©Journal of Sports Science and Medicine (2009) 8, 219-224
http://www.jssm.org

Research article

Effects of acute moderate and strenuous exercise bouts on IL-17 production and inflammatory response in trained rats

Halil Duzova ✉, Yunus Karakoc, Memet Hanifi Emre, Zumrut Yilmaz Dogan and Evren Kilinc
Department of Physiology, Inonu University Faculty of Medicine, 44280 Malatya, Turkey

Abstract
In this study, we aimed to compare the effects of a single bout of acute moderate and strenuous running exercise on the production of interleukin-17 (IL-17), interleukin-6 (IL-6), interleukin-1 receptor antagonist (IL-1ra) and inflammatory response of skeletal muscles in regularly trained rats. Eight week old rats were trained by treadmill running 5 days per week for 13 weeks at the durations of 30 min (moderate) and 60 min (strenuous). Two days after the last training session, the animals were subjected to a single bout of moderate or strenuous exercise and serum samples were analyzed for IL-17, IL-6, IL-1ra levels and myeloperoxidase (MPO) activity of gastrocnemius muscle were determined. IL-17 level significantly increased in strenuous exercise group when compared to that of sedentary controls ($p < 0.01$), On the other hand, only in the moderate exercise group, there was a negative correlation between IL-6 and IL-17 levels ($r = -0.857$ and $p = 0.014$). In conclusion, acute single bout of strenuous exercise increased IL-17 production in trained rats and, this cytokine may be involved in inflammatory process of skeletal muscles.

Key words: Interleukin-17, cytokines, running, exercise, rat.

Introduction

There have been many reports of altered immune function after acute exercise, both increase and decrease, depending on the immune cell investigated (Rowbottom and Green, 2000). The influence of chronic exercise has also been studied in both animal and human models. Several studies using training protocols of varying durations and intensities in human and different animal species support the findings of increased resting levels of endogenous cytotoxicity after voluntary exercise (Pedersen and Hoffman-Goetz, 2000).

Strenuous exercise increases production of several pro- and anti-inflammatory cytokines, endogenous cytokine inhibitors and chemokines (Pedersen et al., 2001). Unaccustomed and strenuous exercise can also cause neutrophil activation and muscle damage that involves protein degradation and ultra structural changes (Komulainen et al., 1998; Peake et al., 2005; Sorichter et al., 1999). High intensity exercise results in neutrophil translocation to the active skeletal muscle, subsequently resulting in oxidative stress. High blood levels of neutrophil myeloperoxidase (MPO) and elastase levels can be elevated immediately post-exercise (Quindry et al. 2003). In addition, phagocyte infiltration in to muscle is found after strenuous exercise (Sorichter et al., 1999; Aoi et al., 2004; Niess et al., 1999; Tidball et al., 1995). Several studies demonstrated that exercise induces production of cytokines, especially interleukin-6 (IL-6) and interleukin-1 receptor antagonist (IL-1ra) (Ostrowski et al., 2000; Ronsen et al., 2002; Rosendal et al., 2005). Ostrowski et al. (2000). found that marathon running resulted in a 100-fold increase in plasma IL-6 concentration whereas a less strenuous treadmill running resulted in only a 25-fold increases.

Plomgaard et al. (2005) reported that skeletal muscle is recently recognized as an endocrine organ with the capacity to produce signaling peptides in response to muscle contractions. It has also been demonstrated that resting healthy human muscles express cytokines in a fiber type specific manner, such as tumor necrosis factor (TNF)-alpha and interleukin-18 (IL-18) is solely expressed by type II fibers, whereas the expression of IL-6 in more prominent in type I compared to type II fibers (Plomgaard et al., 2005).

Several experimental and clinical evidences show that IL-17 family members are involved in specific inflammatory processes leading to the mobilization of granulocytes. Most published evidence supports a role for IL-17A and possible IL-17F, as a promoter of granulopoeisis, neutrophil accumulation, and neutrophil activation in the lung, joint space, central nervous system, and intestinal tissue (Kolls and Linden, 2004). In human, it has been demonstrated that IL-17, a cytokine derived from activated CD4 cells, increases the release of the major human chemoattractant, the C-X-X chemokine, interleukin-8 (IL-8), in human bronchial epithelial and venous endothelial cells in vitro (Laan et al., 1999). On the other hand, it has been showed that IL-17 increases neutrophil elastase and myeloperoxidase concentration in rat airways in vivo (Hoshino et al., 2000). However, the positive in vivo finding on IL-17 contrasts with the negative finding in vitro (Hoshino et al., 2000; Prause et al., 2004).

Although IL-17 is a T cell-derived, proinflammatory cytokine that is suggested to be involved in the development of various inflammatory diseases (Nakae et al., 2003; Sigal, 2004), IL-6 secretion (Borish and Steinke, 2003) and neutrophil activation in tissue (Hoshino et al., 2000), there is not any knowledge about the effects of moderate or strenuous exercise on its production. Likewise, the role of IL-17 and its association with neutrophil activation in inflammatory process in skeletal muscle has not been elucidated in exercise models. Additionally, acute effects of moderate and strenuous running exercise on immune functions have not been evaluated in trained

Received: 23 January 2008 / Accepted: 24 February 2009 / Published (online): 01 June 2009

Table 1. Weekly variation in treadmill speed, inclination, and running time of moderate exercise group.

Days		Weeks 1	2	3	4	5	6	7	8-13
Monday	$cm \cdot sec^{-1}$	17	17	19	22	28	32	37	45
	Grade(°)	5	10	15	15	15	15	18	18
	Minutes	15	15	30	30	30	30	30	30
Tuesday	$cm \cdot sec^{-1}$	17	17	19	22	28	32	37	45
	Grade(°)	5	13	15	15	15	15	18	18
	Minutes	15	15	30	30	30	30	30	30
Wednesday	$cm \cdot sec^{-1}$	17	19	19	22	28	32	37	45
	Grade(°)	8	13	15	15	15	15	18	18
	Minutes	15	15	30	30	30	30	30	30
Thursday	$cm \cdot sec^{-1}$	17	19	19	22	28	32	37	45
	Grade(°)	8	15	15	15	15	15	18	18
	Minutes	15	15	30	30	30	30	30	30
Friday	$cm \cdot sec^{-1}$	17	19	22	28	32	37	45	45
	Grade(°)	10	15	15	15	15	15	18	18
	Minutes	15	30	30	30	30	30	30	30

athletes. In this study, we aimed to compare the acute effects of single bout of moderate and strenuous exercise on the production of IL-17, IL-6, IL-1ra and inflammatory response of skeletal muscle in regularly trained rats.

Methods

Animals

Twenty-five Wistar-Albino adult male rats were used in the study. Principles of laboratory animal care (NIH publication) were followed, and Inonu University Ethic Committee of Experimental Animals (Malatya, Turkey) approved this study protocol. The control (n = 10), 30 min (moderate) exercise (n = 8) and 60 min (strenuous) exercise (n = 7) groups of rats were housed in three groups in colony cages, at ambient temperature of 23 °C with a 12-h/12-h light/dark cycle. The animals had free access to water and pellet chow containing 1.8-2.2 % of calcium, 1.1 % of phosphorus and 2650 kcal/kg energy.

Training protocol

Moderate and strenuous exercises were performed by using an animal treadmill system that allows to four animals to run at the same time. In this study, we used a training protocol for treadmill running described by Rico et al. (1999). As previously described in above cited article, our training protocol was consisted of treadmill running 5 days per week for 13 weeks. The steep grade treadmill incline was used to stimulate high-intensity muscle activity in rats. The rats in moderate and strenuous exercise groups started training 8 weeks old and acquainted to the treadmill exercise with a minimal progression during a week. In this period, running time was gradually increased from 15 min to 30 and 60 min per session for moderate and strenuous exercise groups, respectively. Treadmill speed increased to 45 $cm \cdot sec^{-1}$ with increments of 2-3° to reach a final grade inclination of 18°. The chronological progression in the treadmill speed, grade inclination, and running time are shown in the Table 1 and Table 2. Control rats were kept in the cages at the same environmental conditions and inspected daily to control their health.

Measurements

To evaluate the acute effects of single bout moderate and strenuous exercise, an additional single bout running was performed 48 hours after the training protocols were over. Ten minutes after a single bout of treadmill training (13

Table 2. Weekly variation in treadmill speed, inclination, and running time of strenuous exercise group.

Days		Weeks 1	2	3	4	5	6	7	8-13
Monday	$cm \cdot sec^{-1}$	17	17	19	22	28	32	37	45
	Grade(°)	5	10	15	15	15	15	18	18
	Minutes	15	15	60	60	60	60	60	60
Tuesday	$cm \cdot sec^{-1}$	17	17	19	22	28	32	37	45
	Grade(°)	5	13	15	15	15	15	18	18
	Minutes	15	15	60	60	60	60	60	60
Wednesday	$cm \cdot sec^{-1}$	17	19	19	22	28	32	37	45
	Grade(°)	8	13	15	15	15	15	18	18
	Minutes	15	15	60	60	60	60	60	60
Thursday	$cm \cdot sec^{-1}$	17	19	19	22	28	32	37	45
	Grade(°)	8	15	15	15	15	15	18	18
	Minutes	15	15	60	60	60	60	60	60
Friday	$cm \cdot sec^{-1}$	17	19	22	28	32	37	45	45
	Grade(°)	10	15	15	15	15	15	18	18
	Minutes	15	45	60	60	60	60	60	60

Table 3. Initial body weights of rats in control, moderate and strenuous exercise groups and their alterations at the end of training. Data are means (±SD, grams).

	Initial	At the end of training
Control (n=10)	155.0 (5.7)	232.8 (20.6)
Moderate Exercise (n = 8)	164.0 (4.1)	295.8 (16.7) **
Strenuous Exercise (n = 7)	160.1 (7.9)	269.4 (15,5)

** $p < 0.01$ and difference from initial value.

weeks), blood samples were withdrawn from the abdominal aorta under intraperitoneal ketamine and xylasine anesthesia. Serum IL-6, IL-17 and IL-1ra levels were measured by ELISA (Organon Technica Microwell, Italy) using commercial ELISA kits (rat IL-1ra and IL-6 Bio-source International, Inc., USA; rat IL-17 Market Inc., USA). The minimum detectable limits of IL-1ra, IL-6 and IL-17 were to be 12, 8, 5 $pg \cdot ml^{-1}$, respectively.

In order to evaluate inflammation in skeletal muscles, MPO activity of gastrocnemius muscle was also determined by biochemical technique using UV-Visible Spectrophotometer (Shimadzu UV-1601, Japan) (Bradley et al., 1982). Tissue samples, approximately 200 mg, were homogenized with homogenizer (Tempest Virtishear, Model 278069; The Virtis Company, Gardiner, NY, USA) in 3 ml of 50 $mmol \cdot l^{-1}$ potassium phosphate buffer, pH 6. One milliliter of homogenate was centrifuged at 10,000 *g* for 10 min at 4°C, and pellet was suspended in 1 ml of (50 $mmol \cdot l^{-1}$) potassium phosphate buffer, containing 0.5% hexadecyl–trimethyl ammonium bromide (Sigma) to negate peroxidase activity of hemoglobin and myoglobin and to solubilize membrane-bound MPO. Oxidized *o*-dianisidine forms a stable chromophore absorbing at a 460 nm wavelength. One unit of MPO activity is defined as that required, to degrade 1 μmol of H_2O_2 per minute at 25°C. Protein concentration was determined with Lowry method (Lowry et al., 1951). Values were calculated as mU of MPO per milligram of protein.

Statistics

SPPS for Windows 13.0 version was used to analyze of data. Normality of data was analyzed by Shapiro Wilks normality test. Because of the not normal distribution of all variables ($p < 0.05$), Wilcoxon tests were used to compare body weights of rats between pre- and post-exercise periods. Kruskal-Wallis and Bonferroni Mann-Whitney U tests were used to compare variables among the groups. Spearman's correlation was also used to correlate variables, and $p < 0.05$ was regarded to be statistically significant.

Results

Initial body weights of rats in control, moderate and strenuous exercise groups and their alterations at the end of training protocol were shown in the Table 3. Increase in body weight at the end of training was found to be significant only in moderate exercise group when compared to initial values ($p < 0.01$).

Mean and standard errors of serum IL-1ra levels were found 86.50 ± 19.87; 107.50 ± 14.33; 121.91 ± 22.34 pg/ml in control, moderate and strenuous exercise groups, respectively. They were 56.37 ± 13.58; 232.93 ± 104.63; 165.03 ± 87.18 $pg \cdot ml^{-1}$ for IL-6 and, 52.41 ± 17.98; 90.86 ± 35.13; 308.74 ± 74.60 $pg \cdot ml^{-1}$ for Il-17. Additionally, MPO activities of gastrocnemius muscle were also 26.13 ± 1.43; 26.56 ± 0.95; 32.37 ± 5.24 $U \cdot g^{-1}$ wet tissue in the above mentioned groups, respectively.

Comparison of serum IL-1ra, IL-6, IL-17 levels and muscle MPO activity of rats in control, moderate and strenuous exercise groups were also shown in the Figure 1. In both moderate and strenuous exercise groups, there were no significant changes in serum IL-6, IL-1ra levels or MPO activity when compared to those of sedentary controls. However, IL-17 level was significantly increased in the strenuous exercise group ($p < 0.01$) whereas not changed in the moderate exercise group when compared to the controls ($p > 0.05$). There was not any significant change in any parameters between two exercise groups. Additionally, in moderate exercise group, there was a negative correlation between IL-6 and IL-17 levels ($r = -0.857$ and $p = 0.014$).

Discussion

Our results show that a single bout of strenuous exercise increases serum IL-17 level in rats whereas a single bout of moderate exercise does not change its production in rats trained for two types of exercise model by treadmill running for 13 weeks. In our study, we also found that single bouts of both moderate and strenuous exercise elevated serum IL-6 levels in trained groups of rat, but these elevations were not statistically different from the basal levels of control group. Additionally, IL-1ra level slightly increased in both exercise groups and this result was not correlated to increase in serum IL-6 level in these exercise groups. In both moderate and strenuous exercise groups, there were no significant changes in MPO activities in gatrocnemius muscle and in blood lactate levels when compared to those of controls.

Skeletal muscle has been recognized as an endocrine organ, and muscle cell cultures express several cytokines with potential hormonal effects (Akerstrom et al. 2005). Contracting muscle fibers produce and release IL-6, and plasma levels of this cytokine are markedly elevated in response to physical exercise (Keller et al. 2005). Increased plasma IL-6 is observed after intense, prolonged exercise (Haddad et al., 2005; Rosendal et al., 2005).

It is well known that IL-6 stimulates the production of IL-1ra, which binds to and blocks the IL-1 receptor, thus exerting strong anti-inflammatory effects. With exercise, peak IL-1ra is found 1-2 h after the peak of IL-6. From this, it is assumed that the level of IL-1ra reflects the production of IL-6 (Ronsen et al., 2002). In our study, insignificant increases in IL-6 levels in moderate and strenuous exercise groups may be due to limited number of animals in control and exercise groups or the training protocols we used. However, our findings indicate that IL-6 production may not correlate with the duration of chronic running exercise because the elevation of IL-6 in the strenuous exercise group was less than the moderate exercise group (Figure 1). We found that serum IL-1ra level slightly increased in both exercise groups and this result was not correlated to non-significant increase in serum IL-6 level in these exercise groups. The elevation of IL-6 level may be related to duration of exercise. It was demonstrated that there was a negative correlation between serum IL-6 concentration and running time and positive correlation between plasma IL-6 concentration and running intensity (Ostrowski et al., 2000).

Based on our present data and the literature, one could speculate that a single bout of strenuous exercise increases IL-17 production. This cytokine activates macrophages and fibroblasts, secretion of cytokines and stromal cells, including their expression of intercellular adhesion molecule-1 (ICAM-1), and secretion of cytokines (IL-6, IL-8, IL-11), granulocyte-colony stimulating factor [G-CSF]), prostaglandin E_2, and nitric oxide (Borish et al. 2003; Sigal, 2004). MPO activity is another marker of neutrophil activation. It is a catalyzing enzyme that metabolizes superoxide radicals produced during neutrophil activation (Dularay et al., 1990). It has been speculated that IL-17 can activate neutrophils in association with their recruitment into the airways in vivo (Hoshino et al.,2000). However, similar activation of MPO by IL-17 for the skeletal muscle is not known. In our study, in contrast to plasma IL-6 level, tendencies of increases in serum IL-1ra and IL-17 are parallel to the duration of treadmill exercise. Increase in MPO levels of gastrocnemius muscle of rats especially in strenuous exercise group may also be related to the duration of running exercise. In the whole blood or plasma, biochemical markers strictly correlated with MPO activity may help to determine tissue damage in skeletal muscle of human. From our results, serum or plasma IL-17 level may be a useful biochemical marker to determine acute exercise-induced inflammation in skeletal muscles of trained animals or human subjects. However, we did not show any significant correlation between serum IL-17 level and muscle MPO activity because of limited number of rats in our experimental groups.

Conclusion

In conclusion, in regularly trained rats, a single bout of acute strenuous running exercise markedly elevated IL-17 production, which may be associated with inflammation of skeletal muscle while performing acute exercise. This preliminary result should be supported by forthcoming studies that investigate the role of IL-17 in acute inflammatory process of skeletal muscle.

Acknowledgments

We thank to Prof. Dr. Riza Durmaz and Biologist Ahmet Tuna, from the Department of Microbiology, Inonu University Faculty of Medicine, for analyzing of interleukins and Cemal Yerli for performing treadmill exercise.

This research was supported by Inonu University Scientific Research Foundation (Project number: 2003/33)

References

Akerstrom, T., Steensberg, A., Keller, P., Keller, C., Penkowa, M. and Pedersen, B.K.(2005) Exercise induces interleukin-8 expression in human skeletal muscle. *Journal of Physiology* 563(2), 507-516.

Aoi, W., Naito, Y., Takanami, Y., Kawai, Y., Sakuma, K., Ichikawa, H., Yoshida, N. and Yoshikawa, T. (2004) Oxidative stress and delayed-onset muscle damage after exercise. *Free Radical Biology* and *Medicine* 37(4), 480-487.

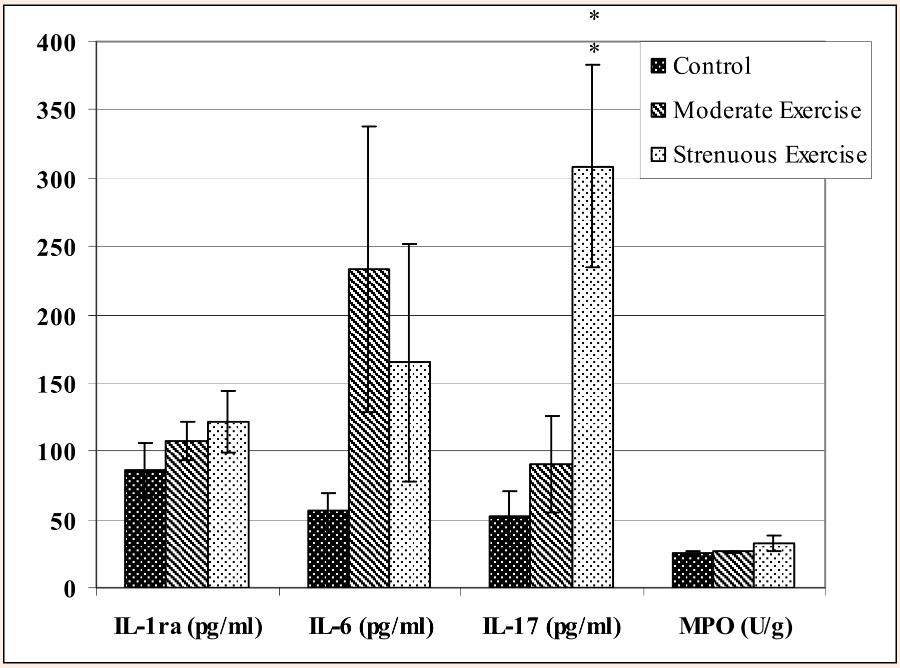

Figure 1. Comparison of serum IL-1ra, IL-6, IL-17 levels, and muscle MPO activities (mean±standard error) among the groups. ** $p < 0.01$ and difference from control group.

Borish, L.C. and Steinke, J.W. (2003) 2. Cytokines and chemokines. *Journal of Allergy* and *Clinical Immunology* 111(Suppl. 2), S460-475.

Bradley, P.P., Priebat, D.A., Christensen R.D. and Rothstein, G. (1982) Measurement of cutaneous inflamation: Estimation of neutrophil content with an enzyme marker. *Journal* of Investigative *Dermatology* 78, 206-209.

Dularay, B., Elson, C.J., Clements-Jewery, S., Damais, C. and Lando, D. (1990) Recombinant human interleukin-1 beta primes human polymorphonuclear leukocytes for stimulus-induced myeloperoxidase release. *Journal* of Leukocyte *Biology* 47(2), 158-163.

Haddad, F., Zaldivar, F., Cooper, D.M. and Adams, G.R. (2005) IL-6-induced skeletal muscle atrophy. *Journal* of *Applied Physiology* 98(3), 911-917.

Hoshino, H., Laan, M., Sjostrand, M., Lotvall, J., Skoogh, B.E. and Linden, A. (2000) Increased elastase and myeloperoxidase activity associated with neutrophil recruitment by IL-17 in airways in vivo. *Journal of Allergy* and *Clinical Immunology* 105(1 Pt 1),143-149.

Keller, P., Penkowa, M., Keller, C.A., Steensberg, A., Fischer, C.P., Giralt, M., Hidalgo, J. and Pedersen, B.K. (2005) Interleukin-6 receptor expression in contracting human skeletal muscle: regulating role of IL-6. *The FASEB Journal* 19(9), 1181-1183. Epub.

Kolls, J.K. and Linden, A. (2004) Interleukin-17 family members and inflammation. *Immunity* 21(4), 467-476.

Komulainen, J., Takala, T.E., Kuipers, H. and Hesselink, M.K. (1998) The disruption of myofibre structures in rat skeletal muscle after forced lengthening contractions. Pflügers Archiv European Journal of Physiology 436(5), 735-741.

Laan, M., Cui, Z.H., Hoshino, H., Lotvall, J., Sjostrand, M., Gruenert, D.C., Skoogh, B.E. and Linden, A. (1999) Neutrophil recruitment by human IL-17 via C-X-C chemokine release in the airways. *The Journal of Immunology* 162(4), 2347-2352.

Lowry, O., Rosenbraugh, N., Farr, L, and Rondall, R. (1951) Protein measurement with the folin–phenol reagent. *Journal* of *Biological Chemistry* 183, 265-275.

Nakae, S., Saijo, S., Horai, R., Sudo, K., Mori, S. and Iwakura, Y. (2003) IL-17 production from activated T cells is required for the spontaneous development of destructive arthritis in mice deficient in IL-1 receptor antagonist. *Proceedings of the National Academy of Sciences USA* (PNAS) 100(10), 5986-5990.

Niess, A.M., Dickhuth, H.H., Northoff, H. and Fehrenbach, E. (1999) Free radicals and oxidative stress in exercise--immunological aspects. *Exercise Immunology* Review. 5, 22-56.

Ostrowski, K., Schjerling, P. and Pedersen, B.K. (2000) Physical activity and plasma interleukin-6 in humans--effect of intensity of exercise. *European Journal* of *Applied Physiology* 83(6), 512-515.

Peake, J.M., Suzuki, K., Wilson, G., Hordern, M., Nosaka, K., Mackinnon, L. and Coombes, JS. (2005) Exercise-induced muscle damage, plasma cytokines, and markers of neutrophil activation. *Medicine* & *Science* in *Sports* & *Exercise* 37(5), 737-745.

Pedersen, B.K. and Hoffman-Goetz, L. (2000) Exercise and the immune system: regulation, integration, and adaptation. Physiological Reviews 80(3), 1055-1081.

Pedersen, B.K., Steensberg, A. and Schjerling, P. (2001) Exercise and interleukin-6. *Current* Opinion in *Hematology* 8(3), 137-141.

Plomgaard, P., Penkowa, M. and Pedersen, B.K. (2005) Fiber type specific expression of TNF-alpha, IL-6 and IL-18 in human skeletal muscles. *Exercise Immunology* Review 11, 53-63.

Prause, O., Bozinovski, S., Anderson, G.P. and Linden, A. (2004) Increased matrix metalloproteinase-9 concentration and activity after stimulation with interleukin-17 in mouse airways. *Thorax*. 59(4), 313-317.

Quindry, J.C., Stone, W.L., King, J. and Broeder, C.E. (2003) The effects of acute exercise on neutrophils and plasma oxidative stress. *Medicine* & *Science* in *Sports* & *Exercise* 35(7), 1139-1145.

Rico, H., Gervas, J.J., Hernandez, E.R., Seco, C., Villa, LF, Revilla, M. and Sanchez-Atrio, A. (1999) Effects of alprazolam supplementation on vertebral and femoral bone mass in rats on strenuous treadmill training exercise. Calcified Tissue International 65(2), 139-142.

Ronsen, O., Lea, T., Bahr, R. and Pedersen, B.K. (2002) Enhanced plasma IL-6 and IL-1ra responses to repeated vs. single bouts of prolonged cycling in elite athletes. *Journal* of *Applied Physiology* 92(6), 2547-2553.

Rosendal, L., Sogaard, K., Kjaer, M., Sjogaard, G., Langberg, H. and Kristiansen, J. (2005) Increase in interstitial interleukin-6 of human skeletal muscle with repetitive low-force exercise. *Journal* of *Applied Physiology* 98(2), 477-481.

Rowbottom, D.G. and Green, K.J. (2000) Acute exercise effects on the immune system. *Medicine* & *Science* in *Sports* & *Exercise* 32(Suppl. 7), S396-405.

Sigal, L.H. (2004) Interleukins of current clinical relevance (Part I). *Journal of Clinical Rheumatology* 10(6), 353-359.

Sorichter, S., Puschendorf, B. and Mair, J. (1999) Skeletal muscle injury induced by eccentric muscle action: muscle proteins as markers of muscle fiber injury. *Exercise Immunology* Review 5, 5-21.

Tidball, J.G. (1995) Inflammatory cell response to acute muscle injury. *Medicine* & *Science* in *Sports* & *Exercise* 27(7), 1022-1032.

Key points

- A single bout of acute strenuous running exercise markedly elevated IL-17 production.
- This preliminary result should be supported by forthcoming studies that investigate the role of IL-17 in acute inflammatory process of skeletal muscle.

AUTHORS BIOGRAPHY

Halil DUZOVA

Employment

Assoc. Prof. of Physiology, Inonu University Faculty of Medicine.

Degree

MD

Research interest

Neutrophil, exercise, cytokin.

E-mail:

hduzova@inonu.edu.tr hduzova@hotmail.com

Yunus KARAKOC

Employment

Assoc. Prof. of Biophysics, Inonu University Faculty of Medicine.

Degree

PhD

Research interest

Hemorheology.

E-mail: ykarakoc@inonu.edu.tr

Memet Hanifi EMRE

Employment

Prof. of Physiology, Inonu University Faculty of Medicine.

Degree

PhD

Research interest

Learning, memory and antioxidant.

E-mail: hemre@inonu.edu.tr

Zumrut Yilmaz DOGAN

Employment

Research Assistant.

Degree

MSc

Research interest

Expermenit animals.

E-mail: byozumrut@hotmail.com

Evren KILINC
Employment
Research Assistant.
Degree
MSc
Research interest
Hemorheology.
E-mail: evren_kilinc@yahoo.com

✉ **Halil Duzova, MD, Assoc. Prof.**
Department of Physiology, Inonu University Faculty of Medicine, 44280 Malatya Turkey