Nutrition Metabol

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AMP-activated protein kinase is required for the anti-adipogenic effects of alpha-linolenic acid

Xihong Zhou, Weiche Wu, Jingqing Chen, Xinxia Wang and Yizhen Wang*

Abstract

Background: n-3 long chain polyunsaturated fatty acid (n-3 LC PUFA) increases β-oxidation and limits lipid accumulation in adipocytes. The current study was conducted to determine whether their precursor alpha-linolenic acid (ALA) could also exert the above effects and how AMP-activated protein kinase (AMPK) was involved.

Methods: AMPKα1$^{-/-}$, AMPKα2$^{-/-}$ mice and wild-type (WT) mice were fed a high-fat diet (HFD) or HFD with ALA. Body weight was recorded weekly and serum was collected. Adipocytes size and expression of key players involved in mitochondrial biogenesis and lipid oxidation were also measured.

Results: Our results showed an elevated serum adiponectin level and a decreased leptin and insulin level in WT mice fed HFD with ALA when compared with WT mice fed HFD. In addition, dietary ALA decreased epididymal adiposity and adipocytes size in WT mice. At protein level, mitochondrial genes (peroxisome proliferator-activated receptor gamma coactivator 1 alpha [PGC1α] and nuclear respiratory factor-1 [nrf1]) and β-oxidation related genes (carnitine palmitoyltransferase 1A [CPT1a] and peroxisome proliferator-activated receptor alpha [PPARα]) were upregulated by dietary ALA in epididymal fat of WT mice. Consistently, dietary ALA also increased mitochondrial genomic DNA copy numbers. Moreover, lipogenesis was repressed by dietary ALA, indicated by that expression of fatty acid synthase (FAS), acetyl CoA carboxylase (ACC) and stearoyl-CoA desaturase 1 (SCD1) were decreased. However, these aforementioned effects were abolished in the AMPKα1 and AMPKα2 knockout mice.

Conclusions: Our results suggest that ALA could improve adipose tissue function and its anti-adipogenic effects are dependent on AMPK.

Keywords: Alpha-linolenic acid, AMP-activated protein kinase, β-oxidation, Mitochondrial biogenesis, Adipose tissue

Introduction

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Materials and methods

Animals and diets

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Statistical analysis

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Results

Effects of ALA on serum insulin, adiponectin and leptin concentration in WT, AMPKα1$^{-/-}$ and AMPKα2$^{-/-}$ mice

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Effects of ALA on HFD-induced fat deposition in white adipose tissue required AMPK

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Table 2 Effects of ALA on fat depots of WT, AMPK**α**1$^{-/-}$ and AMPK**α**2$^{-/-}$ mice fed HFD

	WT		**AMPKα1$^{-/-}$**		**AMPKα2$^{-/-}$**	
	HF	**HF-A**	**HF**	**HF-A**	**HF**	**HF-A**
Final BW (g)	42.6 ± 3.1	32.6 ± 1.8^{ab}	43.1 ± 3.0	42 ± 3.2	45.5 ± 3.4	44.2 ± 3.7
Epididymal						
weight (mg)	2270 ± 158	1224 ± 98^{ab}	2242 ± 201	2137 ± 198	2349 ± 178	2146 ± 184
DNA (μg/mg)	0.32 ± 0.04	0.67 ± 0.05^{ab}	0.29 ± 0.05	0.35 ± 0.06	0.29 ± 0.05	0.36 ± 0.07
Inguinal						
Weight (mg)	1090 ± 42	1037 ± 57	1097 ± 45	1058 ± 55	1102 ± 49	1072 ± 59
DNA (μg/mg)	0.42 ± 0.05	0.5 ± 0.06	0.36 ± 0.04	0.39 ± 0.06	0.38 ± 0.05	0.41 ± 0.07

Note: The values are means ± SE. $^{a}P < 0.05$ for difference between different genotypes with HF-A diet; $^{b}P < 0.05$ for difference between WT mice. BW, body weight. HF, mice fed high-fat diet; HF-A, mice fed high-fat diet with ALA.

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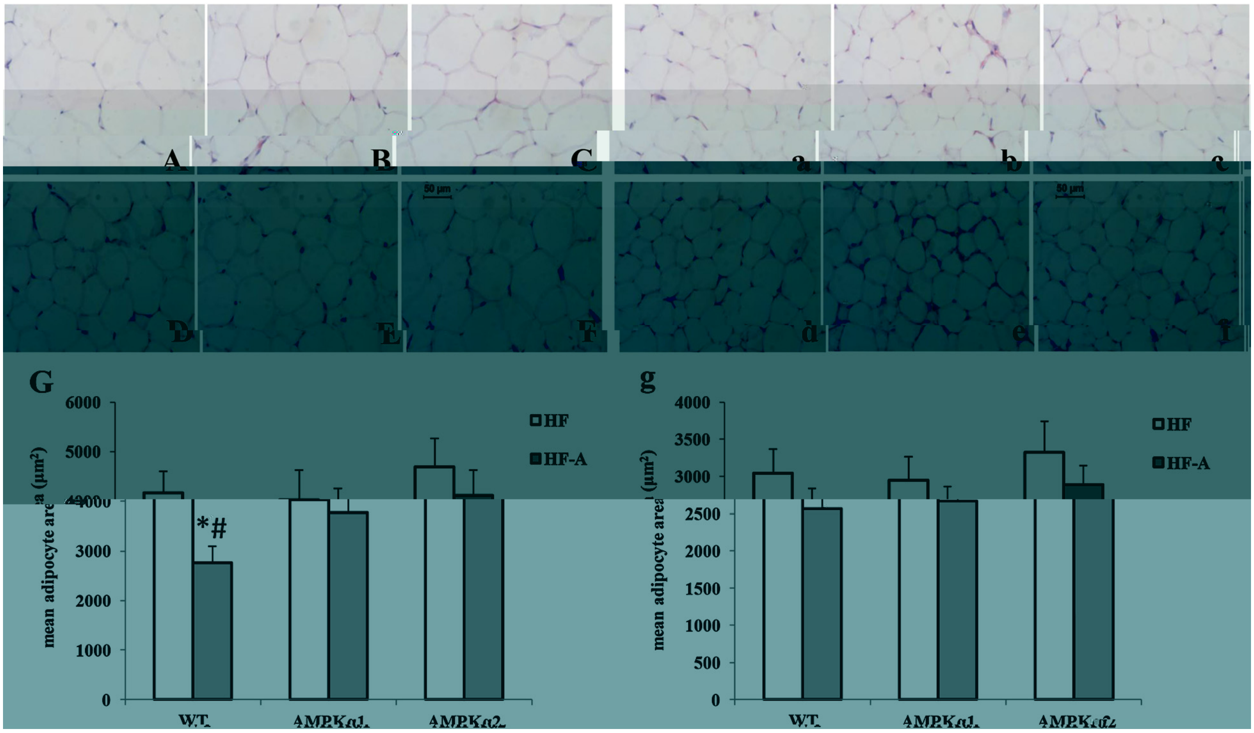

Figure 1 **Adipocyte size in WT, AMPKα1$^{-/-}$ and AMPKα2$^{-/-}$ mice. A**, **a**, WT mice fed HF diet; **B**, **b**, AMPKα1$^{-/-}$ mice fed HF diet; **C**, **c**, AMPKα2$^{-/-}$ mice fed HF diet; **D**, **d**, WT mice fed HF-A diet; **E**, **e**, AMPKα1$^{-/-}$ mice fed HF-A diet; **F**, **f**, AMPKα2$^{-/-}$ mice fed HF-A diet; **G**, **g**, mean adipocyte area in WT mice, AMPKα1$^{-/-}$ and AMPKα2$^{-/-}$ mice (uppercase represents epididymal fat; lowercase represents inguinal fat; cell size, μm^{2}); HF, mice fed high-fat diet; HF-A, mice fed high-fat diet with ALA.

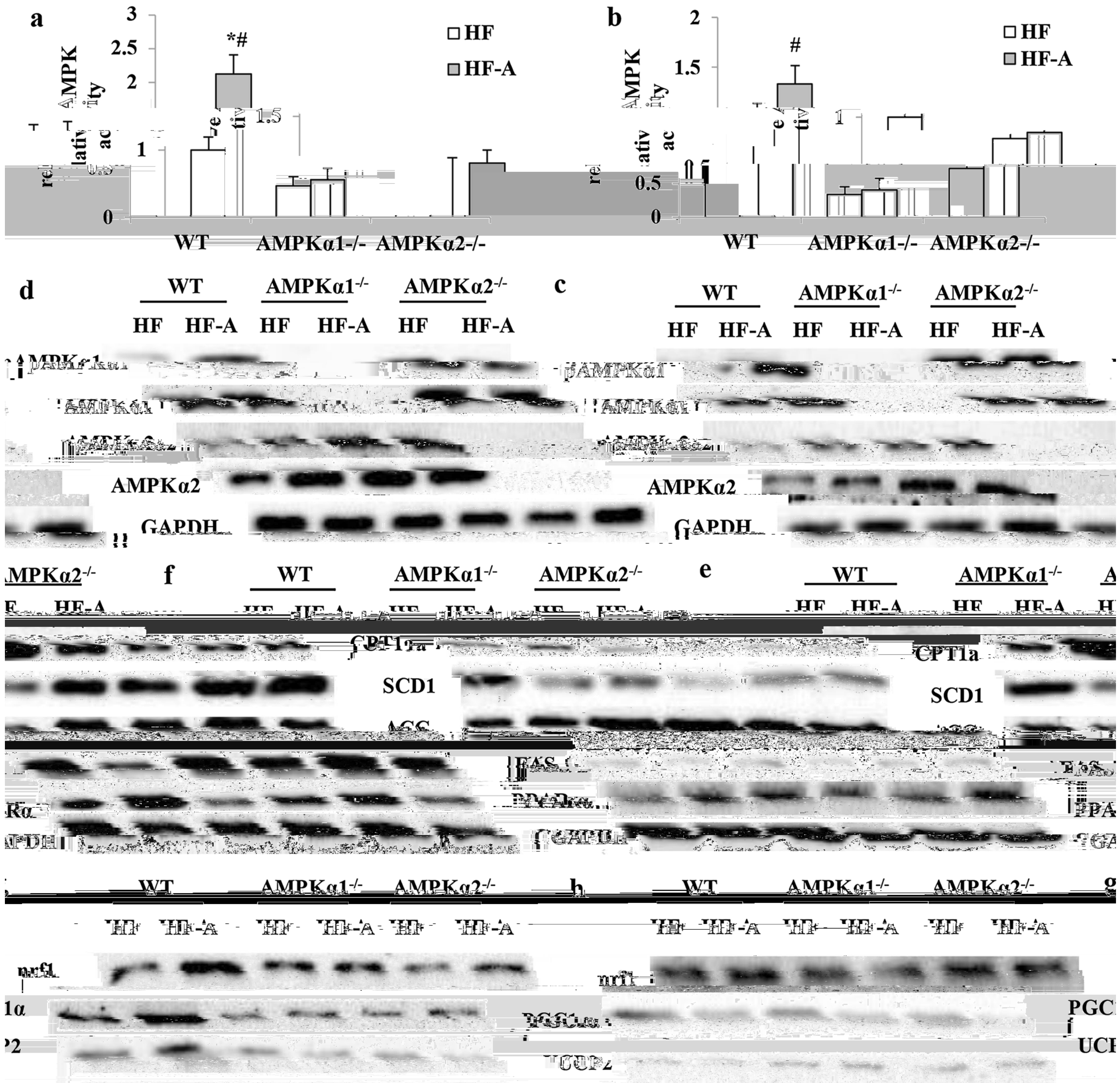

Figure 2 **AMPK activity, protein expression of mitochondrial biogenesis and β-oxidation related genes in WT, AMPKα1$^{-/-}$ and AMPKα2$^{-/-}$ mice.** HF, mice fed high-fat diet; HF-A, mice fed high-fat diet with ALA. (**a**, **c**, **e**, **g**, activity of AMPK and protein expressed in epididymal fat; **b**, **d**, **f**, **h**, activity of AMPK and protein expressed in inguinal fat). The values are means ± SE. #P < 0.05 for difference between different genotypes with HF-A diet; *P < 0.05 for difference between WT mice.

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carried out the experiments and collected the data; WYZ participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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