

# Changes of Interleukin-6 and brain-derived neurotrophic factor levels following acute plyometric training among inactive men

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## Original Article

### Abstract

**Introduction:** Brain-Derived Neurotrophic Factor (BDNF) plays an important role in transmission of nerve impulses, plasticity, growth, and generally in the health of nervous system. Interleukin-6 (IL-6) is involved in immune and inflammatory responses and is produced by immune cells, fibroblasts, endothelial cells, skeletal muscles, and fat tissues. The aim of this study was investigating the changes of IL-6 and BDNF serum concentration following acute plyometric training among inactive men.

**Methods:** This semi-experimental study was conducted at a gymnasium in Yasuj. A total of 18 inactive men voluntarily participated in the study and were randomly divided in two groups: experimental (n=9) and control group (n=9). Subjects in the acute exercise group performed plyometric trainings consist of scissor jump, lateral hop, box jump, diagonal hop, power skipping, and speed skipping. Subjects' blood samples were taken before and after training in order to measurement IL-6 and BDNF levels. The levels of IL-6 and BDNF were measured using an enzyme-linked immunosorbent assay (ELISA) kits. Between group differences and within group differences were analyzed through independent t-test and dependent t-test, respectively, using SPSS 16 software. The level of significance was considered  $P < 0.05$ .

**Results:** The levels of IL-6 after plyometric trainings significantly increased comparing with the control group, but significant changes wasn't observed in BDNF concentrations.

**Conclusion:** Acute plyometric training did not have any effects on the serum level of BDNF as to the short period of training. However, the significant rise of IL-6 was attributed to the subjects' lack of physical fitness.

**Key words:** IL-6, BDNF, Plyometric Trainings

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### Introduction:

Physical activity makes many physiological changes such as changes in the immune system. An area which has drawn attention among experts in

sport medicine and sport sciences is the positive or negative effect of physical activities on the immune system. Cytokines are peptides or proteins that produced or released by the cells of the human immune system and play major role in the immune

response to pathological stimuli like inflammation and tissue injury. The function of cytokines is different and involved in both useful and harmful responses. This depends on the production level of inner restrainers and the interference with other cytokines (1-3). Some believe that more and more intensive physical activities build up body strength against illnesses. On the other hand, studies have shown that light and average activities create an anti-inflammatory environment and reduce the infection risk. On the opposite side, continuous and intensive exercises may increase the oxidative stress, inflammatory reactions and the infection risk (2).

According to research findings, there are many factors including stress and intensive physical activities bringing forth an acute response determined by changes in immune and inflammatory responses such as increased serum levels of IL-6 (2,3). This cytokine is produced by immune cells, fibroblasts, endothelial cells, skeletal muscles and fat tissue (4). Studies show that increased physical activities and improved life style may reduce IL-6 (5,6). Comparing the effects of two periods of aerobic and strength exercises on the levels of IL-6 among men, Donges et al. (2010) argued that strength exercises significantly reduced IL-6 levels (7). On the contrary, Libardi et al. (2012) studied a 16-weeks period of aerobic, strength and combined exercises. They concluded that heightened consumed oxygen and muscular strength did not make any change in the serum levels of IL-6 (8). On the other hand, Brain-Derived Neurotrophic Factor (BDNF) is a member of the protein family of neurotrophins and facilitate the growth and life of neurons and synaptogenesis. BDNF is highly important in the long-term memory (9). BDNF is made both in the central nervous system and other tissues such as vascular endothelium and stored in platelets. There are other environmental resources facilitate the production of BDNF, immune cells and the cells of vascular soft cells. As BDNF released in the central nervous system is distributed inside the blood flow, BDNF changes can be a reflection of changes in its release in the brain (10). BDNF protects brain against the leukemia-related inflammation by adjusting the levels of cells, cytokines and the transcription factor (11). BDNF reduced the inflammation and

apoptosis in mice in the allergic group. The reduced apoptosis decreases inflammation (12). At the time of environmental inflammation in dorsal root ganglion in mice, BDNF expression and synthesis increase. Its expression also increases at the time of environmental inflammation in nervous injuries (13). Several studies examined the effect of different exercises on BDNF. Seifert et al. (2010) observed the effect of strength exercises in the increased BDNF (14). Johnson et al. (2003) reported that BDNF significantly increased after obligatory running on treadmill for 7 nights (15). Yarrow et al. (2010) concluded that intensive strength exercises temporarily increased the BDNF of blood circulation and regular exercises reinforced such response. It did not though any effect on the rest levels of BDNF (16).

Various intensive exercises, including plyometric training, may cause inflammation. Plyometric trainings are a type of explosive exercises that athlete doing them to build up their ability to jump. Eccentric contractions during plyometric trainings cause muscle injuries among humans and animal models. This increases inflammatory indexes such as IL-6 in blood and muscles (17). Therefore, regarding the probable role of BDNF in coping with inflammation, this study aims to examine the BDNF and IL-6 changes following one session plyometric exercises. Literature review also indicates that in research conducted on BDNF, the effects of strength and aerobic exercises are studied. However, the impact of intensive plyometric exercises on BDNF, as a nervous neurotrophic, has yet to be studied. This question is, thus, raised that do plyometric exercises change the serum levels of BDNF? Or does a session plyometric exercises have any effect on the serum levels of IL-6?

## Methods:

Research subjects included 18 inactive healthy men in Yasouj City that voluntarily participated in the study. Having stated the expectations from subjects during the research and presented the required recommendation, the research reminded participants the conditions including not ever doing plyometric exercises. Subjects were then randomly divided into two groups of exercise and control.

The research plan and the potential risks and benefits were explained to each one, and the consent letter was then completed and signed by them. One week before implementing the research protocol, subjects were familiarized with the research steps. Afterwards, several medical examinations were done to be ensured of subjects' health. In the next phase, the general information about subjects including height, weight, and the body mass index were then measured and registered.

One week after the familiarization stage and teaching the implementation techniques, the workout program including various plyometric exercises was performed. At the beginning, subjects did warm up exercises (running slowly and doing stretching exercises) in a Gymnasium for 10 minutes. The main program (consisting of scissor jump, lateral hop, box jump, diagonal hop, power skipping, speed skipping) was then executed. According to the exercise methodology, each activity was repeated in two or three periods with 6 to 12 iterations. At the end of session, there were 5-minute cold-up movements. Acute plyometric training session was held in the afternoon, supervised by the researcher and assistants. Blood samples (5ml for each time) were collected from the antecubital vein in the stages of pre and post-tests in order to measure the serum levels of BDNF and IL-6. The collected blood samples were put in pre-cooled serum tubes and allowed to be clotted within one hour at the room temperature. Samples were then centrifuged in 1300g within 12 minutes at 4°C. The obtained serum was discharged into

Eppendorf tubes and stored at -80°C to be analyzed. BDNF was measured by ELISA using kits specified to human samples based on the instruction of manufacturer (Boster Biological, China) at the range of 31.2-2000 pg/ml and the method sensitivity of >2pg/ml. IL-6 was also measured by ELISA using kits specified to human samples based on the instruction of manufacturer (EK0410 Boster, China) with the method sensitivity of 0.3 pg/ml. As data distribution was natural based on Kolmogorov-Smirnov test, to compare the difference of between and within groups, independent t-test and dependent t-test were used respectively.

### Results:

Table 1 presents mean values and standard deviation of the age, height, and BMI among research various groups. It was hypothesized that BDNF could be affected by age and BMI.

However, independent t-test showed no significant difference between the two groups. Also the independent t-test showed that the intensive plyometric exercises did not have any effect on the serum level of BDNF (Table 2). The serum levels of IL-6 though significantly increased after plyometric exercises in comparison with the control group (Table 2). Also in exercise group the levels of IL-6 in post-test were significantly increased from pre-test ( $P=0.001$ ). Figure 1 depicts BDNF changes among various groups. IL-6 changes have been shown in figure 2.

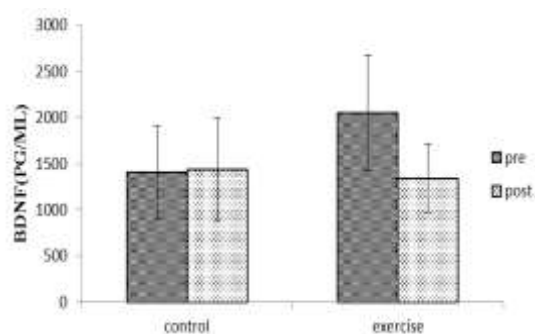
**Table 1. Independent t-test and mean values for age, height, weight, and BMI among various groups**

Group	Age	Height	Weight	BMI
Exercise	22.14±1.34	172.14±3.89	63.85±9.20	21.39±3.06
Control	23.85±2.54	178.57±7.11	71.42±4.5	22.47±1.78
<b>Independent T-test</b>	P=0.09	P=0.03	P=0.04	P=0.46

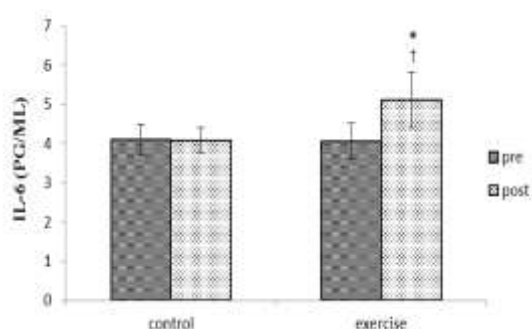
**Table 2. Results of independent t-test for serum levels of BDNF and IL-6**

Factor	Exercise group		Control group		Independent T-test
	Pre	Post	Pre	Post	
BDNF	2050.88±623.18	1343.44±372.51	1404.55±499.19	1636.88±559.44	P=0.209
IL-6	4.06±0.46	5.11±0.71	4.10±0.39	4.08±0.33	P=0.001*

\*: Significantly different from between group  $P \leq 0.05$ .



**Figure 1. Variation of BDNF concentration among different groups**



**Figure 2. Variation of IL-6 concentration among different groups**

\*: significantly different from control group  $p \leq 0.05$ .

†: significantly different from pretest in exercise group  $p \leq 0.05$ .

## Conclusion:

This study examined the effect of intensive plyometric exercises on the serum levels of BDNF and IL-6. Results showed that one session plyometric exercises did not have any effect on the serum level of BDNF. The serum levels of IL-6 though significantly changed after plyometric exercises. While the effect of different physical activities on BDNF has widely studied, this is for the first time that the effect of intensive plyometric exercises on the serum levels of BDNF is studied. You can find many studies conducted on the effect of different physical activities on BDNF. Findings disclose that BDNF is affected by different training stimuli including the intensity, duration, and the type of activity.

Sport protocols, with average or high intensity, have shown that they raise the levels of BDNF (18). Gold et al. (2003) reported that a long session of physical activity (cycling for 30 minutes with the intensity of 60 percent of the maximal oxygen consumption) significantly increase BDNF (19).

Rojas Vega et al. (2006) believed that increasing training session would result in a significant growth of BDNF. However, doing exercise for 10 minutes was shown to be insufficient to significantly increase BDNF comparing with the levels before training (20). Suijo et al. (2013) studied the effect of several voluntary exercises (including aerobic running and strength running over treadmill) for 14 days on the concentration of hippocampal BDNF in mice. Results showed the significant growth of BDNF after 14 days of aerobic and strength running comparing the control group. The growth was though higher in aerobic group than the strength training group. An interesting point was that the researcher found a significant positive correlation between BDNF levels and the workload in the aerobic group. But such correlation was not observed among BDNF and the strength exercises (21). On the other hand, Correia et al. (2010) examined the effect of intensive strength trainings on the serum levels of BDNF. In this study, subjects carried out eccentric and concentric movements (isokinetic contractions) for their elbows and knees for two consecutive days. At the end, measures did not show any significant change in BDNF (22). Our results support Correia's et al. findings, but they are not aligned with other research. The trainings considered for this research may have not been sufficiently intensive to stimulate the release of BDNF. According to Cassilhas et al. (2012), strength trainings affect brain through factors such as insulin growth factor 1(IGF1) and active kinas T (AKT). However, aerobic trainings affect brain by factors such as BDNF (23).

Therefore, insignificantly changed BDNF, in this paper, may be because of doing plyometric exercises, which are a type of strength trainings.

The study also found out that IL-6 increased following one session plyometric exercises. In a research on 14 young cyclists, Paczak et al. (2006) studied the effect of intensive physical activities on the serum levels of IL-6. They observed a significant increase in IL-6 immediately (two hours) after workout (24). Libardi et al. (2012) concluded that there was no change in IL-6 levels after 16 weeks strength, aerobic, or combined exercises (8). Recent studies reported results agreeing or rejecting the findings of this research. Workout program, subjects' preparation, intensity, duration and the

type of training are considered the reasons of results differences (25). IL-6 seems to be more sensitive to the exercise intensity than volume of training. This is the indirect indicator of muscular mass involved in contractive activities. The other effective factor is probably the type of muscle fiber. In this research, as inactive people with relatively low physical fitness were studied and the exercises were comparatively heavy, the type II muscle fiber was more probably worked resulting in a growth in IL-6 (26). Generally, lack of physical fitness and applying high pressures before reaching a good fitness may increase inflammatory markers such as IL-6 in blood and muscles. To increase the production of BDNF and reduction of IL-6 in muscles and blood, the exercises are suggested to be carried out longer and with higher intensity or even at the same time with an allowed supplement.

Due to some limitations, present study was conducted only on men and it did not account for gender differences. Therefore, the results are not generalizable to women. Another study can be done on female subjects to generalize the results to women.

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## تغییرات غلظت اینترلوکین - ۶ و فاکتور نوروتروفیک مشتق از مغز به دنبال تمرین حاد پلیومتریک در مردان غیر فعال

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### چکیده

**مقدمه:** فاکتور نوروتروفیک مشتق از مغز نقش مهمی در انتقال پیام‌های عصبی، تغییرپذیری عصبی، رشد نرونی و به طور کلی سلامت دستگاه عصبی انسان ایفا می‌کند. هدف از این پژوهش، بررسی تأثیر یک جلسه تمرین پلیومتریک بر غلظت سرمی اینترلوکین ۶ و فاکتور نوروتروفیک مشتق از مغز مردان غیرفعال بود. اینترلوکین ۶ در ایمنی و پاسخ‌های التهابی نقش دارد و توسط سلول‌های ایمنی، فیبروبلاستها، سلول‌های اندوتلیال، عضلات اسکلتی و بافت چربی تولید می‌شود.

**روش کار:** این مطالعه به صورت نیمه تجربی در مجموعه ورزشی در شهر یاسوج انجام شد. برای این منظور ۱۸ مرد غیرفعال به صورت داوطلبانه در این تحقیق شرکت نمودند و به طور تصادفی به ۲ گروه تجربی (۹ نفر) و کنترل (۹ نفر) تقسیم شدند. آزمودنی‌های گروه تمرین، تمرینات پلیومتریک شامل (جست سرعتی، جست قدرتی، پرش قیچی، پرش زانو بالا، لی لی از پهلو، لی لی مورب، پرش روی جعبه) را انجام دادند. خون‌گیری از افراد پیش و پس از برنامه تمرینات به منظور اندازه‌گیری اینترلوکین ۶ و BDNF به عمل آمد. سطوح اینترلوکین ۶ و BDNF با استفاده از کیت آزمایشگاهی و روش الایزا اندازه‌گیری شد. تفاوت‌های بین گروهی و درون گروهی به ترتیب با استفاده از آزمون‌های آماری تی مستقل و تی همبسته، با استفاده از نرم افزار SPSS 16 انجام شد. سطح معنی‌داری هم ( $P < 0/05$ ) در نظر گرفته شد.

**نتایج:** غلظت سرمی IL-6 پس از تمرین پلیومتریک حاد در مقایسه با گروه کنترل تغییر معنی‌داری یافت ولی سطوح سرمی BDNF تغییری پیدا نکرد.

**نتیجه‌گیری:** یک جلسه تمرین پلیومتریک تأثیری بر سطوح سرمی BDNF ندارد که می‌تواند به دلیل دوره کوتاه تمرینی باشد. اما افزایش معنی‌دار IL-6 می‌تواند به دلیل عدم آمادگی جسمانی آزمودنی‌ها باشد.

**کلیدواژه‌ها:** BDNF، IL-6، تمرین پلیومتریک

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