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Changes of necdin concentration after a bout of intensive aerobic exercise in obese and lean men

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Abstract

Introduction: Necdin is an important negative regulator of white adipogenesis. The acute effect of aerobic exercise on necdin concentration is unclear; therefore the present study was conducted to determine the effects of a bout of intensive aerobic exercise on necdin concentration in obese and lean men.

Material & Methods: Eighteen sedentary obese (Age: 21.7 ± 2.1 and BMI: 33.7 ± 2.1 kg/m^2; ± SD, n = 9) and lean (Age: 20.5 ± 0.7 and BMI: 17.6 ± 1.6 kg/m^2; ± SD, n = 9) men volunteered to participate in this study. All the subjects were performed the Bruce test as the intensive aerobic exercise. Blood samples were taken before and immediately after the intensive aerobic exercise.

Results: No significant differences were observed at baseline in necdin concentration between obese and lean subjects

(35.8 ± 24.2 *vs.* 21.9 ± 16.2 pg/ml; P = 0.2 respectively). After an intensive aerobic exercise necdin concentration increased significantly in the lean subjects (21.9 ± 16.2 to 65.9 ± 86.1 pg/ml; P = 0.01) however no significant changes were observed in the obese subjects (35.8 ± 24.2 to 36.9 ± 19.3 pg/ml; P = 0.5). The results revealed that necdin concentration was higher in the lean subjects in compare to the obese subjects (P = 0.03) in response to a bout of intensive aerobic exercise.

Conclusion: The results of present study suggest that necdin concentration increases in response to acute aerobic exercise in lean subjects. Future studies are needed to examine the effect of exercise training on necdin levels in the obese subjects.

Keywords: Intensive exercise, Preadipocyte proliferation, Necdin, Obesity, Adipose tissue

1. Introduction

Obesity causes many serious diseases such as type 2 diabetes mellitus, cardiovascular diseases, hypertension, and certain types of cancer (1). Fat mass expands by increasing the volume and/or the number of adipocytes in white adipose tissues. Although increased lipid storage in white adipocytes has been thought to be a major cause of fat mass expansion, recent studies have suggested that adipocyte number is also a key determinant for fat mass (2,3). The number of adipocytes in obese individuals is larger than that in lean individuals, a difference established during childhood and adolescence (2). White adipose tissues are composed mainly of white fat cells (adipocytes) is a highly active metabolic and endocrine organ, which plays an important role in energy storage and metabolism (4). White adipocyte number is most likely controlled by the rate of preadipocyte proliferation, because white adipocytes are terminally differentiated postmitotic cells and arise from their preadipocytes or mesenchymal stem cells residing in white adipose tissues. Therefore, preadipocyte proliferation may contribute to the etiology of obesity. However, the molecular mechanisms that regulate

preadipocyte proliferation during adipose tissue development are still unclear. Necdin that encoded by the NDN gene in humans (5), originally identified as a gene product induced in neurally differentiated embryonal carcinoma stem cells (6). Previous studies demonstrated that postmitotic cells such as neurons and skeletal myocytes are the main resources of necdin gene expression (7,8). Expression of the necdin gene is controlled through genomic imprinting, a placental mammal-specific epigenetic mechanism (9,10). Hayashi et al. (1995) indicated that, necdin might complement retinoblastoma protein to prevent postmitotic neurons from resuming cell proliferation (11). Necdin also, interacts with viral oncoproteins and cellular E2F family proteins (12,13). Furthermore, necdin contribute in apoptosis suppresses (14). It binds to the tumor suppressor protein p53 and inhibits p53-dependent apoptosis, whereas these two proteins suppress cell proliferation (14). These findings suggest that necdin serves as an anti- cell proliferation and anti-apoptotic protein in postmitotic cells (15). Exercise training is a useful strategy for improving obesity and decrease adipocytes (16); however the mechanisms that exercise training effect on obesity not well known. In only available study, Moghadasi et al. (2017) examine the effect of concurrent training on necdin concentration in sedentary middle-aged men. The authors reported that necdin concentration had not significant changes after 8 weeks of concurrent training (17). The acute effect of aerobic exercise on necdin concentration is unclear; therefore the present study was conducted to determine the effects of a bout of intensive aerobic exercise on necdin concentration in obese and lean men.

2. Material & Methods

Subjects

Nine sedentary obese men (BMI: 33.7 ± 2.1 kg/m^2; ± SD) and nine sedentary lean men (BMI: 17.6 ± 1.6 kg/m^2; ± SD) volunteered to participate in this study. All the subjects were asked to complete a personal health and medical history questionnaire, which served as a screening tool. The subjects were given both verbal and written instructions outlining the experimental procedure, and written informed consent was obtained. The study was approved by the Islamic Azad University, Marvdasht branch Ethics Committee.

Measurements

Anthropometric and body composition measurements

Height was measured with a fixed stadiometer (Seca, Germany) and weight was measured with a regularly calibrated electronic scale (Seca, Germany). Body mass index (BMI) was calculated by dividing weight (kg) by height (m^2). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm). Body fat percentage was assessed by skinfold thickness protocol. Skinfold thickness was measured sequentially, in chest, abdominal, and thigh by the same investigator using a skinfold caliper (Harpenden, HSK-BI, British Indicators, West Sussex, UK) and a standard technique (18).

Biochemical analyses

Blood samples were collected at rest (before training) and immediately after a bout of intensive aerobic exercise. Blood sample was obtained by venipuncture and plasma obtained was frozen at –22 °C for subsequent analysis. The plasma necdin level was measured using an enzyme-linked immunosorbent assay (ELISA) kits (BioCEP, China). The sensitivity of kit was 24 pg/ml.

Intensive aerobic exercise

All the subjects were performed the Bruce test as the intensive aerobic exercise. This test includes 7 phases. This test is done on the treadmill and started with low intensity; every 3 minutes. The speed and the gradient (slope) of the device increased up to the level in which the subject could not perform the test anymore and became totally exhausted. For hart rate control during the exercise, each participant was equipped with a heart rate monitor (Polar, FS3c, Finland).

Statistical analysis

All values were expressed as means ± SE. Statistical significance was set at $P<0.05$. To compare parameters of the two groups, the Mann–Whitney U-test using unpaired data was used. Pre *vs.* post-exercise

differences were evaluated using Wilcoxon test. The statistical software program SPSS.19 was used for all data analysis.

3. Results

Anthropometric and body composition parameters of the subjects are presented in Table 1. The results indicated that body weight, BMI, body fat percent and WHR were higher in the obese group in compare to the lean group ($P<0.05$).

Table 1. Anthropometric and body composition parameters (mean ± SD) of the subjects

	Obese group (mean±SD)	Lean group (mean±SD)
Age (Year)	21.7 ± 2.1	20.5 ± 0.7
Body weight (Kg)	107.5 ± 5.7*	59.3 ± 4.5
BMI (Kg/m^2)	33.7 ± 2.1*	17.6 ± 1.6
WHR	1.14 ± 0.01*	0.81 ± 0.04
Body Fat (%)	34.5 ± 2.1*	6.8 ± 1.6

*$P<0.05$ for between-group differences.

Changes of necdin concentration in response to intensive aerobic exercise in the obese and lean subjects are presented in the Figure 1.

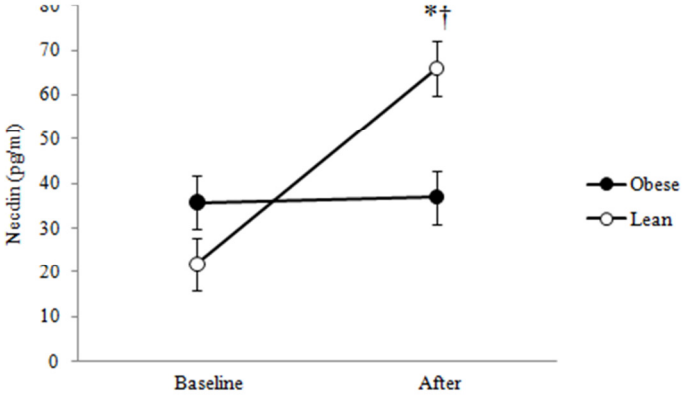

Figure 1. Changes of necdin concentration in response to intensive aerobic exercise in the obese and lean subjects
* Significant differences for Pre-Post exercise; $P<0.05$
† Significant differences for between group; $P<0.05$

No significant differences were observed at baseline in necdin concentration between obese and lean subjects (35.8±24.2 *vs.* 21.9±16.2

pg/ml; P=0.2 respectively). After an intensive aerobic exercise necdin concentration increased significantly in the lean subjects (200.9 % increases; P=0.01) however no significant changes were observed in the obese subjects (3.07% increases; P=0.5). The results revealed that necdin concentration was higher in the lean subjects in compare to the obese subjects (P=0.03) in response to a bout of intensive aerobic exercise.

4. Discussion

Previous studies indicated that necdin serves as an anti- cell proliferation and anti-apoptotic protein in postmitotic cells (15). On the other hand, exercise training is a useful strategy for improving obesity and decrease adipocyte tissue (16); however the mechanisms that exercise training effect on obesity not well known. The aim of present study was to determine the effects of a bout of intensive aerobic exercise on necdin concentration in obese and lean men. Surprising, the results of present study indicated that there are no significant differences in necdin concentration between obese and lean subjects. White adipose tissues are composed mainly of white fat cells (adipocytes), which play a key role in energy storage and metabolism. White adipocytes are terminally differentiated postmitotic cells and arise from their progenitor cells (preadipocytes) or mesenchymal stem cells residing in white adipose tissues. Thus, white adipocyte number is most likely controlled by the rate of preadipocyte proliferation, which may contribute to the etiology of obesity (19). Necdin, which is expressed predominantly in postmitotic neurons, is a pleiotropic protein that possesses anti-mitotic and pro-survival activities. Fujiwara et al. (2012) showed that necdin functions as an intrinsic suppressor of preadipocyte proliferation both *in vivo* and *in vitro* to control the adipocyte number during white adipose tissue development (19). The number of adipocytes in obese individuals is larger than that in lean individuals, a difference established during childhood and adolescence (2). Furthermore, adipocyte number increases in certain depots even in human adults after excessive food intake (3). Because adipocytes are differentiated from multipotent mesenchymal stem cells or preadipocytes residing in white adipose tissues (20-22), stimulated preadipocyte proliferation during white adipose tissue development may contribute primarily to an increase in adipocyte

number. In mice, preadipocytes in the stromal-vascular compartment of white adipose tissues can proliferate in response to excessive calorie intake and differentiate into mature adipocytes (23).

Fujiwara et al. (2012) reported that necdin was expressed in white adipose tissue stromal-vascular cells expressing $CD34^+$ and $Sca\text{-}1^+$ (19), both of which are markers of mesenchymal stem cells or preadipocytes (24). They also indicated that necdin was expressed in αSMA^+ and $PDGFR\beta^+$ vascular cells (19), which potentially differentiate into adipocytes (25). Fujiwara et al. (2012) found that necdin-expressing stromal-vascular cells differentiate not only into adipocytes but also into osteocytes, chondrocytes, myocytes, and neuron-like cells (19). In another study, Pamuklar et al. (2013) demonstrated that necdin gene expression in the adipose tissue were significantly down-regulated after gastric bypass surgery when compared with obese and were similar to levels observed in the lean controls (26). This discrepancy results may be due to study population and necdin assessment. The subjects of the present study were sedentary obese and lean men without any calorie restriction or weight control regimen; however the subjects of the Pamuklar's study underwent the gastric bypass surgery. Furthermore, we were assessed plasma necdin concentration while necdin gene expression was measured in the Pamuklar's study.

The results of the present study revealed that necdin concentration increased significantly in the lean subjects after a bout of intensive aerobic exercise; however no significant changes were observed in the obese subjects. Attempts to determine effects of exercise training on necdin levels are very little and by our knowledge there is only one study that has determined the effects of concurrent training on necdin concentration. Moghadasi et al. (2017) investigated the effects of 8 weeks concurrent training on necdin levels in obese middle-aged men. They reported that necdin concentration had not significant changes after 8 weeks of concurrent training (17). The authors reported that exercise induced-changes in necdin concentration might needs large magnitude of weight reduction and long terms exercise training (17). According to our results, although basal necdin concentration was higher in the obese subjects, but there was no significant differences in the necdin concentration at baseline between the lean and the obese subjects and

necdin concentration was increased significantly in the lean subjects in response to a bout of intensive aerobic exercise thus it seems that adipocyte number, type, intensity, volume and duration of exercise may be attribute in necdin concentration. Further studies are needed to determine the effects of exercise on necdin concentration.

5. Conclusion

The results of present study suggest that there are no significant differences in the necdin concentration between the lean and the obese subjects and necdin concentration increases in response to acute aerobic exercise in lean subjects. It seems that magnitude of weight reduction is the main factor for exercise induced-changes in necdin concentration in the obese subjects; however future studies are needed to examine the effect of exercise training on necdin levels in the obese subjects.

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Conflict of interests: None of the authors declare competing financial interests.

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