生物物理学报 2012, 28(1) 45-52 DOI: 10.3724/SP.J.1260.2012.10061 ISSN: 1000-6737 CN: 11-1992/Q

研究论文

棕榈酸的组织吸收分布及对骨骼肌胰岛素抵抗的影响

彭恭[3], 刘延波[2], 李凌海[1], 刘平生[1]

1. 中国科学院生物物理研究所,北京 100101;
2. 贵州大学生命科学学院,贵阳 550025;
3. 吉林大学第一医院,转化医学研究院,长春 130021

摘要:

脂肪酸代谢紊乱是II型糖尿病的主要致病因素之一。棕榈酸是血液中含量最高的游离脂肪酸。我们建立了大鼠颈静脉置管输注棕榈酸的模型,发现血液中的大部分棕榈酸被骨骼肌组织所吸收。以棕榈酸处理的C2C12骨骼肌细胞为实验模型发现,棕榈酸进入骨骼肌细胞后的中间代谢产物(磷脂和甘油二酯)的累积,会造成内质网应激及胰岛素抵抗。提示血液中棕榈酸含量的升高可能通过骨骼肌的胰岛素抵抗机制,影响II型糖尿病的发生和发展。

关键词: 棕榈酸 胰岛素抵抗 骨骼肌 脂肪酸静脉输注

Insulin Resistance Is Correlated with Palmitic Acid Uptake in Skeletal Muscle Cells

PENG Gong[3], LIU Yanbo[2], LI Linghai[1], LIU Pingsheng[1]

1. Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China;
2. College of Life Science, Guizhou University, Guiyang 550025, China;
3. Institute of Translational Medicine,the First Hospital of Jilin University, Changchun 130021, China

Abstract:

The aberration of palmitic acid metabolism is one of the key factors that have linked to the development and progression of type II diabetes. Palmitic acid is the most abundant free fatty acid in human blood. The mechanism how palmitic acid affects animal body energy homeostasis and leads to such metabolic disease remains elusive. Therefore, we established a rat model with venous fatty acid infusion to investigate the function of palmitic acid in animal blood. Using this model system, we found that half-life of palmitic acid in rat blood was about 30 min and more than half of palmitic acid was uptaken by skeletal muscle. Our further experiments using skeletal muscle cell line C2C12 revealed that palmitic acid was mainly converted to phospholipids, diacylglyceride and triglyceride. Similar to previous studies including our own, accumulated palmitic acid metabolites induced insulin resistance. Taken together, increasing concentration of blood palmitic acid may cause type II diabetes through insulin resistance in skeletal muscle.

Keywords: Palmitic acid Insulin resistance Skeletal muscle Venous fatty acid infusion

收稿日期 2011-04-15 **修回日期** 2011-04-20 **网络版发布日期**

DOI: 10.3724/SP.J.1260.2012.10061

基金项目:

国家自然科学基金项目(30871129, 30971431)

通讯作者: 刘平生,电话:(010)64888517,E-mail:pliu@ibp.ac.cn

作者简介:

作者Email: pliu@ibp.ac.cn

参考文献:

1. Shoelson SE, Herrero L, Naaz A. Obesity, inflammation, and insulin resistance. Gastroenterology, 2007, 132(6): 2169~2180
2. Brindley DN, Wang CN, Mei J, Xu J, Hanna AN. Tumor necrosis factor-alpha and ceramides in insulin resistance. Lipids, 1999, 34 Suppl: S85~88
3. Jazet IM, Pijl H, Meinders AE. Adipose tissue as an endocrine organ: Impact on insulin resistance.

Neth J Med, 2003, 61(6): 194~212
4. Nakamura S, Takamura T, Matsuzawa-Nagata N, Takayama H, Misu H, Noda H, Nabemoto S, Kurita S, Ota T, Ando H, Miyamoto KI, Shuichi K. Palmitate induces insulin resistance in H4IIEC3 hepatocytes through reactive oxygen species produced by mitochondria. J Biol Chem, 2009, 284(22): 14809~14818
5. Ozcan U, Cao Q, Yilmaz E, Lee AH, Iwakoshi NN, Ozdelen E, Tuncman G, Gorgun C, Glimcher LH, Hotamisligil GS. Endoplasmic reticulum stress links obesity, insulin action, and type 2 diabetes. Science, 2004, 306(5695): 457~461
6. Ozcan U, Yilmaz E, Ozcan L, Furuhashi M, Vaillancourt E, Smith RO, Gorgun CZ, Hotamisligil GS. Chemical chaperones reduce ER stress and restore glucose homeostasis in a mouse model of type 2 diabetes. Science, 2006, 313(5790): 1137~1140
7. Singer P, Godicke W, Voigt S, Hajdu I, Weiss M. Postprandial hyperinsulinemia in patients with mild essential hypertension. Hypertension, 1985, 7(2): 182~186
8. Sinha S, Perdomo G, Brown NF, O'Doherty RM. Fatty acid-induced insulin resistance in L6 myotubes is prevented by inhibition of activation and nuclear localization of nuclear factor kappa B. J Biol Chem, 2004, 279(40): 41294~41301
9. Wang X, Yu W, Nawaz A, Guan F, Sun S, Wang C. Palmitate induced insulin resistance by PKCtheta-dependent activation of mTOR/S6K pathway in C2C12 myotubes. Exp Clin Endocrinol Diabetes, 2010, 118(9): 657~661
10. Mason TM, Goh T, Tchipashvili V, Sandhu H, Gupta N, Lewis GF, Giacca A. Prolonged elevation of plasma free fatty acids desensitizes the insulin secretory response to glucose in vivo in rats. Diabetes, 1999, 48(3): 524~530
11. Liu P, Ying Y, Zhao Y, Mundy DI, Zhu M, Anderson RG. Chinese hamster ovary K2 cell lipid droplets appear to be metabolic organelles involved in membrane traffic. J Biol Chem, 2004, 279(5): 3787~3792
12. Peng G, Li LH, Liu Y, Pu J, Zhang SY, Yu JH, Zhao JJ, Liu P. Oleate blocks palmitate-induced abnormal lipid distribution, endoplasmic reticulum expansion and stress, and insulin resistance in skeletal muscle. Endocrinology, 2011, 152(6): 2206
13. Montell E, Turini M, Marotta M, Roberts M, Noe V, Ciudad CJ, Mace K, Gomez-Foix AM. DAG accumulation from saturated fatty acids desensitizes insulin stimulation of glucose uptake in muscle cells. Am J Physiol Endocrinol Metab, 2001, 280(2): E229~237
14. Sabin MA, Stewart CE, Crowne EC, Turner SJ, Hunt LP, Welsh GI, Grohmann MJ, Holly JM, Shield JP. Fatty acid-induced defects in insulin signalling, in myotubes derived from children, are related to ceramide production from palmitate rather than the accumulation of intramyocellular lipid. J Cell Physiol, 2007, 211(1): 244~252
15. Garland PB, Randle PJ. Regulation of glucose uptake by muscles. 10. Effects of alloxan-diabetes, starvation, hypophysectomy and adrenalectomy, and of fatty acids, ketone bodies and pyruvate, on the glycerol output and concentrations of free fatty acids, long-chain fatty acyl-coenzyme A, glycerol phosphate and citrate-cycle intermediates in rat heart and diaphragm muscles. Biochem J, 1964, 93(3): 678~687
16. Zhang SY, Du YL, Wang Y, Liu PS. Lipid droplet —— A cellular organelle for lipid metabolism. Acta Biophys Sin, 2010, 26(2): 1~10

本刊中的类似文章

文章评论

反馈人		邮箱地址	
反馈标题		验证码	8446