Comparative Exercise Physiology, 2018; 14 (1): 55-61

How high-fat diet and high-intensity interval training affect lipid metabolism in the liver and visceral adipose tissue of rats

M. Ebrahimi[1], R. Fathi[1*], Z. Ansari Pirsaraei[2], E. Talebi Garakani[1] and M. Najafi[2]

[1]Department of Exercise Biochemistry and Metabolism, University of Mazandaran, Shahid Beheshti Ave, Babolsar 47416-13534, Iran; [2]Department of animal science and fishery, Sari Agricultural Sciences and Natural Resources University, Farah Abad, Sari 4818168984, Iran; r.fathi@umz.ac.ir

Received: 31 May 2017 / Accepted: 1 August 2017

RESEARCH ARTICLE

Abstract

Lipogenic and lipolytic pathways are tightly regulated by nuclear receptors and binding proteins, such as farnesoid x receptor (*FXR*) and sterol regulatory element binding protein 1c (*SREBP-1c*). We designed this research to study the effects of high-intensity interval training (HIIT) and high-fat diet (HFD) on hepatic and adipose *FXR* and *SREBP-1c* gene expression beside the plasma levels of lipid profile and insulin. 24 male Wistar rats were randomly divided into normal (~12% fat) and HFD (~56% fat) groups with or without participating in the 8 weeks HIIT protocol. Results from two-way ANOVA and Pearson tests ($P<0.05$) showed that the HFD rats experienced a larger weight gain correlated with dyslipidemia and hyperinsulinemia, higher hepatic and adipose *SREBP-1c* expression and lower hepatic *FXR* expression compared with normal diet fed rats. Although HIIT rats showed higher hepatic *FXR* and lower hepatic and adipose *SREBP-1c* expression and lower weight gain compared with untrained rats, plasma lipid profile levels had not any significant difference between trained and untrained rats. Interestingly, hepatic *FXR* expression was negatively correlated with weight gain and *SREBP-1c* expression in both tissues while only the hepatic *SREBP-1c* was positively correlated to insulin levels. In conclusion, HFD-induced dyslipidemia could occur via the activation of the hepatic *SREBP-1c* pathway under the insulin effect. Although HIIT rats showed lower *SREBP-1c* correlated to hepatic *FXR* activation it seems diet is more effective on lipid profile than HIIT. Also, in presence of HFD, HIIT only affects adipose lipolysis.

Keywords: HIIT, high fat diet, *FXR*, *SREBP-1c*, insulin, lipid profile

1. Introduction

Postprandial high fat diet (HFD)-induced dyslipidemia has been shown to be an independent risk factor for metabolic and cardiovascular diseases (Tan *et al.,* 2014). Lifestyle interventions are mostly used for lipid lowering effects. It has been shown in human studies, that even one session of aerobic (Kolifa *et al.,* 2004) or resistant (Petitt *et al.,* 2003) exercise can reduce postprandial triglyceride (TG) content in a sex-independent manner that apparently is related to increased lipoprotein lipase activity and decreased endogenous hepatic very low-density lipoprotein (VLDL) secretion (Tan *et al.,* 2014). Increased hepatic lipolytic pathways after exercise appear to decrease liver free fatty acid stores, resulting in decreased endogenous hepatic synthesis and secretion of TG-rich VLDLs (Magkos, 2009). Lipogenic and lipolytic pathways are regulated by hormones and transcriptional factors, such as insulin (Tan *et al.,* 2014), farnesoid x receptor (*FXR*) (Ma *et al.,* 2013), peroxisome proliferator-activated receptor alpha (*PPAR*α) (Zhang *et al.,* 2009), liver x receptor (*LXR*) and sterol regulatory element binding protein-1c (*SREBP-1c*) (Kohjima *et al.,* 2008). *FXR* and *PPAR-α* activate target genes in lipolytic pathways and elevate fatty acid oxidation (Calkin and Tontonoz, 2012) while *SREBP-1c* and *LXR* induce lipogenesis through activating lipogenic enzymes under the insulin effect (Ferre and Foufelle, 2010).

Lately, high-intensity interval training (HIIT), including high-intensity aerobic training with low intensity or rest time in between, has been considered as a beneficial intervention for health, because of the fat oxidation enhancement (Talanian *et al.,* 2007) and the TG level reduction (Tan *et al.,* 2014). It has also been reported that

chronic HIIT protocols compared with the steady-state training result in decreased TG levels (Freese *et al.,* 2011), total and abdominal fat and insulin resistance (Trapp *et al.,* 2008); but it's still unclear how this model of training affects transcriptional factors involved in lipid metabolism and which pathway is targeted by HIIT protocol. Considering the limited literature relevant to HIIT protocols in high fat diet fed rats, we have studied the tissue expression of key regulatory genes and plasma levels of lipid profile and insulin following an HIIT protocol in a high-fat diet model of rats to see if high-fat diet affect hepatic and adipose lipid metabolism by activating lipogenic pathways and whether or not HIIT have lipid lowering effects in high-fat diet fed rats via lipolytic pathways.

2. Material and methods

Animals

24 male *Wistar* rats (six weeks old) weighing 150.30±28.98 (g) were obtained from the Pasteur Institute (Amol, Mazandaran/Iran) and were kept in a lab with 12:12 light/dark cycle, 45 to 55% of humidity and 20-24 °C temperature. All animals had *ad libitum* access to food and tap water. After two weeks of acclimatisation to the environment, rats were divided randomly into the untrained-normal diet (n=6), untrained-HFD (n=6), HIIT-normal diet (n=6) and HIIT-HFD (n=6) groups.

All procedures conform to the policies established by the National Research Council Guide for the Care and Use of Laboratory Animals and have been approved by a local ethical committee of the University of Mazandaran in animal sciences.

Diet

Normal diet consisted of standard rat food (~12% calories from fat). High fat/high cholesterol diet (~56% calories from fat) according to Srinivasan *et al.* (2005) included normal pellet diet (365 g/kg), lard (310 g/kg that we replaced it with sheep fat), casein (250 g/kg), cholesterol (10 g/kg), vitamins and minerals (60 g/kg), DL-Methionine (3 g/kg), yeast (1 g/kg) and sodium chloride (1 g/kg) which was produced by the Behparvar company (Babol, Iran).

Training

Two weeks after initiation of the diet intervention, HIIT groups underwent sprint training on the treadmill, five days/week for eight weeks. The running speed gradually increased to 65-70 m/min with the number of sprint sets and resting periods being adjusted to enable all animals to run at the target speed. The initial treadmill speed was 20-30 m/min in the first week and was increased gradually to 65-70 m/min for the final week. Each training session consisted of 10 sets of 1 min sprint running and the sprint running sets were separated by 2 min of inactive recovery periods (Arabzadeh *et al.,* 2016).

Blood and tissue sampling

72 h after the last session of exercise (from 8:00 AM to 12:00 PM) rats were anaesthetised intraperitoneally by a combination of ketamine (75 mg/kg) and xylazine (35 mg/kg). After the complete anaesthesia blood samples were collected directly from the right ventricle into the syringes pre-treated with the ethylenediaminetetraacetic acid (EDTA). Samples were centrifuged at 5,000 rpm for 15 min, then plasma samples were collected for further analysis. Liver and visceral adipose tissue were removed and transferred to RNase-DNase free tubes after washing with normal saline and were kept in -80 °C until assay.

Biochemical analysis

Plasma cholesterol (CHOL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels were measured using the enzymatic photometric method (Parsazmoon kit, Pars Azmoon Inc., Tehran, Iran); TG level was measured using the enzymatic colorimetric method (Parsazmoon kit); and insulin level was measured by ELISA kit (Mercodia Co, Sweden, sensitivity: 1 mU/l).

Molecular analysis

To measure the relative gene expression, three samples of both tissues selected randomly from each group (according to the MIQE guidelines) (Bustin *et al.,* 2009); *FXR* and *SREBP-1c* primers for rats were designed (Table 1) (Côté *et al.,* 2013). 50-80 mg of tissue samples were homogenised by liquid nitrogen and an Accuzol kit (Bioneer, Daejeon, Republic of Korea) was used for total RNA extraction according to the manufacturer's instruction. In order to

Table 1. Real-time PCR primer sequences.

Gene	Oligo Forward	Oligo Reverse
FXR	CCACGACCAAGCTATGCAG	TCTCTGTTTGCTGTATGAGTCCA
SREBP-1c	TACAGCGTGGCTGGGAAC	GGCTGAGCGATACAGTTCAA
β-actin	CTGGAACGGTGAAGGTGACA	AAGGGACTTCCTGTAACAATGCA

avoid genomic contamination, 10 µl of RNA samples were purified using a DNase kit (Thermo Scientific Co., Waltham, MA, USA) and then cDNA was synthesised using oligo (dT) primers and reverse transcription (RT) kit (Bioneer). Relative gene expression was determined using the QuantiFast SYBER Green PCR kit (Qiagen Co., Hilden, Germany) with real-time PCR reaction. β-actin was used as a pre-validated reference gene. $2^{-\Delta\Delta CT}$ (Livak method) was used for expression analysis of genes (Livak and Schmittgen, 2001).

Statistical analysis

Values are expressed as a mean ± standard deviation. Shapiro-Wilk test was used for the data distribution normality test. Statistical analysis was performed by two-way ANOVA for non-repeated measures and Pearson correlation test was used for the study of the relationship between factors (P<0.05). All data were analysed by SPSS 22 software (Chicago, IL, USA).

3. Results

Weight gain

Compared to the untrained-normal diet group, untrained-HFD rats showed larger weight gain (~40%) (P<0.001); HIIT-normal diet rats compared with untrained-normal diet rats had almost 14% (P<0.001) and HIIT-HFD rats compared with untrained-HFD group had ~12% lower weight gain (P<0.001); the interaction effect of diet and exercise on weight gain did not reach statistical significance (P=0.442) (Table 2).

Plasma lipid profile and insulin levels

Untrained-HFD rats showed ~122% higher LDL (P<0.001), ~56% higher HDL (P<0.001), ~35% higher CHOL (P<0.001) and ~47% higher insulin (P<0.001) levels compared to untrained-normal diet rats, while TG level was found to be statistically non-significant different between groups (P=0.081). Also, no differences were observed in the lipid profile and insulin levels between trained and untrained rats (P≥0.05); regardless of the non-significant interaction effect of diet and exercise on lipid profile (P≥0.05), HIIT-HFD rats showed significantly higher insulin levels than HIIT-normal diet group (P=0.001) (Table 3). It was noteworthy that plasma LDL (r=0.715, P<0.001), HDL (r=0.575, P<0.001), CHOL (r=0.706, P<0.001) and insulin (r=0.692, P<0.001) levels were positively correlated with weight gain; the plasma insulin level was also correlated to the LDL (r=0.542, P=0.006), HDL (r=0.667, P<0.001), CHOL (r=0.647, P<0.001) and TG (r=0.420, P=0.041) levels, positively.

FXR relative gene expression

Our results showed that untrained-HFD rats had significantly lower hepatic (P=0.006) and not adipose (P=0.810) *FXR* expression compared to untrained-normal diet fed rats. Both HIIT groups had higher hepatic *FXR*

Table 2. Weight changes (g, mean ± standard deviation) of trained and untrained rats fed with normal and high fat diet.[1,2]

Group/factor	Untrained-normal diet	Untrained-HFD	HIIT-normal diet	HIIT-HFD
Initial weight	307.50±30.55	302.33±20.64	305.00±27.09	295.33±46.71
Final weight	368.00±31.16	386.83±23.61	357.17±26.78	369.50±47.64
Weight gain	60.50±1.87	84.50±3.83*	52.17±2.04**	74.17±4.07**

[1] HFD = high fat diet; HIIT = high-intensity interval training.
[2] * = significantly different compared to untrained-normal diet group; ** = significantly different from untrained rats with the same diet.

Table 3. Plasma factors (mean ± standard deviation) of trained and untrained rats fed with normal and high fat diet.[1,2]

Groups	Untrained-normal diet	Untrained-HFD	HIIT-normal diet	HIIT-HFD
LDL (mg/dl)	15.00±3.22	33.33±3.67*	17.83±8.42	31.83±7.14
HDL (mg/dl)	19.33±3.88	30.17±3.31*	23.00±6.78	33.83±2.23
CHOL (mg/dl)	66.83±10.72	90.00±7.18*	69.33±9.93	89.50±5.24
TG (mg/dl)	94.50±24.12	112.50±29.48	89.67±18.14	120.00±48.78
Insulin (ng/ml)	0.075±0.018	0.110±0.016*	0.037±0.017	0.147±0.034

[1] HFD = high-fat diet; HIIT = high-intensity interval training; LDL = low-density lipoprotein; HDL = high-density lipoprotein; CHOL = cholesterol; TG = triglyceride.
[2] * = significantly different compared to untrained-normal diet group.

relative gene expression compared to the untrained rats with the same diet (P<0.001), while the adipose *FXR* expression was not different between trained and untrained rats (P=0.058). The interaction effect of diet and exercise on hepatic *FXR* was not significant (P=0.124); however, the HIIT-HF diet fed rats compared to HIIT-normal diet fed rats showed higher adipose *FXR* expression (P=0.001) (Figure 1).

SREBP-1c relative gene expression

Untrained-HFD rats compared with untrained-normal diet rats showed almost 56% higher hepatic (P=0.016) and 47% higher adipose (P=0.044) *SREBP-1c* relative gene expression. Furthermore, HIIT groups had a lower hepatic (P=0.029) and adipose (P<0.001) *SREBP-1c* expression compared to untrained groups with the same diet. Although the interaction effect of diet and exercise on hepatic *SREBP-1c* was not significant (P=0.736), HIIT-HFD rats had lesser adipose *SREBP-1c* expression than HIIT-normal diet rats (P=0.003) (Figure 2). Surprisingly, hepatic *FXR* showed a negative relationship with weight gain (r=-0.668, P=0.017), hepatic *SREBP-1c* (r=-0.724, P=0.008) and adipose *SREBP-1c* (r=-0.747, P=0.005) gene expression. It is interesting that hepatic but not adipose *SREBP-1c* expression had a significant positive relationship with weight gain (r=0.797, P<0.001) and plasma insulin level (r=0.661, P=0.019).

4. Discussion

According to our findings and as we expected, HFD rats experienced more weight gain and dyslipidemia that was correlated to insulin levels. It has been previously reported that high fat-high cholesterol diets increase weight, plasma LDL, TG and cholesterol levels (Otunola *et al.,* 2010; Wen *et al.,* 2013); also in the study by Srinivasan *et al.* (2005) high fat diet, containing lard, increased plasma TG levels; while HFD in our study – containing sheep fat instead of lard – had not any significant effect on TG levels. The saturated fatty acids content in 100 g lard and sheep fat is similar but although the sheep fat cholesterol is slightly higher than lard, it yet contains higher levels of monounsaturated fatty acids (Alfred *et al*., 2002). Thereby, it seems that dietary fat type plays an important role in plasma lipid profile content. Despite previous findings that have shown lipid profile improvement in order to the enhancement of whole-body lipid oxidation by exercise training (Hawley and Yeo, 2014; Wen *et al.,* 2013), lipid profile in the HIIT rats was not different from the untrained rats in both dietary groups. Considering the lower weight gain in the HIIT trained rats, more weeks of HIIT, maybe accompanied by calorie intake restriction, could improve lipid profile levels and hyperinsulinemia.

Similar to other studies (Gao *et al.,* 2015), HFD caused hyperinsulinemia that could be a result of insulin resistance (Srinivasan *et al.,* 2005). Insulin resistance could increase free fatty acids (FFA) flow to the liver by elevating lipolysis in peripheral adipose tissue. Also, higher levels of insulin can activate *de novo* lipogenesis and inhibit FFA oxidation in liver and cause fat accumulation in hepatocytes (Conlon *et al.,* 2013). As we observed, this hyperinsulinemia was correlated to dyslipidemia, weight gain and hepatic (not adipose) *SREBP-1c* expression that may show the role of hyperinsulinemia in lipogenic pathways.

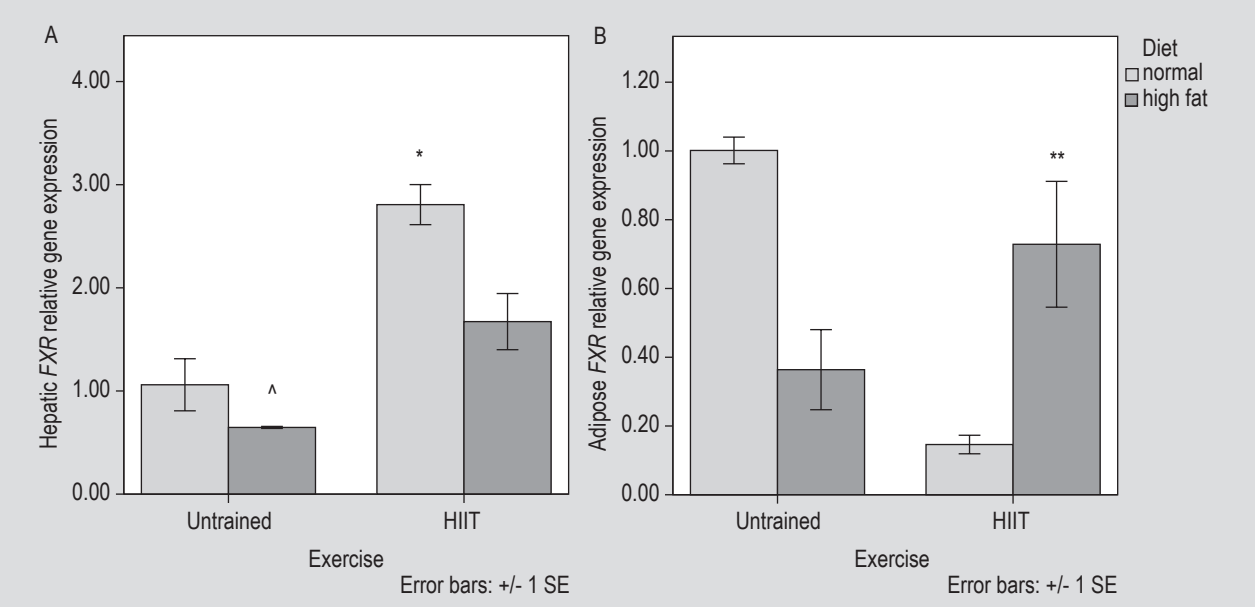

Figure 1. (A) Hepatic and (B) adipose *FXR* relative gene expression (mean ± standard deviation). Significant effect of diet (^), high intensity interval training (HIIT) (*) and the interaction effect of diet and HIIT (**).

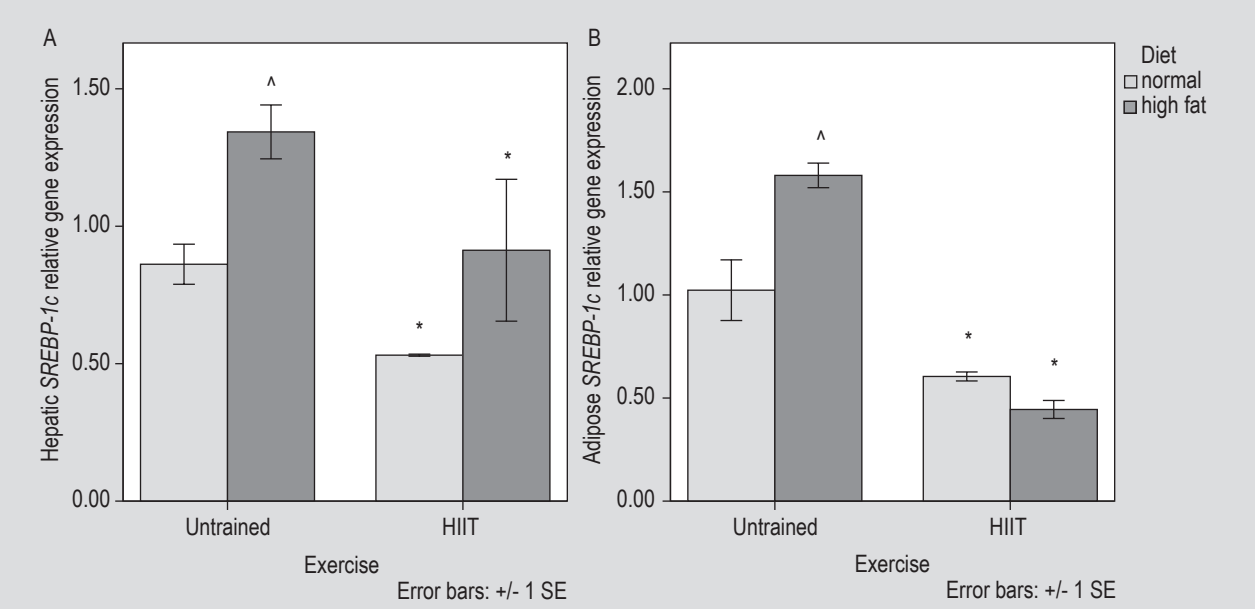

Figure 2. (A) Hepatic and (B) adipose *SREBP-1c* relative gene expression (mean ± standard deviation). Significant effect of diet (^) and high intensity interval training (HIIT) (*).

Hepatic *FXR* relative gene expression and not adipose expression was lower in HFD rats. Some researchers have also reported lesser hepatic *FXR* expression by HFD (Ichimura *et al.,* 2015). *FXR* plays a key role in the cholesterol and bile acid homoeostasis (Yang *et al.,* 2015). Activation of *FXR* has been shown to modulate hepatic *de novo* lipogenic pathways, up-regulating the expression of the very low-density lipoprotein receptor (VLDL-R) and triglyceride clearance. Additionally, *FXR* seems to be involved in reverse cholesterol transport, a process that results in the delivery of cholesterol from peripheral tissues to the liver for biliary disposal and consequent faecal elimination (Gadaleta *et al.,* 2015). Thereby, reduced *FXR* expression could induce lesser fat removal and oxidation. According to our findings, lower hepatic *FXR* relative gene expression in HFD rats may explain dyslipidemia induced by HFD. On the other hand, HIIT-normal and HIIT-HFD rats compared with untrained rats with the same diets showed higher hepatic and not adipose *FXR* expression but regardless of higher hepatic *FXR* expression and lower weight gain in HIIT rats, lipid profile was similar between groups. It's noteworthy that HIIT-HFD rats compared with HIIT-normal diet rats showed higher adipose *FXR* expression. It seems that in presence of high-fat diet, HIIT activates adipose *FXR* to enhance lipolysis only in adipose tissue.

Both hepatic and adipose *SREBP-1c* expression tended to be higher in HFD rats and lower in HIIT groups. It has been shown that excess calorie intake can activate *de novo* fatty acid synthesis and esterification to TGs primarily in the liver (Viscarra *et al.,* 2017). The main factor in this pathway seems to be *SREBP-1c* that activates its target genes, such as fatty acid synthase (*FAS*), acetyl-CoA carboxylase (*ACC*) and stearoyl-CoA desaturase 1 (*SCD-1*) and this pathway in the liver is controlled by the hepatic insulin signalling, even under the severe insulin resistance states, such as obesity or diabetes (Yilmaz *et al.,* 2016). Paying attention to the positive correlation between plasma insulin and hepatic *SREBP-1c* but not its adipose expression, it seems that high plasma levels of insulin after the HFD consumption has activated hepatic *de novo* lipogenesis through *SREBP-1c* expression and subsequently the hepatic *FXR* expression has been suppressed. Furthermore, the inhibition of hepatic *FXR* by *SREBP-1c* that had been also previously reported (Karagianni and Talianidis, 2015), may have been caused decreased lipolysis, dyslipidemia and more weight gain. Generally, *FXR* down-regulation by *SREBP-1c* seems to be occurring via the induction of small heterodimer partner (*SHP*), as it is not observed in SHP-null mice (Gadaleta *et al.,* 2015).

HFD rats showed higher adipose *SREBP-1c* expression independent of plasma insulin levels that unlike to the liver tissue it was not accompanied with lower adipose *FXR* expression. Also, it seems that in presence of HFD notwithstanding of hyperinsulinemia, higher adipose *FXR* expression by HIIT suppresses adipose *SREBP-1c* and thereby causes adipose lipolysis. These mechanisms are not completely understood and yet need to be studied.

5. Conclusions

High-fat diet fed rats in this research experienced more weight gain and dyslipidemia probably via activation of the *SREBP-1c* pathway in the liver tissue under the insulin

effect. HIIT seems to enhance hepatic *FXR* activity and inhibits hepatic and adipose *SREBP-1c* expression but despite lower weight gain in HIIT rats, the lipid profile improvement by this type of exercise needs more studies. It seems that diet has more effect on lipid profile than exercise and in presence of HFD, HIIT enhances only adipose lipolysis and has no effect on hepatic metabolism. We did our best to eliminate limitations of the study using homogenisation of the groups by age, gender, weight and presence of the control group, but monitoring the initial metabolic state of each rat would be helpful for a better conclusion. Because rats had *ad libitum* access to the food, we suggest measuring the food consumption to see whether rats with high-fat diet had consumed the same quantity of food compared with normal diet rats.

References

Alfred, T., Matthäus, B. and Fiebig, H.-J., 2002. Fats and fatty oils. In: Ullmann's encyclopedia of industrial chemistry. Wiley-VCH, Weinheim, Germany. DOI: 10.1002/14356007.a10_173.pub2.

Arabzadeh, E., Mirdar, S. and Moradiani, H., 2016. *Nigella sativa* supplementation attenuates exercise-induced bronchoconstriction in the maturing rat: a histometric and histologic study. Comparative Clinical Pathology 25: 1-5.

Bustin, S.A., Benes, V., Garson, J.A., Hellemans, J., Huggett, J., Kubista, M., Mueller, R., Nolan, T., Pfaffl, M.W., Shipley, G.L., Vandesompele, J. and Wittwer, C.T., 2009. The MIQE guidelines: minimum information for publication of quantitative real-time PCR experiments. Clinical Chemistry 55: 611-622.

Calkin, A.C. and Tontonoz, P., 2012. Transcriptional integration of metabolism by the nuclear sterol-activated receptors LXR and FXR. Nature Reviews Molecular Cell Biology 13: 213-224.

Conlon, B.A., Beasley, J.M., Aebersold, K., Jhangiani, S.S. and Wylie-Rosett, J., 2013. Nutritional management of insulin resistance in nonalcoholic fatty liver disease (NAFLD). Nutrients 5: 4093-4114.

Côté, I., Sock, E.T.N., Lévy, E. and Lavoie, J.M., 2013. An atherogenic diet decreases liver FXR gene expression and causes severe hepatic steatosis and hepatic cholesterol accumulation: effect of endurance training. European Journal of Nutrition 52: 1523-1532.

Ferre, P. and Foufelle, F., 2010. Hepatic steatosis: a role for *de novo* lipogenesis and the transcription factor SREBP-1c. Diabetes, Obesity and Metabolism 12 Suppl. 2: 83-92.

Freese, E.C., Levine, A.S., Chapman, D.P., Hausman, D.B. and Cureton, K.J., 2011. Effects of acute sprint interval cycling and energy replacement on postprandial lipemia. Journal of Applied Physiology 111: 1584-1589.

Gadaleta, R.M., Cariello, M., Sabbà, C. and Moschetta, A., 2015. Tissue-specific actions of FXR in metabolism and cancer. Biochimica et Biophysica Acta – Molecular and Cell Biology of Lipids 1851: 30-39.

Gao, M., Ma, Y. and Liu, D., 2015. High-fat diet-induced adiposity, adipose inflammation, hepatic steatosis and hyperinsulinemia in outbred CD-1 mice. PLoS ONE 10: e0119784.

Hawley, J.A. and Yeo, W.K., 2014. Metabolic adaptations to a high-fat diet. In: Maughan, R.J. (ed.) The encyclopaedia of sports medicine: an IOC medical commission publication. Vol. 19. Wiley, Hoboken, NJ, USA, pp. 166-173.

Ichimura, M., Kawase, M., Masuzumi, M., Sakaki, M., Nagata, Y., Tanaka, K., Suruga, K., Tamaru, S., Kato, S. and Tsuneyama, K., 2015. High-fat and high-cholesterol diet rapidly induces non-alcoholic steatohepatitis with advanced fibrosis in Sprague-Dawley rats. Hepatology Research 45: 458-469.

Karagianni, P. and Talianidis, I., 2015. Transcription factor networks regulating hepatic fatty acid metabolism. Biochimica et Biophysica Acta – Molecular and Cell Biology of Lipids 1851: 2-8.

Kohjima, M., Higuchi, N., Kato, M., Kotoh, K., Yoshimoto, T., Fujino, T., Yada, M., Yada, R., Harada, N. and Enjoji, M., 2008. SREBP-1c, regulated by the insulin and AMPK signalling pathways, plays a role in nonalcoholic fatty liver disease. International Journal of Molecular Medicine 21: 507-512.

Kolifa, M., Petridou, A. and Mougios, V., 2004. Effect of prior exercise on lipemia after a meal of moderate fat content. European Journal of Clinical Nutrition 58: 1327-1335.

Livak, K.J. and Schmittgen, T.D., 2001. Analysis of relative gene expression data using real-time quantitative PCR and the $2^{-\Delta\Delta CT}$ method. Methods 25: 402-408.

Ma, Y., Huang, Y., Yan, L., Gao, M. and Liu, D., 2013. Synthetic FXR agonist GW4064 prevents diet-induced hepatic steatosis and insulin resistance. Pharmaceutical Research 30: 1447-1457.

Magkos, F., 2009. Basal very low-density lipoprotein metabolism in response to exercise: mechanisms of hypotriacylglycerolemia. Progress in Lipid Research 48: 171-190.

Otunola, G.A., Oloyede, O.B., Oladij, A.T. and Afolayan, A.A., 2010. Effects of diet-induced hypercholesterolemia on the lipid profile and some enzyme activities in female Wistar rats. African Journal of Biochemical Research 4: 149-154.

Petitt, D.S., Arngrímsson, S.A. and Cureton, K.J., 2003. Effect of resistance exercise on postprandial lipemia. Journal of Applied Physiology 94: 694-700.

Srinivasan, K., Viswanad, B., Asrat, L., Kaul, C.L. and Ramarao, P., 2005. Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: a model for type 2 diabetes and pharmacological screening. Pharmaceutical Research 52: 313-320.

Talanian, J.L., Galloway, S.D., Heigenhauser, G.J., Bonen, A. and Spriet, L.L., 2007. Two weeks of high-intensity aerobic interval training increases the capacity for fat oxidation during exercise in women. Journal of Applied Physiology 102: 1439-1447.

Tan, M., Fat, R.C.M., Boutcher, Y.N. and Boutcher, S.H., 2014. Effect of high-intensity intermittent exercise on postprandial plasma triacylglycerol in sedentary young women. International Journal of Sport Nutrition and Exercise Metabolism 24: 110-118.

Trapp, E., Chisholm, D., Freund, J. and Boutcher, S., 2008. The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. International Journal of Obesity 32: 684-691.

Viscarra, J.A., Wang, Y., Hong, I.H. and Sul, H.S., 2017. Transcriptional activation of lipogenesis by insulin requires phosphorylation of MED17 by CK2. Science Signaling 10: eaai8596.

Wen, S., Jadhav, K.S., Williamson, D.L. and Rideout, T.C., 2013. Treadmill exercise training modulates hepatic cholesterol metabolism and circulating PCSK9 concentration in high-fat-fed mice. Journal of Lipids 2013: 908048.

Yang, Z., Cappello, T. and Wang, L., 2015. Emerging role of microRNAs in lipid metabolism. Acta Pharmaceutica Sinica B 5: 145-150.

Yilmaz, M., Claiborn, K.C. and Hotamisligil, G.S., 2016. *De novo* lipogenesis products and endogenous lipokines. Diabetes 65: 1800-1807.

Zhang, H., He, Y., Chung, P.K., Tong, T.K., Fu, F.H., Chen, Y. and Jiao, G., 2009. Effects of 12 weeks of exercise on hepatic TNF-α and PPARα in an animal model of high-fat diet-induced nonalcoholic steatohepatitis. Journal of Exercise Science and Fitness 7: 18-23.