Brazilian Journal of Biomotricity
ISSN: 1981-6324
marcomachado@brjb.com.br
Universidade Iguaçu
Brasil

Damirchi, Arsalan; Rahmani-Nia, Farhad; Mehrabani, Javad
EFFECT OF A SINGLE BOUT GRADED EXERCISE ON THE CYTOKINES RESPONSE AND INSULIN RESISTANCE INDEX
Universidade Iguaçu
Itaperuna, Brasil

Available in: http://www.redalyc.org/articulo.oa?id=93018957008
EFFECT OF A SINGLE BOUT GRADED EXERCISE ON THE CYTOKINES RESPONSE AND INSULIN RESISTANCE INDEX

Arsalan Damirchi, Farhad Rahmani-Nia, Javad Mehrabani

Department of Exercise physiology, University of Guilan, Rasht, Iran

Corresponding author:
Dr. Arsalan Damirchi
Associate Professor in Exercise Physiology
Department of Exercise physiology
University of Guilan, Rasht, Iran
P.O. Box: 1438
Phone: 0098-131-6690685
Fax: 0098-131-6690675
E-mail: arsaland388@gmail.com

Submitted for publication: Apr 2011
Accepted for publication: May 2011

ABSTRACT
DAMIRCHI, A.; RAHMANI-NIA, F.; MEHRABANI, J. Effect of a single bout graded exercise on the cytokines response and insulin resistance index. Brazilian Journal of Biomotricity, v. 5, n. 2, p. 132-140, 2011.Interleukin-1 beta (IL-1 beta) the same as Lipocalin-2 (LCN2) is identified a new acute phase protein that secreted by adipose tissue. Effects of acute trainings, particularly the graded exhaustive exercise on these adipokine is unknown. We examine the changes of these adipokines in nine obese (Ob) and nine normal weight (NW) inactive middle-aged (37-49 yrs) males in response to a Bruce treadmill running. Body mass index (BMI), body fat percent (BFP), waist circumference (WC), and waist to hip ratio (WHR) were higher in Ob subjects than the NW. The initial IL-1 beta concentration were 0.08±0.011 pg/ml in Ob and 0.06±0.012 pg/ml in NW subjects (p=0.043). After the exercise, concentration of IL-1 beta was significantly higher than the pre-exercise in Ob (0.21±0.016 pg/ml; p=0.0001) and NW (0.17±0.015 pg/ml; P=0.002) subjects. The LCN2 concentrations were 152.4±29.3 µg/l and 141±36.5 µg/l in Ob and NW subjects at baseline, respectively (P=0.001). After the exercise, concentration of IL-1 beta was significantly higher than the pre-exercise in Ob (0.21±0.016 pg/ml; p=0.0001) and NW (0.17±0.015 pg/ml; P=0.002) subjects. The LCN2 concentrations were 152.4±29.3 µg/l and 141±36.5 µg/l in Ob and NW subjects at baseline, respectively (P=0.001). LCN2 concentration was increased in Ob subjects by 9.2% (152.4±29.3 to 176.9±30.5 µg/l; P=0.012) and NW by 11% (141±36.5 to 155.7±37.3 µg/l; P=0.032) after exercise than the baseline. The HOMA-IR was decrease significantly by 75% in OB (2.8±0.5 to 1.6±0.5) and by 44.4% in NW (2.6±0.9 to 1.8±0.8) after the exercise. Participation in acute incremental exercise may be led to more increasing of blood inflammatory markers in obese and non-obese males and these changes are considerable in obese individuals. So, it seems participation in an exhaustive graded exercise may not be a useful effort for inactive males.

Key Words: Acute exercise, Obesity, Interleukin-1 beta, Lipocalin-2, Insulin resistance.
INTRODUCTION

Acute exercises lead to an increase in pro-inflammatory markers in the circulatory pathway. This status results in metabolic changes during exercise such as increasing of glucose use (BEAVERS et al. 2010) and blood LA accumulation (BLOOMER & COLE, 2009). Thus, acute exercise activates an immune response and increases inflammatory cytokines in circulation. During inflammation, Lipocalin-2 (LCN2) is produced in different organs, such as adipocytes (WANG et al., 2007) and liver (COSTA et al., 2010). That seems to be an attractive candidate that potentially relates obesity-linked inflammation (SHEN et al., 2006; WANG et al., 2007; YAN et al., 2007). Indeed, measurement of LCN2 might be a striking marker for obesity-related metabolic and cardiovascular diseases (WANG et al., 2007). The response of LCN2 to a single bout of graded exercise is not investigated in obese inactive individuals yet. Only in a study performed by Spiropoulos et al. (2010), it was shown that LCN2 concentrations reached to maximum value in athletes who participated in an ultra-distance foot race (SPIROPOULOS et al., 2010). The reason of this increase is not clear. That seems elevation of leukocyte and interleukin 1 beta (IL-1 beta) concentrations is effective. Spiropoulos et al. showed an increase in leukocyte turnover after an ultra-distance race (SPIROPOULOS et al., 2010). Sommer et al. (2009), also, have reported that increase of LCN2 concentration is due to IL-1 beta effect (SOMMER et al., 2009). They showed that an upregulation of LCN2 by IL-1 beta implicating a potential role of this adipocyte-secreted acute phase reactant in the development of insulin resistance, obesity, and associated disorders, including cardiovascular disease (SOMMER et al., 2009). IL-1 beta is one of the most potent pro-inflammatory cytokine that has the metabolic and immunologic function (BOURKE et al., 2003). Drenth et al. has been show the IL-1 beta production increased two-fold in ten recreational trained athletes immediately after the 5-km run (DRETH et al., 1998). This cytokine expressed by many cells, including monocytes and neutrophils (METKAR et al., 2008) and via CRP effect, it has been associated with increased cardiovascular risk (LAMANTE et al., 2002).

Taking into account that exercise intensity could affect the immune response and a graded training has severe problems, some authors have suggested that the metabolism complication induced by this type of exercise could initiate apoptotic processes, resulting in the lymphopenia observed after this type of exercise (LAMANTE et al., 2002; YAN et al., 2007).

Generally, this objective that performing an exhaustive exercise is useful or hurtful is problematic. Many studies have been shown take part in a single bout graded exercise lead to concentration of inflammatory markers, including acute-phase proteins and adipokines in circulation (CANCELLO et al., 2005; TATARANNA & ORTEGA, 2005). Although the effect of an acute graded exercise on the immune function and response of more adipokines is confirmed, but the response of IL-1 beta and LCN2 to this type of exercise has not been investigated yet. Our goal in this study was to determine interleukin-1 beta and lipocalin-2 response and insulin resistance index to an exhaustive exercise (graded Bruce protocol).

MATERIAL AND METHODS

Participants

Eighteen middle-aged male (37-49 yrs) who had volunteered to this take part, nine obese and nine normal-weight sedentary male were divided in two groups according to BMI classification and did not participation in a regular exercise program. For inclusion,
screening session (7-day before exercise), all participants were asked to complete a health and readiness questionnaire and obtained a consent form. The subjects were familiarized with protocol and walked on the treadmill. The subjects who had been smoking, cardiovascular diseases, bypass surgery, diabetes, chronic kidney and liver disease, or were taking medication that could have affected the results were excluded (MOHEBBI et al., 2009). The subjects were guided not to do any exercise and do not change their diet until the measurement day. Second day (6-day before exercise), all subjects completed a graded test to volitional exhaustion by measuring maximal oxygen uptake (VO2max) with an automated open circuit gas analysis system (Cosmed, Quark b2, Italy) at baseline.

Procedure and measurements

On the test day, body composition components were measured using a Body Composition Analyzer (Inbody 3.0®, Biospace Co Ltd, Seoul, Korea) as well as on the screening session. Blood pressures were assessed above the left brachial artery after 30 minutes rest in the prone state with an electronic sphygmomanometer (HESTIA Mannheim, Japan). After warming up (5 min treadmill jogging and stretching), the subjects completed a graded exercise treadmill according to the Bruce protocol (HEYWARD & STOLARCZYK, 1996; BRUCE et al., 1973). In this protocol, the treadmill is set up with the stage 1 (speed 2.74 km/hr), and grade of slope (10% that increases by 2% per stage). Exercise heart rate was recorded using a telemetric device with monitor (Polar, Kempele, Finland). The exercise was stopped when the subjects were exhausted or perceived exertion (stress) was 19 according to Borg 6-20 perception of effort scale (BRUCE et al., 1973; BORG, 1982). Then the subjects had a 5 min cooling down. All the measurements were done in two sequential mornings from 800-10:00 AM.

Blood sampling

The samples were collected after 12 hours overnight fasting. They kept at -20 °C for subsequent assay. Samples were obtained by venipuncture after 45 min resting before the exercise. The collection procedure was repeated immediately after exercise. IL-1 beta and LCN2 were assessed with specific enzyme linked sorbent immuno assays (ELISA, R&D Systems, Minneapolis, MN). All samples were analyzed in duplicates or triplicates. According to the manufacturer, the intra-assay CVs for IL-1 beta and LCN2 were less than 1.0% and 1.7%, respectively. The enzymatic RANDOX Laboratories LC, UK, test was used for LA accumulation. Glucose level was determined by enzymatic (GOD-PAP, Glucose Oxidase-Amino Antipyrine) colorimetric method (Pars Azmoun, Tehran, Iran) and insulin level was measured by a radioimmunoassay (RIA). Insulin resistance index was calculated regarding the homeostasis model assessment (HOMA-IR) according to the formula (ESTEVE et al., 2009): HOMA-IR = [fasting glucose (mmol/l) × fasting insulin (mU/l) / 22.5]. Total leukocyte count was determined by a laboratory routine method.

Data analysis

Findings are shown as mean ± standard deviation (SD). Mann whitney U or student t tests were used for the analysis of the before/after changes in measured variables. A SPSS software, Ver. 13 (SPSS Inc., Chicago, IL) was used and p<0.05 was considered statistically significant.

RESULTS

Somatic and physiological variables

Data have been shown in table 1 (characteristics and body composition) and table 2
(physiological variables). The Ob subjects had higher measures in body mass, BMI, fat mass, lean mass, waist circumference, waist-hip ratio, and lower values in running time and maximal oxygen uptake than NW (p<0.05).

Table 1- Values of characteristics and body composition components in the participants (mean ± SD).

<table>
<thead>
<tr>
<th>Variable Group</th>
<th>Age (yrs)</th>
<th>Body mass (kg)</th>
<th>BMI (kg/m²)</th>
<th>PF (%)</th>
<th>FM (kg)</th>
<th>LM (kg)</th>
<th>WC (cm)</th>
<th>WHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ob (n=9)</td>
<td>43.2±4.6</td>
<td>87.7±10.2</td>
<td>31.4±1.6</td>
<td>24.0±3.2</td>
<td>20.8±4.6</td>
<td>65.9±7</td>
<td>89.8±3.8</td>
<td>0.93±0.03</td>
</tr>
<tr>
<td>NW (n=9)</td>
<td>42.9±4.4</td>
<td>69.5±6.2</td>
<td>23.0±1.7</td>
<td>17.8±3.4</td>
<td>12.4±2.8</td>
<td>57.1±5.1</td>
<td>78±3.7</td>
<td>0.82±0.04</td>
</tr>
<tr>
<td>Sig*</td>
<td>0.913</td>
<td>0.002*</td>
<td>0.0001*</td>
<td>0.002*</td>
<td>0.001*</td>
<td>0.014*</td>
<td>0.0001*</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

* All data are expressed as the mean ± SD. Independent t test or Mann Whitney U was used to compare means of components between the Ob (obese) and NW (normal weight) groups. BMI: body mass index; PF: percentage of fat; FM: fat mass; LM: lean mass; WC: waist circumference; WHR: waist-hip ratio.

Table 2- Values of physiological parameters linked to the exercise (mean ± SD).

<table>
<thead>
<tr>
<th>Variable Group</th>
<th>Running time (min:s)</th>
<th>Maximal uptake (ml/kg/min)</th>
<th>Oxygen stress perception</th>
<th>RHR (b/min)</th>
<th>MHR (b/min)</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ob (n=9)</td>
<td>12.48±2.1</td>
<td>31.6±1</td>
<td>18.4±1.3</td>
<td>81±2.3</td>
<td>174±3.2</td>
<td>126.1±14.6</td>
<td>80.2±8.8</td>
</tr>
<tr>
<td>NW (n=9)</td>
<td>14.57±2.3</td>
<td>34.1±1.5</td>
<td>18.2±1.4</td>
<td>79±3.4</td>
<td>173±3</td>
<td>120.1±12</td>
<td>79.8±7.7</td>
</tr>
<tr>
<td>Sig*</td>
<td>0.001*</td>
<td>0.002*</td>
<td>0.112</td>
<td>0.151</td>
<td>0.244</td>
<td>0.386</td>
<td>0.906</td>
</tr>
</tbody>
</table>

Independent t test or Mann whitney U was used to compare means of parameters between the Ob and NW groups. RHR: rest heart rate; MHR: maximal heart rate; BP= blood pressure.

Cytokine response

The changes of IL-1 beta and LCN2 before and after the exercise are presented in table 3. The initial IL-1 beta concentration was 0.08±0.011 pg/ml in Ob and 0.06±0.012 pg/ml in NW subjects (P=0.043). After the exercise, concentration of IL-1 beta was significantly higher than the pre-exercise in Ob (0.21±0.016 pg/ml; P=0.0001) and NW (0.17±0.015 pg/ml; P=0.002) subjects. The LCN2 concentrations were 152.4±29.3 µg/l and 141±36.5 µg/l in Ob and NW subjects at the baseline, respectively (P=0.001). LCN2 concentration was increased in Ob subjects by 9.2% (152.4±29.3 to 176.9±30.5 µg/l; P=0.012) and NW by 11% (141±36.5 to 155.7±37.3 µg/l; P=0.032) after than the baseline.
After the graded exercise, a significant decrease was observed in HOMA-IR (table 4) in obese (2.6±0.9 vs. 1.8±0.8; \( p < 0.001 \)) and normal-weight (2.8±0.5 vs. 1.6±0.5; \( p < 0.001 \)) subjects after the treadmill exercise. Moreover, insulin level decreased in both obese (11.8±8.9 vs. 9.2±5.5 mU/l; \( P = 0.012 \)) and normal-weight (12.1±9.1 vs. 7.6±5.2 mU/l; \( P = 0.002 \)) individuals after exercise in comparison with baseline. Furthermore, total leukocyte counts were raised significantly in Ob subjects by 15.9% (7.9±2.2 to 12.6±2.7 ×10⁹cell.L⁻¹; \( P = 0.001 \)) and NW by 13.9% (8.2±2.3 to 11.4±2.5 ×10⁹cell.L⁻¹; \( P = 0.002 \)) than the baseline. LA level also was elevated by 4.2 fold in Ob group (1.7±0.2 to 7.2±0.4 mmol/l; \( P = 0.0001 \)) and by 3.6 fold in NW group (1.9±0.2 to 6.8±0.5 mmol/l; \( P = 0.0001 \)).

Table 4- Values of Insulin (mU/l), Glucose (mmol/l), HOMA-IR, Leukocyte count (×10⁹cell.L⁻¹), and blood lactate (mmol/l) in Ob and NW subjects before/after a graded treadmill exercise (\( mean \pm SD \)).

<table>
<thead>
<tr>
<th>Variable Group</th>
<th>Insulin Before</th>
<th>After</th>
<th>Glucose Before</th>
<th>After</th>
<th>HOMA Before</th>
<th>After</th>
<th>Leukocyte Before</th>
<th>After</th>
<th>Leukocyte Blood lactate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ob (n=9)</td>
<td>11.8±8.9</td>
<td>9.2±5.5 †</td>
<td>5.6±0.6</td>
<td>4.5±0.3 †</td>
<td>2.6±0.9</td>
<td>1.8±0.8 †</td>
<td>7.9±2.2</td>
<td>12.6±2.7 †</td>
<td>1.7±0.2</td>
</tr>
<tr>
<td>NW (n=9)</td>
<td>12.1±9.1</td>
<td>7.6±5.2 †</td>
<td>5.4±0.6</td>
<td>4.6±0.5 †</td>
<td>2.8±0.5</td>
<td>1.6±0.5 †</td>
<td>8.2±2.3</td>
<td>11.4±2.5 †</td>
<td>1.9±0.2</td>
</tr>
</tbody>
</table>

Independent \( t \) test or Mann whitney U was used to compare of the independent groups (\( p < 0.05 \)); paired \( t \) test to before/after changes (\( p < 0.05 \)). Ob: obese; NW: normal weight; HOMA: homeostasis model assessment; BLa: blood lactate.

**DISCUSSION**

In this investigation, we assessed the effect of a single bout treadmill exercise on the adipocytokines that are related with inflammation and cardiovascular diseases in obese and normal weight male. We observed a notable increase in concentration of IL-1 beta, LCN2 and leukocyte in both groups, particularly in obese individuals. IL-1 beta is a major pro-inflammatory marker that is linked to obesity-induced diseases. It seems the increasing of IL-1 beta is a common response to acute exercise. Moldoveanu et al. (MOLDOVEANU, et al., 2000) in a unique investigation have been showing a considerable increase in IL-1 beta concentration in ten untrained men due to a 60 min ergometer exercise with 60-65% \( V_O2 \)peak before and after 60 min treadmill running with same intensity. They showed an initial plasma IL-1 beta concentration of 0.04 pg/ml had increased to 0.19 and 0.59 pg/ml by 60 and 180 min into exercise, respectively. Same to
them, we find a significant elevation of 0.08 and 0.06 to 0.21 and 0.17 pg/ml in Ob and NW subjects after the exercise than the baseline. In agreement, Drenth et al. has been show a double increasing in IL-1 beta production after the 5-km run (DRENTH et al. 1998). It may be due to actions of TNFα and interleukin-1 receptor antagonist (IL-1ra) in a whole-blood culture system that stimulated with bacterial lipopolysaccharide (LPS) (DRENTH et al. 1998). It is clear that a single bout exercise induced an elevation in circulating pro-inflammatory markers (MOLDOVEANU et al., 2000; SHEK et al., 1995). It seems the observed changes in the present study are predictable. It may be due to metabolic events and immune function during exercise, including the increase of glucose use, lactate accumulation and leukocyte counts (MOLDOVEANU et al., 2000); also, during exercise, metabolic changes may results in decreased TNFα and IL-1 beta production (PEDERSEN et al., 2003). It is due to activation of an immune response during acute exercise that enhances lipid and glucose metabolism. However, although IL-1 beta has traditionally been understood to be a main inducer cytokine of acute phase reactions, the majority of studies have shown that the circulating concentration of this cytokine is either unchanged following exercise, or exhibits relatively small, delayed increments (SUZUKI et al., 2002). It need to more studies to achieve stronger results. In turn, chronic exercise can lead to lower basal levels of circulating inflammatory markers, as well as reduce the inflammatory response to acute exercise (BEAVERS et al. 2010).

The response of LCN2 to acute exercise is unknown; although Choi et al (CHOI et al., 2009) did not observe any changes in LCN2 concentration after 8 weeks exercise training in obese women, we observed a notable elevation in LCN2 concentration in obese than normal-weight individuals, same as IL-1 beta and level and leukocyte count. This event may be is due to increase that’s expression in fat cells (LAW et al., 2010), metabolism process, increase of other inflammatory signs, including hs-CRP and leukocyte count. We observed a considerable increase in hs-CRP (data not shown) and leukocyte concentrations after the exercise. It has reported that the acute exercise results in a first, rapid and profound neutrophilia (increase in blood neutrophil count) which is linked to intensity and duration of exercise. This increase is likely due to demargination caused by shear stress and catecholamines (WALSH et al., 2011).

There has been showing a positive relation between LCN2 and hs-CRP concentrations (CHOI et al., 2009). Furthermore, increasing of LCN2 secretion from fat cells may be stimulated by lipopolysaccharides (LPS) that suggesting LCN2 as an acute phase protein (WANG et al., 2007). It, also, can impair energy homeostasis and systemic metabolism by TNFα effect and other inflammatory markers (PEDERSEN et al., 2003) and increased the risk for insulin resistance (CHOI et al., 2009; YAN et al., 2007) and diabetes (WANG et al., 2007). It is likely that there is a complex interconnection between LCN2, metabolic complications due to obesity and inflammation. Body mass and fat percentage can be effective. It has been suggested that the increased fat mass might account for the elevated the LCN2 concentration in obese individuals (CHOI et al., 2009; WANG et al., 2007). So, LCN2 can be used by researchers and clinicians as an inflammatory marker same as IL-6, TNFα and hs-CRP (CHOI et al., 2009; WANG et al., 2007). Clearly the response of LCN2 to acute exercises did not investigate and need to more studies. According to findings, it seems the exercise-induced acute phase inflammation results in an increase in IL-1 beta and LCN2 in obese and normal-weight individuals.

We showed also an elevation in insulin values after the exercise. Insulin has a critical role in the metabolism process and identified as major component of metabolism complications such as insulin resistance and type 2 diabetes mellitus. That reaction to single bout or longitudinal training might be different. It has been demonstrated that single bout of exercise increases the glucose disposal by means of insulin in normal and obese
individuals that had insulin resistance (CIOLAC & GUIMARAES, 1998). These changes may be a reflex of an increase in glucose uptake during exercise. There are situations in which the acute exercise does not increase the insulin sensibility, and it may even worsen it. The insulin sensibility is decreased after the marathon running same to after incremental exhaustive exercises (CIOLAC & GUIMARAES, 1998). This discussion is in contrast with our finding.

PRACTICAL APPLICATION

In summary, the results of this study indicate that the concentration of IL-1 beta and LCN2 same as HOMA-IR were increased in normal weighted and obese males after the graded exercise. These changes were more considerable in obese individuals.

ACKNOWLEDGMENT

We most appreciate all the participants of this research. The study was supported by a grant from University of Guilan, Research Division.

REFERENCES


