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Original Article

Effects of a Single Session of Eccentric or Concentric Resistance Exercise on Relative Expression of BDNF, PAX7 and IGF-1 in Young Men

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ABSTRACT

Background and Objectives: The aim of the present study was to investigate effectsof a single sessionof eccentric or concentric resistance exercise on relative expression of BDNF, PAX7 and IGF-1 in healthy participants.

Materials and Methods: In a field trial, ten healthy young men were randomly assigned into two equal groupsof concentric and eccentric contractions. Isokinetic contraction protocols included eccentric and concentric knee extensions with maximum power. The torques assigned were similar in the two groups. At the beginning and end ofthe exercise, biopsies of the lateral broad muscle tissue were collectedto assess relative expression of BDNF, PAX7 and IGF-1.

Results: Statistically significant increases were seen in BDNF and PAX7 expression rates of the concentric exercise group (p= 0.021 and p= 0.014, respectively). Results showed that IGF-1 protein significantly increased after concentric and eccentric exercises (p= 0.005 and p= 0.022, respectively). In eccentric exercise group, BDNF and PAX7 expression rates increasedsignificantly (p=0.034 and p= 0.034, respectively).

Conclusions: Based on the findings, a single session of eccentric and concentric exercise changes factors involved in skeletal muscle strength and hypertrophy. In addition, these changes were totally more in eccentric contraction group, compared to concentric contraction group. It can be recommended to focus further on eccentric exercisesto increase hypertrophy and muscle strength.Furthermore, these findingscan be used to prevent obesity and type 2 diabetes.

Keywords: Muscular contractions, Metaboliceffects, exercise modes, hypertrophy, Satellite cells

Introduction

In a variety of physiological and psychological disorders,neuromuscular biomarkers play important roles in responses of physiological systems to exercise and physical activities and areaffectedby nutritional and metabolic conditions (1–3). Regular physical activity can be used as a complementary therapy.In fact, amino acid (AA) turnover is a major factor in causing structural changes in muscles and is controlled by various muscle contractions as well as signal pathways (1). Pathological changes in neuromuscular biomarkers are associated toinflammation, obesity, insulin resistance and diabetes (4). Brain-derived neurotrophic factor (BDNF) has been identified as the most important regulator of neuronal differentiation, synaptic plasticity and cell death process (5). It plays important roles in learning and memory (6). The neurotrophic factor is the most important known trophic factor in the nervous system (7). The brain-derived neurotrophic factor, despite its name, is not only present in the brain, but is naturally expressed in various tissues and cells, including retina, kidneys and prostate (8). Gharakhanlu et al. reported significant increases in IGF-1 levels in non-athlete men after plyometric exercises, some of which are eccentric in nature (9). Trained rats have been shown to include higher levels of BDNF in their veins,compared to that inactive rats have (9). Previous studies have suggested that increased BDNF levels strongly dependon intensity (10), duration (11) and frequency (12) of the activities. Moreover, BDNF treatment improves insulin sensitivity (13). Recent studies have shown close relationships between BDNF and satellite cell differentiation in skeletal muscles after muscle injuries (14). Bo Li et al. foundthat the BDNF levels were significantly lower in patients with T2DM, compared to those in control participants (15).

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Satellite cells are small mononuclear cells between the basement and cytoplasmic membranes that are activated in muscles, which form myoblasts in response to pressures from heavy exercisesor blows and eventually turn into muscle fibers. In fact, these cells are specific stem cells that are found in almost every tissue and play roles in the normal growth, replacement and repair of tissues after chemical and mechanical damages. Numbers of satellite cells depend on animal species and age, types of muscle fibers and cell locations parallel to the fibers (16).Satellite cells are activated in response to physiological stimuli such as exercises and pathological conditions such as injuries and diseases to produce myoblasts capable of being synthesized and diagnosed. These cells can combine with existing muscle fibers, repair damaged muscle fibers or alternate with each other to form new muscle fibers (17). Scientific studies on effects of training on satellite cells have investigated effects of two types of resistance and endurance activities on these cells. Dungan et al. (2005) investigated effects of heavy resistance training and detraining on satellite cells in human skeletal muscles. These studies have shown that excessive pressures and strains and releases of inflammatory substances as well as growth factors produced by the resistance exercise activities can increase activities of the satellite cells and stimulate them to re-enter the cell cycle and proliferation (18). Based on the studies, satellite cells are regulated by PAX7, a cell cycle activating factor responsible for activating and regulating satellite cell reserves (19). Karyono et al. (2015) showed that moderate and low intensity trainings increased PAX7 expression, whereas high intensity training decreased PAX7 expression, compared to other groups (19). These results revealthat types of the exercise can affect PAX7 changes.

Insulin-like growth factors are a family of growth-promoting peptides that play important roles in tissue growth and development (20). The IGF-1 is a single-chain 70-AA polypeptide produced by the liver through stimulation, secreted by growth hormone and released into the bloodstream (21). Increases in IGF-1 and MGF wereobserved in young men after a one-week of strength training (22). However, they were no different mRNA expression of the both isoforms in the elderly (23). Itwas shownin a study with no strongassociations with exercisesthat the eccentric part was essential for the positive expression of IGF-1 gene since only the concentric part of movements did not lead to positive expressions of this gene. Most studies of participants with no history of resistance training reported no changes in IGF-1 mRNA expression after exercises (24, 25). Nowadays, roles of muscle contraction manipulation in resistance training arereported important as most training and rehabilitation programs involve concentric and eccentric contractions during each repetition (1). Studies have shown that eccentric exercise is metabolically lower than concentric exercise; however, it always leads to further muscle damages and greater inflammatory responses (26). Hortobagyi et al. (1996) concluded that extraversion activities were more adaptive relative to introversion activities (27) while Kay et al. (2000) achieved similar neurological adaptations in the two types of the exercises (28). Based on these data, potential roles of BDNF, PAX7 and IGF-1 in regulating human skeletal muscle masses and strength adaptations in response to resistance exercisesare considered. Associations between neuromuscular biomarkers, inflammation, obesity and diabetes have been verified. Since studies on signaling pathways of the muscle growth factors in humans and theirgeneralization to real groups can provide further accurate schemes of the molecular-cellular events and ultimately adaptability to coaches and sports scientists as well as further human generalizability compared to animal studies, this study was carried out on human samples.Therefore, the aim of the present study wasto investigate relative expressions of BDNF, PAX7 and IGF-1 in response to eccentric and concentric exercisesin young men.

Materials and Methods

Participants

From 18 to 30-year-old healthy active young men (people who carried out resistance exercises for at least three days for general health and physical activity promotion), ten men were randomly assigned into concentric (n=5) and eccentric (n=5) groups. The present trial study was a simple randomized individual study using a table of random numbers and correct concealment. Since this was based on regular activities, participants did not consume specific supplements or foods. National ID card numbers of the eligible participants were recorded and numbers of the participants were divided by ten. Considering numbers and the table of random numbers, participants were selected and grouped in intervention and control groups. Human studies must meet health needs of the population or community, where they are carried out. Ethical requirements are met when successful interventions or other benefits of such studies are made available to the public. To meet the ethical requirements, planning and management processes were carried out before the beginning of the study and monitored and assessed until the end of the processes, making results available to competent authorities and study populations. Competence and skills of the expert researchers and safe conditions of the study environment were approved by the ethics committees before and during the implementation. The ethics code of this study was IR.UT.SPORT.REC.1397.029 issued by the University of Tehran and registered at the Ministry of Health of the Islamic Republic of Iran. As soon as controversial issues were found in human commitments

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and principles, study was discontinued. Receiving informed consents from the participants as well as ensuring their voluntariness and unconditional withdrawal from the study were integral parts of the researcher stasks.

The American College of Sports Medicine (ACSM) guidelines were used to assess health of the participants and minimize risks associated with their cardiovascular system. Participants were not undergone surgeries since six months prior to the study or on medications at the time of the study. After selection of the participants, objectives and procedures of the study were described to them and the participants signed consent forms for participating in the study. Demographic characteristics of the participants are presented in Table 3.Participants attended two sessions in the laboratory. Purpose of the first session was to familiarize the participants with the laboratory environment and the isokinetic system (Biodex Isokinetic Dynamometer, USA), measure their height and weight, explain Borg exercise pressure questionnaires to them and assess their torques. In the second session, participants randomly carried out one of the eccentric and concentric protocols at 8:00–9:00 AM. After assessing the 60° angle, isokinetic device was adjusted to impose the highest pressure on the athletes. Since the device is often used to rehabilitate people in post-recovery conditions, it did not impose the necessary pressure on the athletes to carry out the exhausting protocol of this study. Therefore, researchers should design exercise protocols including sets, repetitions and rest times for the athletes to reach exhaustionstates.in this study, waves of force in isokinetic machine monitor existed and each repetition of the athletes was shown based on the value of the force used.

Concentric and eccentric exerciseprotocols

Participants rested for 10 min at each session and the procedures were reviewed to ensure that they understood how the exercise must be performed. Then,participantswere seated on a dynamometer chair and settings were made to prepare the device. These settings included 90° orientation of tilt dynamometer, 90° of seat orientation, 85° of seat back tilt, 0–90° range of motion. Moreover, dynamometer rotation axis was selected on the sagittal plane withthe line passing through the external condyle.Specific warming with the isokinetic system included twosets of fiveand the rest time between each set included 30 s. Then, participantscarried out one of the two isokinetic muscle contraction protocols thatwas randomly assigned to their right foot. At the end of the exercise, the leg was fixed with no pressures until the biopsy was carried out. Biopsy of each participantwas carried out 3–4 h after completion of the exercise protocol. During implementation of the protocol at the end of each set, the pressure perception was measured using Borg 20-point scale (RPE). Participantswere asked to report a number on the Borg scale after completing each set. When participants declared number 20, verbal encouragementsurged him to continue further two sets and when they were unable to fully implement the protocol, the exercise was stopped.Isokinetic contraction protocols included eccentric and concentric knee extensions with maximum power and angular velocity of 60° per second. Torques assigned to each participantwere assumed equal to match the workload in the two protocols with a rotational speed of 60° per second. Contractions maximally consisted of a 12 sets of tenrepetitions for the right leg and a rest time of 30 seconds between each set. Obviously, eccentric exercise time was longer than concentric exercise one.Exercise protocols in eccentric and concentric groups arepresented in Table1.

Table1. Exerciseprotocols in eccentric and concentric groups

Group	Number of sets	Number ofmovements	Rest between the sets
Eccentric	Max of 12 sets	10 repetitions	30 s at low speed
Concentric	Max of 12 sets	10 repetitions	30 s at high speed

Muscle tissue sampling

At the beginning and the end of the study, biopsies of the lateral broad muscle tissues were collectedin a completely hygienic sterilized environment. The biopsy procedure was carried outin distal and proximal directions of the lateral broad muscles. Baseline biopsy specimens were collected by orthopedic surgeonsfor the first time and 3–4 h after the trainingsin Baqiyatallah Hospital, Tehran, Iran (29). Dermal muscle biopsies (15–20 mg) were collectedfrom the medial parts of the lateral broad muscles at the midpoint between the patella and the greater trochanter of the thigh witha depth of 1–2 cm based onthe previously approved procedures. Biopsy sitewas cleaned and its hair was completely removed. Then, the site was washed with disinfectant soap and disinfected with alcohol. Furthermore, biopsy site was disinfected with betadine. A small area of the cleansed skin, approximately 2 cm in diameter, was anesthetized with a subcutaneous injection of 0.1 ml of lidocaine. Following anesthesia, a 16-inch needle aspiration biopsy specimen (Tru-Core I Biopsy Instrument, Techniques Device Technologies, USA) was placed at approximately 1-cm depth of the muscle tissue to extract the sample. After the initial biopsy, subsequent biopsy of the muscle tissue was extractedclose to the previous site using pre-biopsy and needle depth markers. After muscle biopsies, adipose tissueswereremoved from the muscle samples. Samples were stored immediately at -80° C until use. In each of the two sessions, two muscle specimens were collected;from which,tenmuscle specimens were totally collected for each group during the study and 20 specimens overall. In general, the muscle samples were collectedat the baseline and 3–4 h after the exercises.

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Relative expressions of BDNF and PAX7in tissues

To assessthe relativeexpressions of BDNF and PAX7 genes, tissue analysis was carried out in each group using real-time polymerase chain reaction (PCR). Primer design was first carried out; then, whole RNA was extracted from the tissues and converted to cDNA. ThecDNA was amplified using PCR and analyzed for relativeexpressions of the highlighted genes.The RT-qPCR was used to verify quantitative relativeexpressions of the studied genes. The whole-cell RNA was extractedbased on the manuals by the manufacturer using kiazol solution (Sinagen, Iran)and subjected to DNase I (Fermentas, USA) to ensure genomic DNA decontamination. Then, quality of the RNA was assessed using spectrophotometer (QiagenDPI-1, Germany). Single-stranded cDNA was prepared using primers (Oligo dt MWG-Biotech, Germany) and reverse transcriptase enzymes (Fermentas, USA) based on the stablishedprotocols. Each PCR reaction was carried out using PCR master mix (Applied BioSystems, USA), SYBER Green andABI Step One (Applied Biosystems, Sequences Detection Systems, USA) based on the manufacturer instruction. Generally, 40 cycles were usedfor each real-time PCR set using the following temperatures of 94° C for 20 s, 58–60° C for 30 s and 72° C for 30 s, respectively.Melting diagrams were recorded to check the accuracy of PCR reactions and assessed for each gene individually at each reaction time with negative control diagrams to check possible contaminations. Expression ratios of the genes were assessedusing comparative method of the threshold cycle.Specific standard curves for each gene were plotted using at least fivelogarithmic concentrations diluted from positive controls. Target gene expression was normalized to the reference gene and the expression of healthy group genes was considered as calibrator.Formula E represents efficiency and is achieved using standard curves for the genes.The sequence of primers used in PCR is presented in Table 2. The reference gene included hGAP.

Table 2. Sequences of the primers used in real-time PCR

Gene	F/R	Primer (5’ → 3’)
BDNF	F	TTATTCCCACCATCCCACCTCT
	R	CCTCTTCCCTTTTCCCTTACCA
PAX7	F	CAAGCAGAAGAAGGAGTTGGAG
	R	CGAGATGAGTTAGAAGTTGATG
hGAP	F	GCAGGGATGATGTTCTGG
	R	CTTTGGTATCGTGGAAGGAC

F/R, forward/reverse primers

The IGF-1expression in tissues

Immunocytochemistry (ICC) was used to measure tissue IGF-1 expression. In general, this method is used to locate or detect subcellular locations of the specific antigens or proteins using labeled antibodies; in which,the antigen-antibody complex is characterized by enzymatic markers and fluorescence dyes or radioactive detection markers. Therefore, cell suspensions were cultured on sterile gelatin lamellae. After 24 h, lamellae were washed with PBS and fixed in 4% paraformaldehyde for 4 min at refrigerated temperature. Lamellae were incubated at ambient temperature for 20 min after washing with PBS in 2-normalHCL.Then, lamellae were exposed to 0.3% Triton X-100[2]for 30 min. Triton permeates cell membranes to antibodies. Then, 10% goat serum was added to the cells for 1.5 h. Goat serum proteins covernon-specific antigenic sites, preventing non-specific reactions. Cells were incubated for 1 h with the primary diluted antibody at a ratio of 1:100 in PBS at refrigerated temperature using humid chamber.Use of parafilm and wet conditions preventeddrying of the antibodies. Then, cells were washed twice with PBS and exposed to the secondary antibody conjugating with a dilution of 1:200 for 60 min at 37° C in darkness. After washing threetimes with PBS, PI or DAPI was used to the samples to stain the cell nuclei. Samples were then studies using fluorescent microscopy.

Statistical analysis

Descriptive and inferential statistical methods were used to analyze data. Descriptive statistics were used to calculate the mean and standard deviation (SD) of the data and inferential statistics were used to compare the groups. Kolmogorov-Smirnov test was used to check the normality of data distribution. Significant t-test ($p \leq 0.05$) was used to compare within-group means. Covariance test was used to compare the two groups. Analysis of covariance (ANCOVA) was used to neutralize effects of the pre-test. The SPSS Software v.21 (IBM Analytics, USA) was used to analyze data and Excel 2013 to design charts. A summary of the statistical results is presented in Tables 3 and 5.

Results

Descriptive data linked to demographic indicators of the participants are presented in Table 3.

Table 3. Demographic indicators of the participants in the two groups

Exercise group	Variable	Mean ±SD
Concentric	Weight (kg)	71.50±8.16
Eccentric	Weight (kg)	72.10±9.61
Concentric	BMI (kg/m^2)	23.45±2.26
Eccentric	BMI (kg/m^2)	24.26±1.97
Concentric	Height (cm)	178.80±4.26
Eccentric	Height (cm)	176.26±4.67
Concentric	Age (year)	26.76±3.45
Eccentric	Age (year)	25.15±2.68

SD, standard deviation

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Based on the results of Table 5, significant differences were seen between the pre and post-test values of BDNF in concentric and eccentric exercise groups ($p \leq 0.05$). However, no significant differences were seen between the pre and post-test values of PAX7 in concentric and eccentric exercise groups(Table 5). Significant differences were observedbetween the pre and post-test values of IGF-1 in concentric and eccentric exercise groups ($p \leq 0.05$).Covariance test was used to assess effects between the groups.To homogenize selected samples and eliminate interfering factors, paired test was used to calculate homogeneity of the samples before pre and post-tests In Table 5, all values are significant based on the reported *p*valuesand their trend was ascending in the two groups.Results of the ANCOVAtable show that there is a significant difference between the two groups in IGF-1 post-test values (p = 0.014,F = 26.227). Based on the results of Table 5, the F value of the intervening variable (BDNF pre-test) is 0.089 and the significance value is p = 0.775, thereforeit can be said that the variable is selected correctly. In addition, results of the ANCOVAtable show that there is no significant difference between the various groups in BDNF post-test values (p = 0.439 and F=0.673).Based on the results of Table 5, the F value of the intervening variable (PAX7 pre-test) is 0.508 and the significance level is p = 0.947, thereforeit can be said that the variable is selected correctly. In addition, results of the ANCOVAtable show that there is no significant difference between the various groups in PAX7 post-test values (p = 0.336 and F = 1.068). Eccentricexercise group ($p \leq 0.05$). Nevertheless, no significant differenceswere reportedbetween preand post-test PAX7 levels of the concentric and eccentric exercise groups ($p \geq 0.05$). Significant differenceswere seenbetween pre and post-test IGF-1 levels in concentric and eccentric exercise groups ($p \leq 0.05$). Protein levels in pre and post-tests in the lateral broad muscles of the two groups using fluorescence microscopy are shown in Fig. 1.

Table 4. Results of the analysis of covariance in post-test values of BDNF, PAX7 and IGF-1 for the effect. assessment of the groups

Variable	Source	DF	Mean squares	F-value	*p*-value
BDNF	Pre-test BDNF	1	-009E1.262	0.089	0.775
	Group	1	-009E9.588	0.673	0.439
	Error	7	-008E1.425		
	Total	10			
PAX7	Pre-test PAX7	1	0.005	0.508	0.947
	Group	1	1.135	1.068	0.336
	Error	7	1.063		
	Total	10			
IGF1	Pre-test IGF1	1	34.085	6.138	0.089
	Group	1	145.908	26.275	0.014
	Error	7	5.553		
	Total	10			

DF, degrees of freedom

Table 5. Results of the dependent sample t-test to compare the means of pre and post-test BDNF, PAX7 and IGF-1 levels in the two groups

Variable	Exercise group	Mean difference	t	DF	*p*-value
BDNF	Concentric	-0.00014	-3.702	4	0.021
	Eccentric	-0.00020	-3.159	4	0.034
PAX7	Concentric	-0.0560	1.789	4	0.014
	Eccentric	-0.721	-1.178	4	0.034
IGF-1	Concentric	-37.406	-13.735	4	0.005
	Eccentric	-33.386	-6.598	4	0.022

DF, degrees of freedom

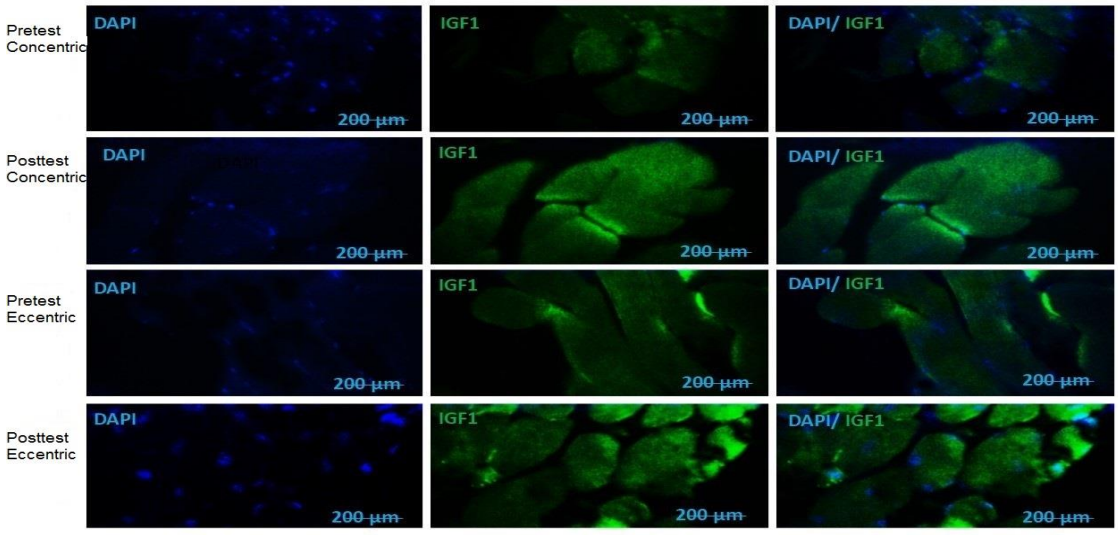

Figure 1. Illustration of IGF-1 protein levels in pre and post-tests in lateral broad muscles of the two groups using fluorescence microscopy.The IGF-1 staining by DAPI in eccentric and concentric groups before and after the tests. Photos are representative of vastus lateralis muscle samples from pre and post-test biopsies of a participant stained with anti-AGF-1.

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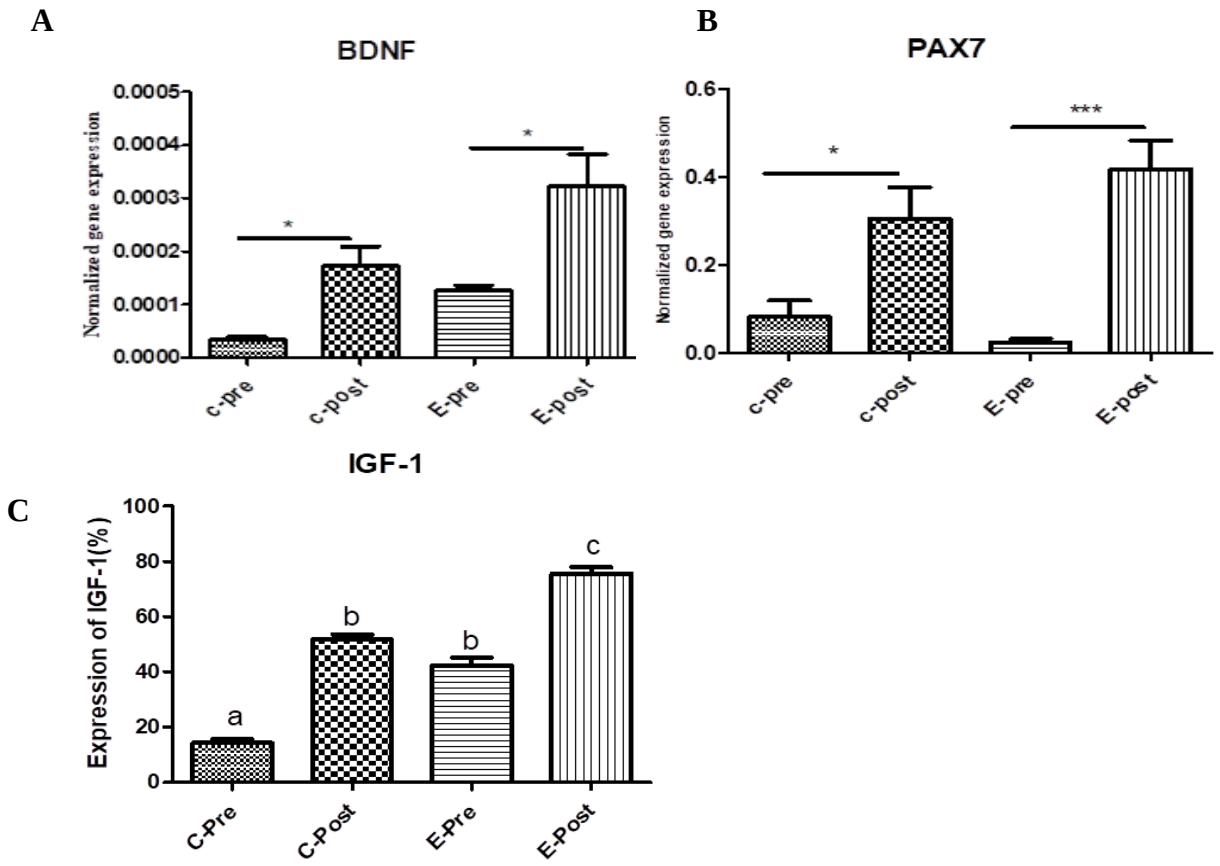

Figure2. Relative expressions of BDNF (A), PAX7 (B) and IGF-1 (C) in pre and post-tests of the two groups. *Significant differencesbetween the preand post-test levels ($p \leq 0.05$). No significant differences were seen between the pre and post-test levels of BDNF and PAX7 in concentric and eccentric exercise groupsbased on the statistical analysis ($p \leq 0.05$). Furthermore, no significant differences were seen between the pre and post-test levels of IGF-1 in concentric and eccentric exercise groups ($p \geq 0.05$).

Discussion

The aim of the present study was to assess effects of a single session of eccentric or concentric resistance exercise on relative expressions of BDNF, PAX7 and IGF-1 in healthy participants. Although this issue is widely verified and empirically accepted based on the principles of repetition, little is known about the molecular mechanisms underlying RE training-induced adaptations. One hypothesis is that following each exercise session, an acute transcriptional response occurs of higher magnitudes following the successive sessions (5). This results in accumulation of cognate proteins (gain of function); thereby, enabling or augmenting key biological processes needed for the adaptation (9, 16, 40). Although this theoretically sounds, principles of repetition during RE training should be explained at various levels (e.g., DNA modifications, mRNA levels, protein levels and posttranslational modifications). Recent high-throughput studies have elucidated transcriptional responses to RE training (26). The fact that muscle contractions can affect muscle hypertrophy due to AA turnover is another metabolic aspect of the present study (1). In the present study, significant differences were seen between pre and post-test BDNF levels of the concentric and eccentric exercise groups. Furthermore, significant differences were seen between pre and post-test PAX7 levels of the concentric and eccentric exercise groups. Significant differences were also observed between pre and post-test IGF-1levels in concentric and eccentric exercise groups.

It has been shown that metabolic efficiency of the eccentric contractions is lower than that of concentric and isometric contractions (1). This is affectedby various factors that trigger neuromuscular signaling pathways. Two mechanisms may generally interact,obesity-related insulin resistance and decreased insulin signaling in the brain may be exacerbated by the chronic peripheral and CNS inflammatory environment associated with obesity. These changes verify changes of IGF-1 in the present study.In fact, IGF-1 is a single-chain 70-AA polypeptide that is produced due to the growth hormone through liver stimulation and is secreted into the bloodstream (21). In the present study, responses to IGF-1 and its expression in eccentric and concentric resistance exercisesin healthy

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participants wereinvestigated. Results showed that intragroup changes of IGF-1 after one session of exercise were significant in eccentric and concentric groups. Intergroup changes showed statistical differences between the two groups. Researchers have reported increased IGF-1 mRNA expression in untrained individuals at various time points after exercises (25, 30, 31). In trainedparticipants, IGF-1 expression increased after exercises.After chronic exercises, baseline IGF-1 levels were upregulated (32). In addition, studies showed that 24 and 48 h after acute exercises, positive IGF-1 upregulation occurred in trained individuals. In untrained individuals, this positive upregulation was not observed (24, 25). The IGF-1 receptor expression was upregulated 2 h after exercises, suggesting that this upregulation was likely to occur more frequently in slow-stressed cords (31). The IGF-1 receptor expressionup to 6 h after exercises suggested that the IGF-1 system might be involved in resistance exercise adaptations (33). In a study with no strong correlations with intensity of exercises, the eccentric partwas shownessential for positive IGF-1Ea expressions, only the concentric part of movements did not lead to positive expressions of this gene (34). Despite increasing total volumes of low intensity exercises, IGF-1R activation increased by 60–65 and 80–85% of one maximum repetition (1RM) 2 and 6 h after exercises (33). Similarly, IGF-1Ea and MRF mRNA expressions increased equally by 60–65 and 80–85% of 1RM 2 h after exercises(31). Based on specific effects of the contraction typesin this study, the eccentric exerciserelativelyincluded highereffects on IGF-1 isoform changes.Bamman et al. (2001) investigatedIGF-1 expression 48 h after eccentric and concentric exercisesin young participants. Results of the study revealed increases only in eccentric contractions(35). In contrast, Adam et al. (2004) reportedthat prolonged eccentric exercisesincluded no effects on IGF-1Ea and MGF levels in muscles of female rats, whereas increases were reported in concentric and isometric contractions (36).

Differences in nature of the stimulation typesappear to contribute to differences in results. It is noteworthy that differences were seen between the groupsin the present study. Muscle damages have been shown to increase IGF-1 in human and rat muscles (37, 38). Exercises in this study appear to trigger injuries, which did not occur in Adam et al. study. Results showed that the relative expression of BDNF in the eccentric group was higher than that in the concentric group with no significant differences. Pedard et al. (2018) showed that exercise-induced increases in BDNF depended on the contraction types (39). Goekint et al. (2010) (40) and Yarrow et al. (2010) (41) were the first researchers to study BDNF responses induced by resistance trainings. Yarow et al. reported a 32% increase in serum BDNF following resistance trainings, whereas Goekint et al. showed a 4% change in BDNF levels following acute resistance trainings. Goekint et al. stated that the intensity of their resistance trainings was low with relatively long rest periods. Yarrow et al. investigated resistance trainings at two various intensities, one consisted of foursets with sixrepetitions of concentric and eccentric contractions and the other one consisted of threesets of sixrepetitions with concentric and eccentric contractions and 100% of one maximal repetition (1RM) (41). The researchers showed temporary increases in BDNF in the twogroups, independent of exercises.Groups were similar according to the volumeof exercises. It is likely that acute strength trainings can stimulate peripheral BDNF underconditions, where the exercise loads are sufficiently intense.Therefore, it can be concluded that the exercise protocols used in the eccentric group of the current study include good intensities to stimulate production of this trophic factor and are good reasons for significant increases in post-exercise BDNF levels. A few studies have assessed thePAX7 changes. In the present study, results showed significant increases in PAX7 in the twogroups. These changes were greater in eccentric group, compared to the baseline. In a study, Karyono et al. (2018) investigated effects of endurance trainings on PAX7 expression changes in rats. Their results showed that low, moderate and high intensity trainings resulted in increased PAX7, which was associated with satellite cells (19). Several studies on satellite cells have investigated the expression of PAX7. The PAX7 is a transcription factor in satellite cells closeto the nucleus and is essential for myogenic and satellite cell regenerations. Sophie et al. (2014) reported that exercise training did not reservedlyincrease satellite cells but rather increased cells that were activated due to the regeneration of muscle fibers (42). However, Schefer et al. (2010) showed that satellite cells per muscle fiber increased after moderate intensity trainings(43).Eileton et al. showed that physical activity and increased BDNF levels improved insulin sensitivity(13). In another study, Bo Lee et al. found that mean serum BDNF levels were significantly lower in patients with T2DM than in controls (15). In the present study, it was shown that eccentric and concentric exercises increased expression of PAX7 in lateral broad muscles. Several adaptations such as increased strength and lean mass are resulted from repetitive resistance exercises due to the high degrees of skeletal muscle flexibility in response to exercise pressures. Various exercise stimuli in resistance exercises can elicit various molecular responses associated with specific adaptations of the skeletal muscles to the types of resistance exercises. Prescribing resistance programsshould be carried outwith careful considerations of manipulating variables. Exercise variables include intensity, volume and time under stress. Hence, manipulation of these variables can affect the results.

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Conclusion

In general, a session of eccentric or concentric exercise leads to significant changes in factors involved in strength and hypertrophy of the skeletal muscles. Since pathological changes in neuromuscular biomarkers are associated with inflammation, obesity, insulin resistance and diabetes, these exercises can be used to prevent these problems, especially in elderly people with sarcopenia. Moreover, these changes are generally greater in eccentric contraction than concentric contraction. Therefore, it can be recommended that athletes who tend to increase muscle hypertrophy and strength should further focus on concentric exercises.

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