device. The eccentric contraction was performed at > 90% of maximal load eccentric strength, and the concentric component was passive (i.e. investigator moved the limb back to the starting position). Visual feedback of the force signal was provided to each individual. Participants were verbally encouraged to maintain the contraction levels during the task. At the end of each set, the rating of perceived exertion (RPE) was determined using the 20-point scale. One participant was not able to maintain the intensity level during the whole task and performed only ten sets.

**Concentric protocol**

The protocol was similar to the eccentric one, but the individuals performed concentric contractions at 90% of their maximal instead of eccentric ones. The eccentric portion of the movement was passive (i.e. the investigator returned the limb to initial position). Visual feedback was also provided, and individuals reported their RPE between sets. All participants performed the full concentric protocol.

**Muscle biopsy**

Two samples were collected: (1) 4 weeks before the eccentric/concentric protocol and (2) immediately after the concentric/eccentric protocol. Tissue biopsies were collected from the mid-portion of the vastus lateralis muscle in the morning (11–12 am). The area was locally anaesthetized (0.1 ml of lidocaine), and a Bergström needle was used. The samples were cleaned from blood and connective tissue, then frozen immediately in liquid nitrogen and stored at −80 °C until gene expression analysis.

**Gene expression**

Expression of Myosin Heavy Chain (MHC) I, IIA, IIX, Myo-D, MRF4, Murf, Atrogin-1, Decorin, Myonection, and IL-15 was identified with real-time Polymerase Chain Reaction (PCR). Total RNA was extracted based on the Cinna Gen protocol using kiazol solution (Cinnacolon, Iran). To ensure no contamination with genomic DNA,
the samples were first exposed to DNase (DNase I Ferments). The quality of extracted RNAs was evaluated with a spectrophotometric device (DPI-1, Kiagen). For reverse-transcribed of RNAs to cDNA used Strand cDNA Synthesis Kit (Oligo dt MWG-Biotech, Germany). The PCR reaction was conducted using the PCR master mix (Applied Biosystems) and Syber Green in the ABI Step One (Applied Biosystems, Sequences Detection Systems, Foster City, CA). For each Real-Time PCR cycle, a total of 40 cycles were considered, and the temperatures for each cycle were set at 94 °C for 20 s, 60–58 °C for the 30 s, and 72 °C for 30 s, respectively. The primer sequence is shown in Table 2. The expression of GAPDH confirmed that PCR conditions were optimized. Melting diagrams were performed to check the accuracy of PCR reactions. They were evaluated for each gene individually and at each reaction time, along with negative control diagrams to check for contamination in each reaction. Relative expression of the gene was analyzed using Prism software after manually setting the baseline and threshold. The RT-PCR data were analyzed using the delta-delta cycle threshold (ΔΔCt) method. All Real-time PCR procedures were performed in triplicate.

### Statistical analysis

Statistical analysis was conducted using SPSS software (version 21; IBM, Chicago, IL) and reported as mean ± SD. The normality of the data and equality of variances was tested using the Shapiro–Wilk and Levine test, respectively. Mixed-design repeated measures analysis of variance (ANOVA) was run to analyses differences across time (baseline vs follow-up) and groups (eccentric vs concentric) in all variables (Myo-D, MRF4, IL-15, Myonection, Decorin, MHC I, IIA, IIX, Atrogin-1, and Murf mRNA expression). Where an interaction effect was observed, independent samples t-test was performed to compare variables at baseline and follow-up change between eccentric and concentric groups. In addition, changes over time (baseline vs follow-up) in each group were assessed using paired t-test. Partial eta squared effect size was reported for group×time interaction. For all statistical analyses, an alpha of p ≤ 0.05 was considered statistically significant for all comparisons.

### Result

#### RPE

The results showed that there were statistically significant interaction effects (group×time) for RPE score (F (1,16) = 9.550, P = 0.010, ηp2 = 0.386). According to the follow-up tests, significant differences in RPE scores were observed in the set 7 to 12 values between CON and ECC groups (P ≤ 0.05). Moreover, the results showed that compared to the CON, RPE scores were significantly lower in the ECC group (P ≤ 0.05, Fig. 1).

#### MyoD

A two-way mixed ANOVA with repeated measures showed that there were statistically significant interaction effects (group×time) for MyoD (F (1,16) = 9.396, P = 0.007, ηp2 = 0.369). The follow-up tests showed significant differences in MyoD at the follow-up values between CON and ECC groups (P = 0.004). Moreover, the paired t-test results showed that MyoD significantly increased in both CON and ECC groups (P ≤ 0.05, Fig. 2A).

#### MRF4

The results showed that there were statistically significant interaction effects (group×time) for MRF4 (F (1,16) = 10.005, P = 0.006, ηp2 = 0.385). According to the follow-up tests, significant differences in MRF4 were observed at the follow-up values between CON and ECC groups (P = 0.005). Moreover, the paired t-test results showed that compared

### Table 2

| Gene     | Forward/reverse | Primer (5′–3′) |
|----------|-----------------|----------------|
| MyoD     | F               | GGTGGGGGATAGTGGGTGGG |
|          | R               | TGGGCAAGGGAGGAGGAGGAGGAG |
| MRF4     | F               | GATAACGGGTAAGGAAGGAGGAG |
|          | R               | AAGGATTAGGTGGCAGAAGGGT |
| IL-15    | F               | GAGGGATTTGTGATGGTAGGGATGG |
|          | R               | ACAGAAGTGACTCGGTAGGGA |
| Myonectin| F               | AGGTGGTGATGAGAGTAGGTT |
|          | R               | TACTCTGGGAAATCTGGGA |
| Decorin  | F               | TGAAGGGAGAAGACATGGA |
|          | R               | GGAAGATAGGGAGGAGGAGGAGG |
| MHC I    | F               | CATTGGAGGACTGGAGGAGGAG |
|          | R               | TGCGTCTACGTCGTAGGGG |
| MHC IIA  | F               | AGCGAGAGAAGGAGGAAAGGTA |
|          | R               | CACTCTAGGGGAGGGAGG |
| MHC IIX  | F               | GCAGGGAGGAGTACAGAACAGG |
|          | R               | TTGGGGTCTCTGGAAATGG |
| Atrogin-1| F               | ACTCCACACCCCTCTACACCT |
|          | R               | TCTCCTACATCACACCCACA |
| MuRF-1   | F               | TGTCGACCATCATCATCATA |
|          | R               | AACATCTCTTCTCTCTACCTC |
| GAPDH    | F               | GCAGGGATGATGATCTG |
|          | R               | CTTTGGTAGCTGGAGGAGAAGGAGGAG |
to the baseline level, MRF4 significantly increased in both CON and ECC groups (P ≤ 0.05, Fig. 2B).

**IL-15**

A two-way mixed ANOVA with repeated measures showed that there were no statistically significant interaction effects (group × time) for IL-15 (F(1.16) = 3.679, P = 0.073, ηp² = 0.187). However, the main effect of time showed a statistically significant increase in IL-15 from baseline to follow-up (P ≤ 0.05) in the CON group. Moreover, there was a significant difference in IL-15 at the follow-up values between CON and ECC groups (P = 0.024, Fig. 2C).

**Myonection**

A two-way mixed ANOVA with repeated measures showed that there were no statistically significant interaction effects (group × time) for Myonection (F(1.16) = 2.315, P = 0.148, ηp² = 0.126). However, the main effect of time showed a statistically significant increase in Myonection from baseline to follow-up (P ≤ 0.05) in both CON and ECC groups. Moreover, there was no significant difference in Myonection at the

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**Fig. 1** RPE score in different sets during the Eccentric and Concentric contractions protocols. The results showed a significant difference between Eccentric and Concentric groups in RPE score from set 7 to 12 (P < 0.05). Each value is presented as the mean ± SE (n = 9). *Statistical analysis indicates the significant difference between RPE score in different sets during the Eccentric and Concentric contractions: p ≤ 0.05

**Fig. 2** Gene expression of MyoD (A), MRF4 (B), IL-15 (C), and Myonection (D) in the vastus lateralis muscle in response to Eccentric and Concentric contractions. The expression levels of MyoD, MRF4 and Myonection significantly increased in both eccentric and concentric groups from baseline to follow-up (P < 0.05). However, IL-15 increased significantly only in the concentric group (P < 0.05). Each value is presented as the mean ± SE (n = 9). *Statistical analysis indicates the significant difference between baseline and follow-up: p ≤ 0.05. ≠Statistical analysis indicates the significant difference between groups at follow-up: p ≤ 0.05
follow-up values between CON and ECC groups (P = 0.102, Fig. 2D).

**Decorin**

A two-way mixed ANOVA with repeated measures showed that there were statistically significant interaction effects (group × time) for Decorin (F(1.16) = 16.062, P = 0.001, ηp² = 0.501). According to the follow-up tests, significant differences in Decorin were observed at the baseline and follow-up values between CON and ECC groups (P ≤ 0.05). Moreover, the paired t test results showed that Decorin significantly increased in both CON and ECC groups (P ≤ 0.05, Fig. 3A).

**MHC I**

A two-way mixed ANOVA with repeated measures showed that there were no statistically significant interaction effects (group × time) for MHC I (F(1.16) = 0.082, P = 0.778, ηp² = 0.005). However, the main effect of time showed a statistically significant decrease in MHC I from baseline to follow-up in the CON group (P ≤ 0.05). Moreover, there was no significant difference in MHC I at the follow-up values between CON and ECC groups (P = 0.079, Fig. 3B).

**MHC IIA**

The results showed that there were no statistically significant interaction effects (group × time) for MHC IIA (F(1.16) = 2.130, P = 0.164, ηp² = 0.117). However, the main effect of time showed a statistically significant increase in MHC IIA from baseline to follow-up in the CON group (P ≤ 0.05). Moreover, there was no significant difference in MHC IIA at the follow-up values between CON and ECC groups (P = 0.251, Fig. 3C).

**MHC IIX**

The results showed that there were no statistically significant interaction effects (group × time) for MHC IIX (F(1.16) = 0.024, P = 0.878, ηp² = 0.002). However, the main effect of time showed a statistically significant increase in MHC IIX from baseline to follow-up in the ECC group (P ≤ 0.05). Moreover, there was no significant difference in
MHC IIX at the follow-up values between CON and ECC groups (P = 0.537, Fig. 3D).

**Atrogin-1**

A two-way mixed ANOVA with repeated measures showed that there were statistically significant interaction effects (group × time) for Atrogin-1 (F (1.16) = 7.159, P = 0.017, ηp2 = 0.309). The paired t-test results showed that compared to the baseline level, Atrogin-1 significantly decreased in the ECC group (P ≤ 0.05). Moreover, there was no significant difference in Atrogin-1 at the follow-up values between CON and ECC groups (P = 0.601, Fig. 4A).

**MuRF1**

The results showed that there were no statistically significant interaction effects (group × time) for MuRF1 (F (1.16) = 3.954, P = 0.064, ηp2 = 0.198). Moreover, there was no significant main effect of time (P = 0.971, Fig. 4B).

**Discussion**

This study investigates the effects of two types of contractions on gene expression of myogenesis factors, including muscle hypertrophy. The results showed that compared to the CON, RPE scores were significantly lower in the ECC group (P ≤ 0.05). Moreover, a significant difference in MyoD, MRF4, IL-15, and Decorin was observed at the follow-up values between CON and ECC groups (P ≤ 0.05). Moreover, the results showed that compared to the baseline level, MyoD, MRF4, Myonection, and Decorin significantly increased in both CON and ECC groups (P ≤ 0.05). MHC I, MHC IIA, IL-15 showed statistically significant changes from baseline to follow-up in the CON group (P ≤ 0.05). On the other hand, MHC IIX and Atrogin-1 showed a statistically significant change from baseline to follow-up in the ECC group (P ≤ 0.05).

The results showed RPE score was different between CON and ECC contractions. In this regard, the ECC group showed a significantly lower RPE score than the CON group from set 7 to set 12. Peñailillo et al. found that RPE was lower during eccentric than concentric cycling (Peñailillo et al. 2018). These findings were expected and are similar to previous studies comparing eccentric and concentric exercise (Aiüillo et al. 2013; Hollander et al. 2003). Another study showed that average RPE was 22% lower during eccentric compared with concentric cycling (Aiüillo et al. 2013). Previously showed that eccentric muscle contractions may result in lower physiological strain when compared to concentric exercise (Aiüillo et al. 2013; Perrey et al. 2001). The lower metabolic cost of ECC contraction is likely attributable to the less motor unit activation and consume less oxygen and energy for a given muscle force than concentric contraction (Hody et al. 2019). Kellis and Baltzopoulos (Kellis and Baltzopoulos 1998) reported that VL EMG amplitudes during maximal eccentric isokinetic knee extensor contractions at different velocities were 11–52% lower than during concentric contractions, which may be attributed to a smaller portion of the motoneuron pool being recruited during eccentric contractions (Hollander et al. 2003).

The results have been shown expression of MHC IIA and MHC I mRNA significantly changed in the CON group, while MHC IIX significantly increased in the ECC group. In this regard, previously demonstrated that the expression of MHC I, MHC IIA, and MHC IIX increased in the response of a single high-intensity resistance training (Wilborn et al. 2009; Willoughby and Nelson 2002). Moreover, remobilization of the soleus muscle in the flat treadmill induced increases of MHC I content. At the same time, eccentric training did not show significant changes in this type of MHC protein (Cornachione et al. 2011). Hence, muscle contraction tends to be a modulator of MHC isoforms, despite the type of contraction. Several factors have
now been identified, which stimulate an increase in muscle volume after mechanical loading (Sotiropoulos et al. 2006; Tortorella et al. 2001). It has been found that some of these effectors affect myoblast hypertrophy (Berkes and Tapscott 2005; Wei and Paterson 2001). In line with previous researches, we have demonstrated that ECC and CON muscle contraction is adequate for the upregulation of Myo-D, MRF-4 and myonectin mRNA levels in the VL muscle. Previous research showed a significant increase only in MRF-4 in the eccentric group (Imaoka et al. 2015; O’Reilly et al. 2008). Psilander et al. found a single heavy-resistance exercise bout considerably upregulated expression of Myo-D and MRF-4 mRNA (Psilander et al. 2003). The importance of these findings is that the Myo-D and MRF-4 probably have the primary role in controlling MHC genes. Previous researches have represented that the expression of Myo-D and myogenin are related to alterations of isoform composition of MHC compared to muscle mass (Mozdziak et al. 1998; Willoughby and Nelson 2002). Moreover, myonectin, a novel myokine, affects fat metabolism and reduces the amount of circulating lipids (Seldin et al. 2012). Seldin et al. represented that voluntary exercise by wheel running increased the expression of the myonectin gene (Seldin et al. 2012). Pourranjbar et al. have shown that engaging in aerobic training increased significantly myonectin in obese women (Pourranjbar et al. 2018). Also, myonectin has been demonstrated to promote the uptake of fatty acids in cultured adipocytes and hepatocytes and suppress the circulating of free fatty acid levels in mice (Seldin et al. 2013); furthermore, the erythroid modulator of iron metabolism and hemoglobin synthesis (Kautz et al. 2014a, b).

Moreover, in the present work, CON and ECC exercise increased IL-15 mRNA expression in the VL muscle, and there was a significant difference between CON and ECC in IL-15 follow-up values. In that way, the IL-15 increased significantly after a single leg maximal isokinetic eccentric resistance exercise (Dieli-Conwright et al. 2009). Furthermore, Bazgir et al. have shown that ECC and CON resistance exercise considerably increased IL-15 serum in non-athlete individuals (Bazgir et al. 2015). The resistance exercise could also induce the increase of IL-15 mRNA in the vastus lateralis muscle (Nielsen et al. 2007). As a consequence, improvements of IL-15 mRNA expression will be predicted after resistance exercise training. Quinn et al. indicated the increase and decrease in IL-15 mRNA levels in muscle and circulation, respectively, the sequence of a single bout of running exercise in the animal model (Quinn et al. 2014). It seems that contraction-induced muscle tissue secretion of IL-15 might lead to these differences. It must be indicated that the type of skeletal fiber, intensity, the volume of training, and metabolic status could affect alteration of IL-15 mRNA after exercise (Molanouri Shamsi et al. 2015).

Furthermore, the results reported that a single bout of CON and ECC contraction changed the decorin mRNA level in the VL muscle. Simultaneously, the results have shown a significant difference in decorin mRNA expression in the follow-up measures between the two groups. In this regard, a single bout of endurance activity could increase the decorin mRNA in skeletal muscle (Heinemeyer et al. 2013). Decorin has been shown to improve the response of an acute resistance exercise bout; however, it returns to the baseline level after an hour of exercise (Kanzleiter et al. 2014). The most important result of this study is that concentric muscle contraction produced more decorin mRNA expression immediately post-exercise. Moreover, there were significant differences between the ECC and CON contraction in Decorin, indicating that Decorin might distinguish between the hypertrophic responses (Bugera et al. 2018).

Atrogin-1 and MuRF1 are present in the degradation of muscle proteins and are assumed to have a significant role in muscle atrophy in disease conditions (Bodine et al. 2001; Gomes et al. 2001). Resistance training, known as a positive modulator of muscle health, controlled the levels of MuRF1 and atrogin-1 mRNA, while the mode of contraction and type of exercise might play a significant role (Stefanetti et al. 2014). To clear the effect of type of contraction on these targets of atrophy, isolated ECC and CON contraction were used in this study. The results showed that Atrogin-1 mRNA expression was sensitive to single-bout muscle contraction in a contraction mode-dependent manner. Atrogin-1 mRNA levels decreased significantly in the ECC group. In this regard, ECC contraction downregulated the expression of MuRF1 and Atrogin-1 mRNA, while CON exercise produced a consistent upregulation of FOXO1 and MURF1, under the same contraction times (Nedergaard et al. 2007; Stefanetti et al. 2014). Atrogin-1 was attenuated after the ECC-exercised muscle, in which CON contractions have not considerable effect (Kostek et al. 2007). In another study, Coffey et al. indicated that Atrogin-1 mRNA levels tend to reduce following a single endurance exercise bout, while there was no significant alteration in strength athletes (Coffey et al. 2006).

Moreover, in line with previous researches increasing MuRF-1 mRNA has been presented in this study (Fry et al. 2013; Glynn et al. 2010). In contrast, a study conducted by Churchley et al. showed a decrease in MuRF mRNA following an acute resistance training bout (Churchley et al. 2007). It seems that the different behaviour of the Atrogin-1 and MuRF in response to resistance training may suggest that they have different roles in the proteolysis process. Moreover, it would be possible that a single bout of resistance training could trigger adequate muscle damage and activate these negative regulators of muscle growth (Mascher et al. 2008; Stefanetti et al. 2014).
Limitation

There have been some possible limitations in this research, which must be considered in the following studies. The sample limitation of muscle biopsy might have a tangible effect on results due to transient response. For future research, this possibility can be discussed by thought increasing sample research. Besides, it must be mentioned that results taken as a consequence are focused on alterations in mRNA, while protein changes remain unclear in current work. Moreover, the following studies should consider the lack of a control group and the use of only one control gene in the current research.

Conclusion

This study investigated the single bout of isolated ECC and CON contraction on several myogenic regulatory factors. In this study, it was found that participants reported greater RPE during concentric compared to eccentric exercise. Our results showed that muscle contraction has variable effects on mRNA expression of MyoD, MRF4, IL-15, and Decorin, IL-15 and MHC isoforms. Moreover, Atrogin-1, which is known as a negative regulator of muscle growth, showed different alterations following ECC and CON contraction. Therefore, it provides a new vision into how the type of contraction in resistance exercise influences myogenic factors.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

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