河南师范大学
NENAN NORMAL UNIVERSITY

肌肉糖代谢

水产动物营养与饲料系　杨丽萍

2016年10月29日

厚德博学·止于至善

内容概要

- 一、OGL实验肌肉对糖的储存与利用
- 二、肌肉对糖的吸收的调节
- 三、高脂、低碳食品短期摄食对肌肉糖代谢关键酶活的影响
- 四、碳水化合物再投喂，对肌肉PDK活性的快速扭转作用

葡萄糖耐量（OGTT）

- OGTT实验
- 血糖下调。
- 一般观点认为，主要进入肌肉、内脏、脂肪？

一、OGL实验肌肉对糖的储存与利用

Skeletal Muscle Glycolysis, Oxidation, and Storage of an Oral Glucose Load

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一、OGL实验肌肉对糖的储存与利用

- Glucose, [^{14}C]glucose specific activity, [3H]glucose specific activity,
- Alanine, lactate, pyruvate, 0_2, $C0_2$, and insulin concentrations
- Whole body glucose and lipid oxidation.
- Nonprotein respiratory quotient was calculated from the calorimetric values and urinary nitrogen excretion。

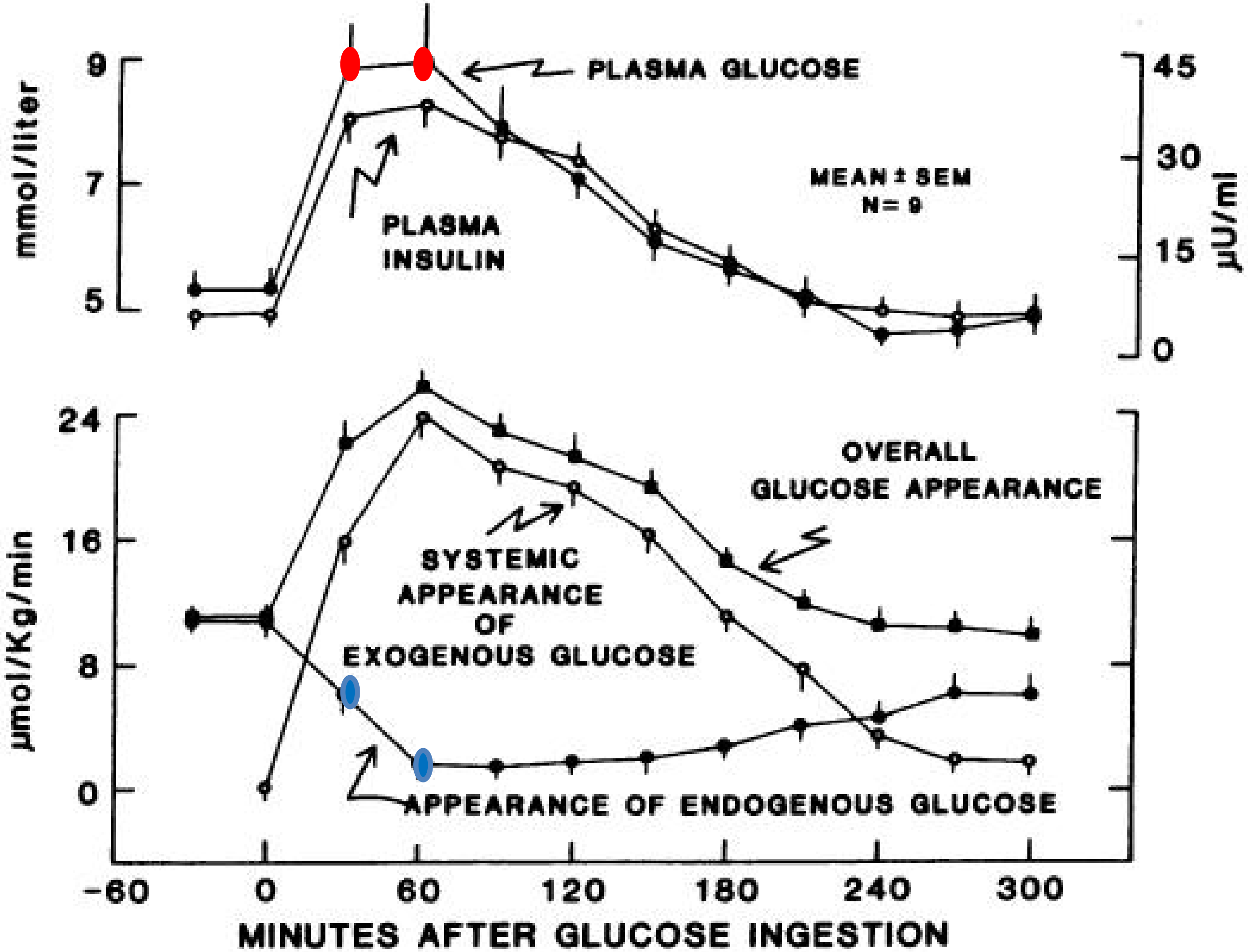
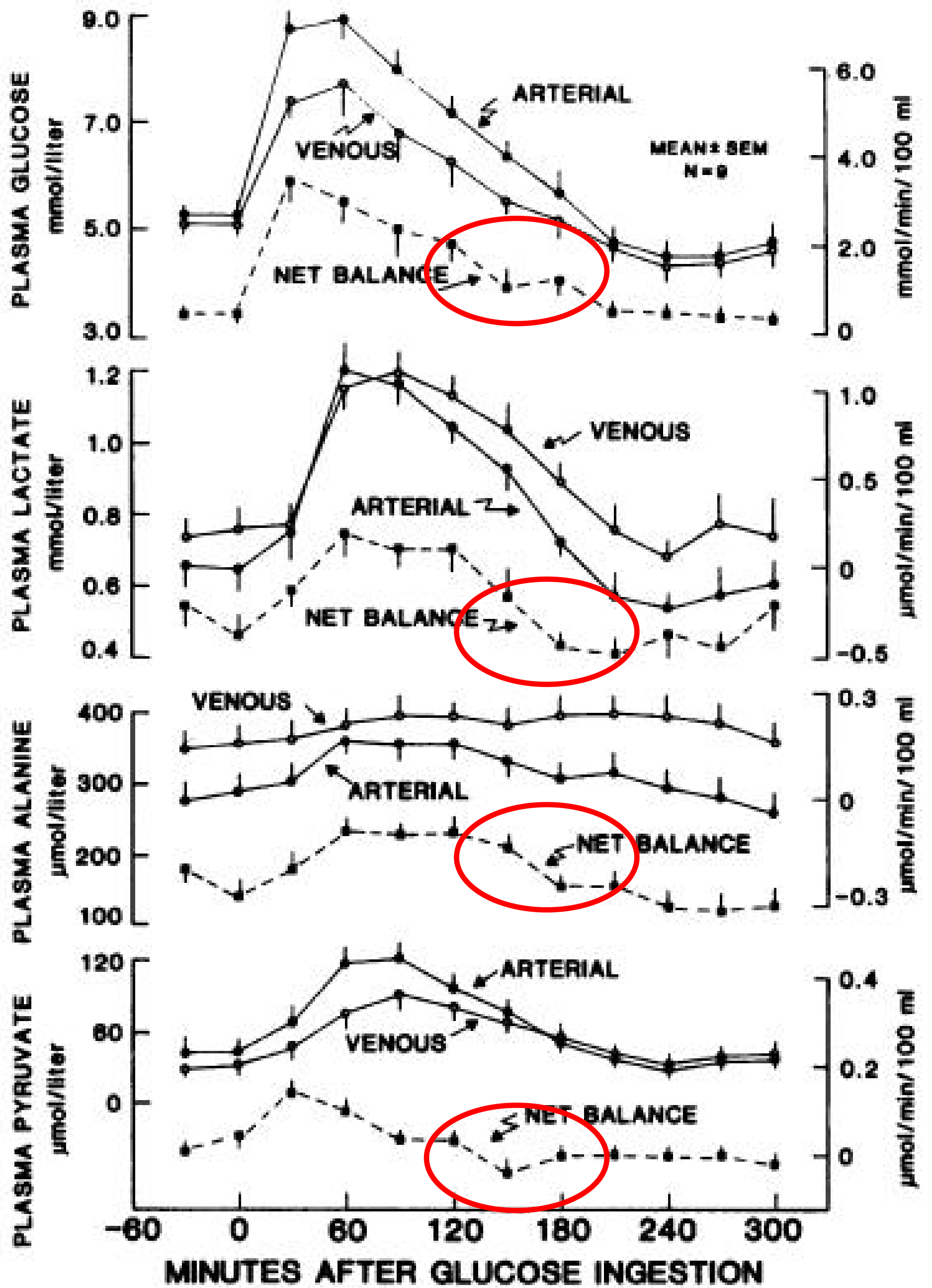


Figure 1. Plasma glucose and insulin concentrations and rates of systemic appearance of endogenous glucose, orally administered glucose, and oral plus endogenous glucose after ingestion of a 1-g/kg glucose load in nine normal volunteers.

静脉血、动脉血血糖、乳酸、丙氨酸、丙酮酸变化



口服葡萄糖负荷后肌肉葡萄糖代谢过程

Table I. Muscle Glucose Metabolism during Assimilation of Oral Glucose Load

	Forearm tissue (μmol/100 ml)*		Total body muscle (g)	
	Overall	Oral glucose	Overall	Oral glucose
Uptake	406±59	268±43	27.3±4.3	17.9±2.9
Glycolysis	60.2±16.6	37.9±11.5	4.0±1.5	2.5±0.9
Lactate release	35.6±12.2	22.9±7.8	2.3±1.1	1.5±0.7
Alanine release	30.5±6.0	18.9±3.6	2.1±0.5	1.3±0.3
Pyruvate release	−6.4±2.9	−4.0±1.8	−0.4±0.2	−0.3±0.1
Oxidation	208±28	138±22	13.6±2.0	8.9±1.4
Storage	138±54	91.5±35.4	9.8±3.7	6.4±2.3

* Micromoles as glucose equivalents calculated as (*a*) sum of lactate, alanine, and pyruvate release, (*b*) glucose uptake minus glycolysis plus oxidation, and (*c*) as described in Methods.

2.5/17.9=15%

OXIDIZED 25g (37%) 36%

STORED 43g (63%) 15%

一、OGL实验肌肉对糖的储存与利用

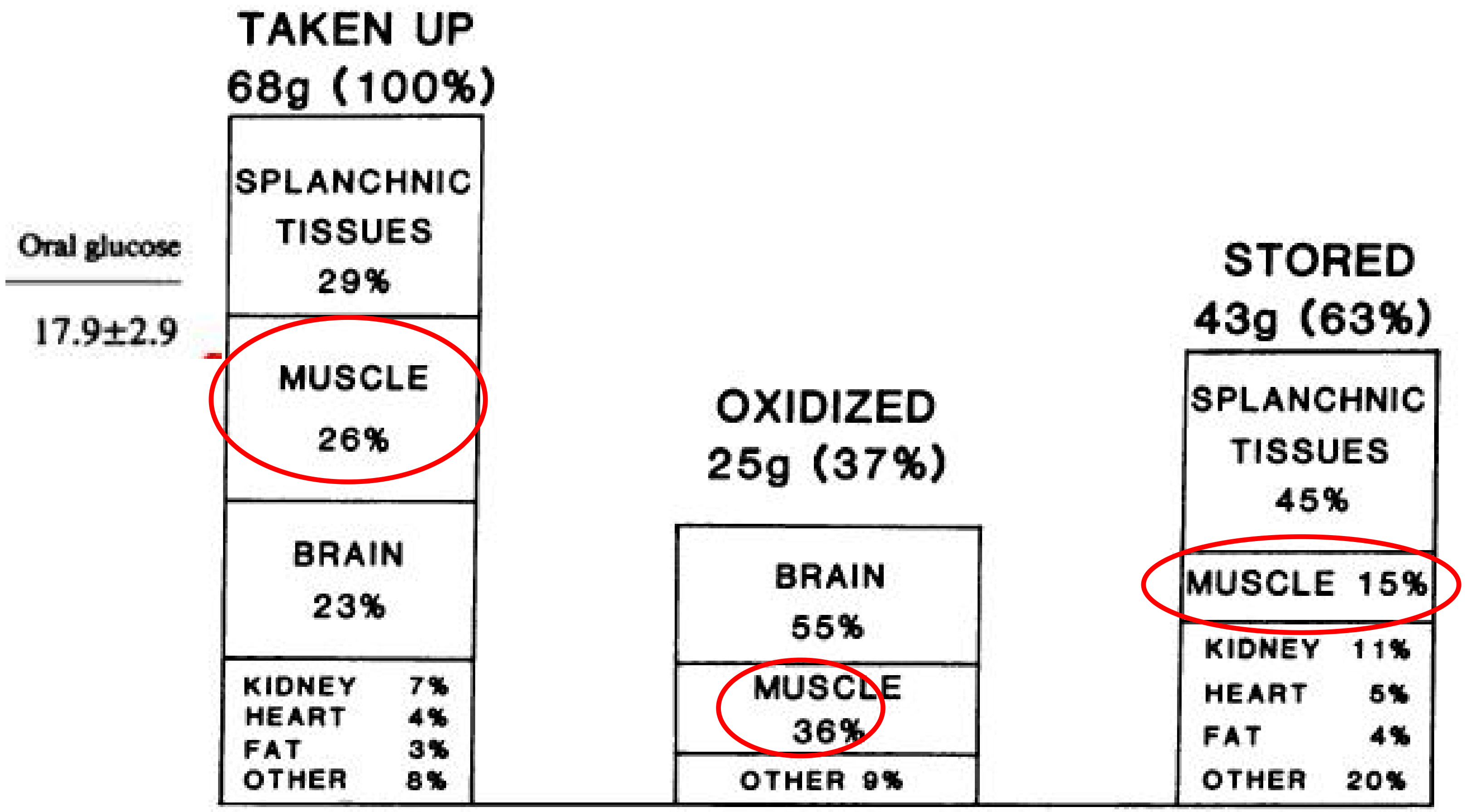


Figure 4. Overview of metabolic fate of 68-g oral glucose load in normal human volunteers. Values for kidney storage actually represent net uptake and may include glucose that was metabolized.

结论：

- 1.OGL实验后进入肌肉的 糖为17.9±2.9g，占总摄取糖的15%。
- 2.糖进入肌肉后，用于氧化的占绝大部分：8.9±1.7g 。
- 3.糖原 储存6.4±1.3g 。
- 4.糖酵解2.5±0.9g。

二、肌肉对糖的吸收的调节

- It is generally regarded that much of the control over rates of uptake is posited within the proximal steps of delivery, transport, and phosphorylation of glucose, with glucose transport as the main locus of control.
- [^{15}O]H_2O，[^{11}C]3-OMG,和 [^{18}F]FDG
- 胰岛素处理+饥饿组
- 比目鱼肌和胫骨前肌

二、肌肉对糖的吸收的调节

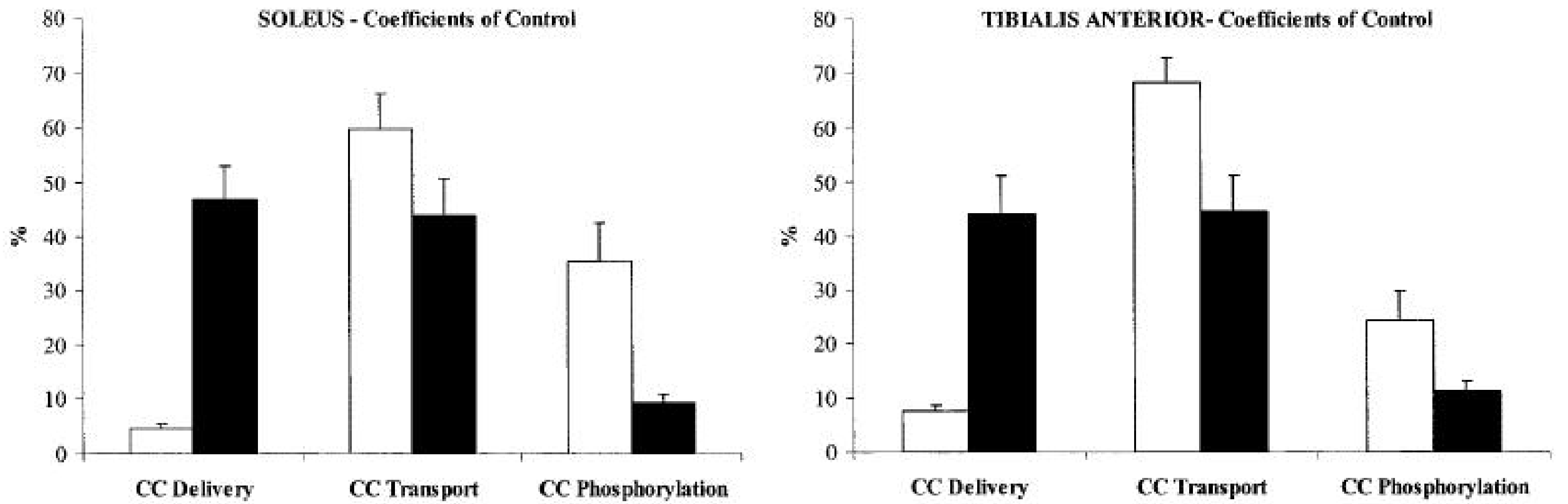


FIG. 5. The coefficients of control governing rates of glucose uptake during basal (□) and insulin (■) are shown for soleus and tibialis anterior muscle.

比目鱼肌

胫骨前肌

DIABETES, VOL. 55, NOVEMBER 2006

三、高脂、低碳食品短期摄食对肌肉糖代谢关键酶活的影响

J Appl Physiol 98: 100–107, 2005.
First published August 13, 2004; doi:10.1152/japplphysiol.00686.2004.

Enzymatic regulation of glucose disposal in human skeletal muscle after a high-fat, low-carbohydrate diet

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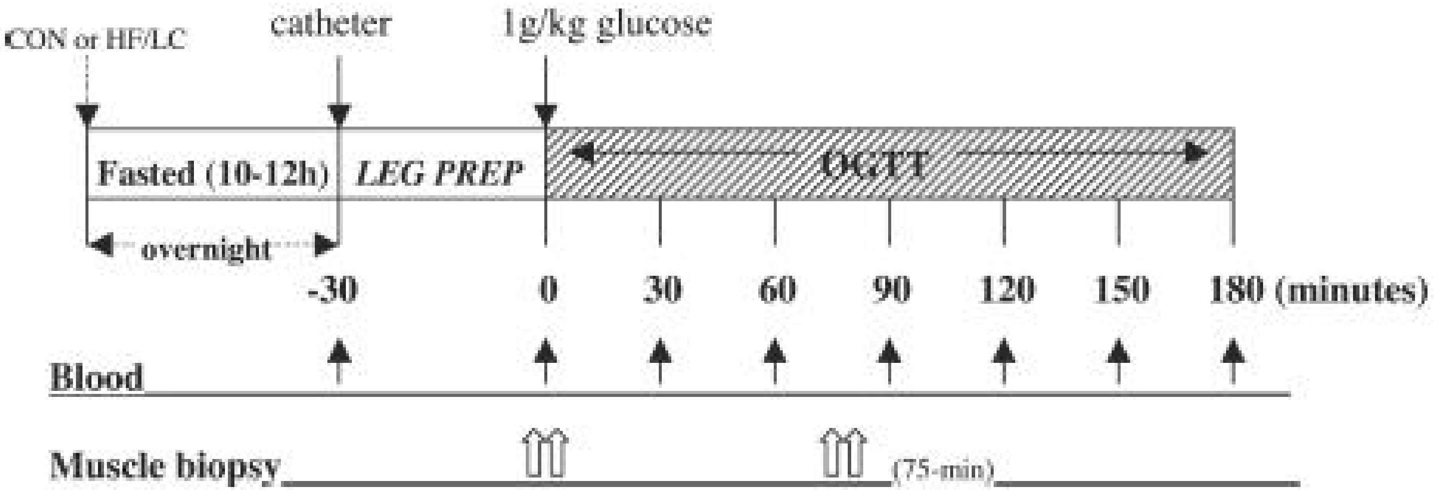
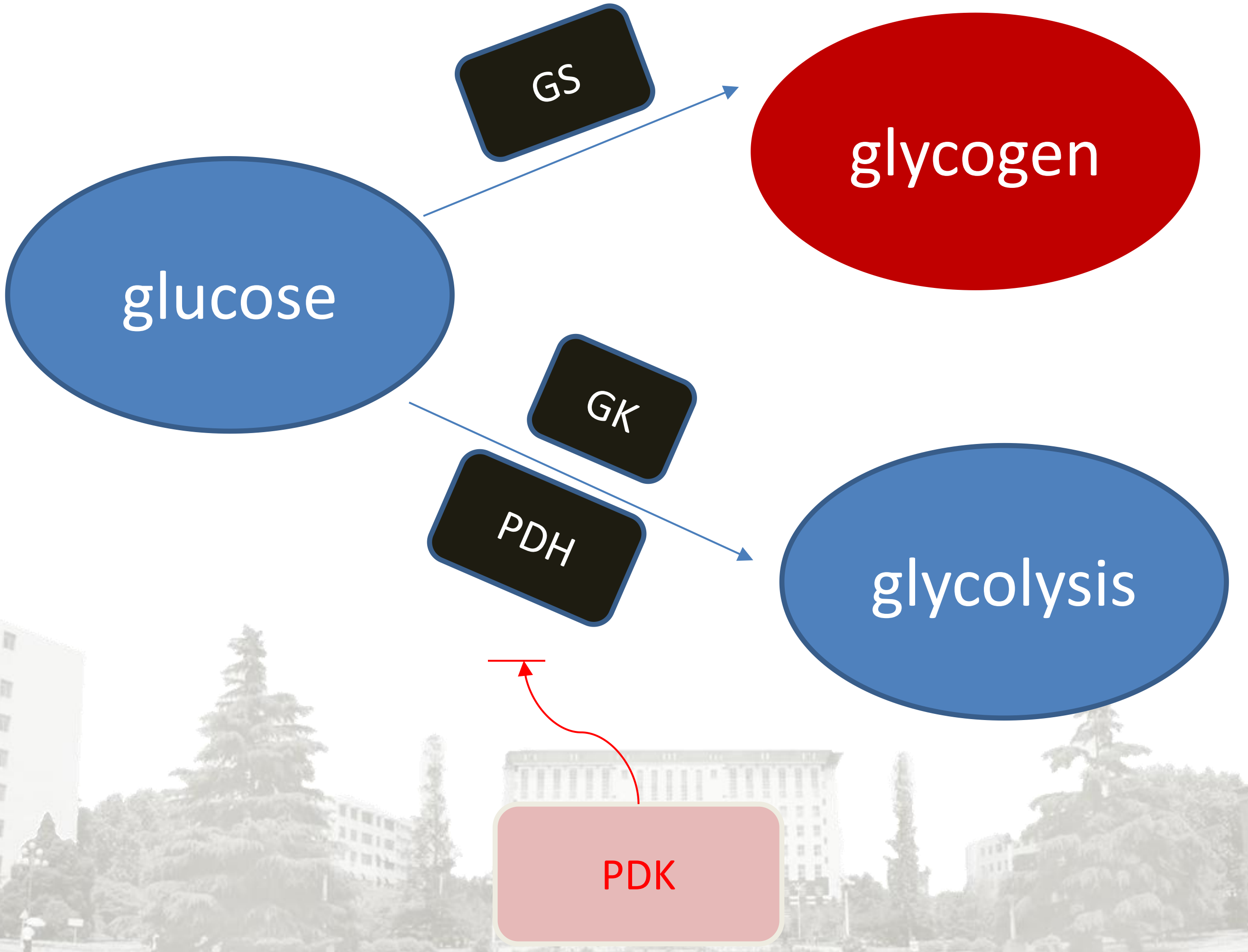


3.1肌肉对糖的利用途径



3.2 血糖及胰岛素变化

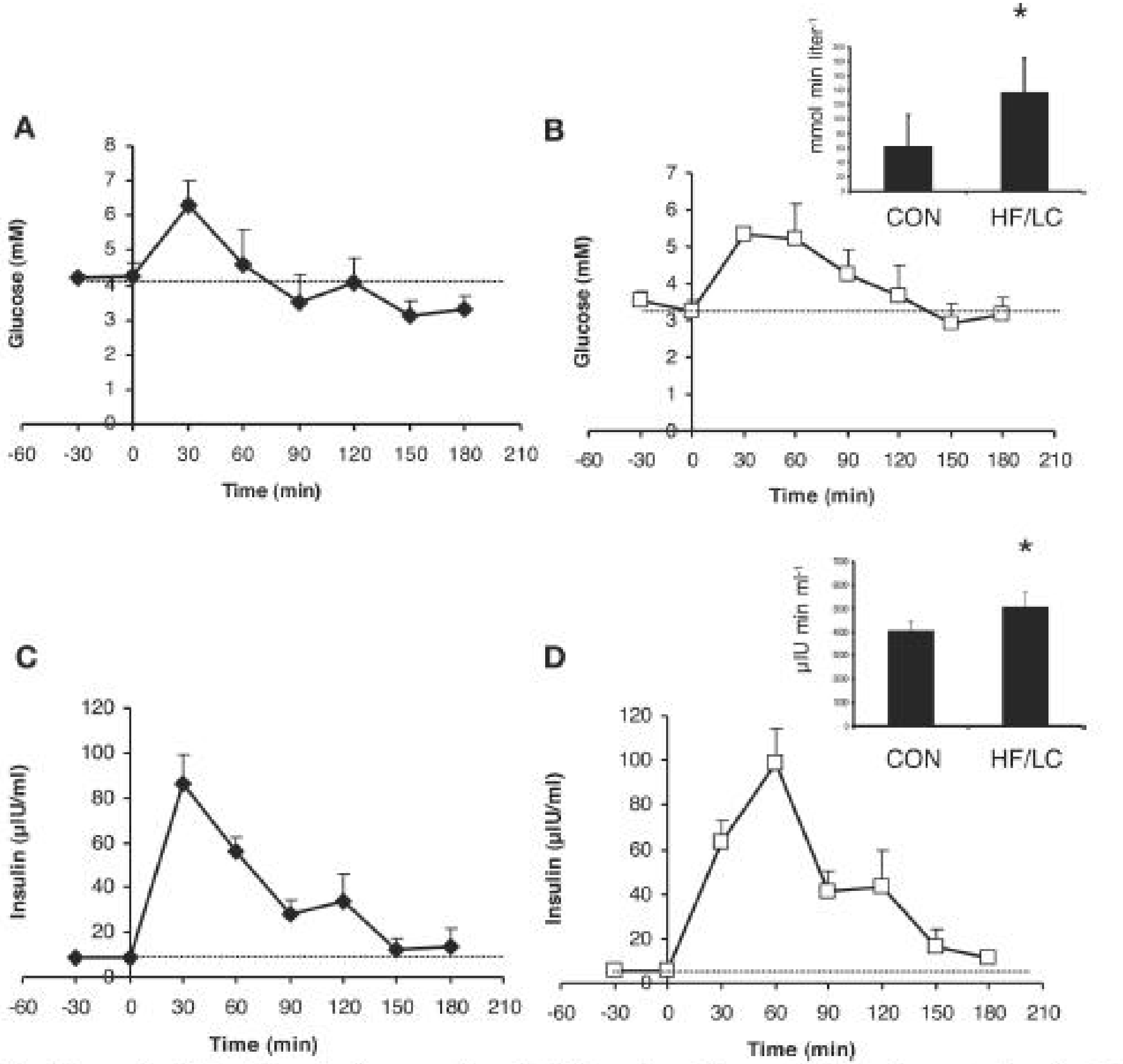


Fig. 2. Whole blood glucose (*A* and *B*) and plasma insulin concentrations (*C* and *D*) over time during an oral glucose tolerance test after a Con diet (*A* and *C*; ◆) or a HF/LC diet (*B* and *D*; □). Values are means ± SE. Dotted lines, mean fasting glucose and insulin concentrations. *Insets*, area under the glucose (*top*) and insulin (*bottom*) curves after Con and HF/LC diets, respectively. *Significantly different from control, $P < 0.05$.

3.2血清FFA及羟基丁酸、丙三醇、乳酸

Table 2. *Plasma FFA and whole blood β-hydroxybutyrate, glycerol, and lactate responses during an OGTT after a Con or HF/LC diet*

Time, min (OGTT)	FFA		β-Hydroxybutyrate		Glycerol		Lactate	
	Con	HF/LC	Con	HF/LC	Con	HF/LC	Con	HF/LC
−30	0.30±0.08	0.52±0.08*	0.10±0.02	0.31±0.09*	0.04±0.01	0.05±0.01	0.4±0.1	0.3±0.1
0	0.31±0.07	0.45±0.06	0.13±0.04	0.28±0.08*	0.05±0.01	0.04±0.01	0.3±0.1	0.1±0.1
30	0.21±0.06	0.27±0.05	0.07±0.02	0.16±0.05	0.03±0.01	0.03±0.01	0.4±0.1	0.1±0.1
60	0.12±0.05†	0.12±0.04†	0.04±0.01†	0.09±0.04†	0.02±0.01†	0.03±0.01[b]	0.4±0.2	0.2±0.1
90	0.11±0.05†	0.07±0.03†	0.04±0.01†	0.05±0.01†	0.02±0.01†	0.02±0.001†	0.5±0.2	0.3±0.1
120	0.09±0.03†	0.06±0.04†	0.04±0.01†	0.04±0.01†	0.02±0.01†	0.02±0.01†	0.3±0.1	0.2±0.1
150	0.22±0.05	0.27±0.14	0.06±0.02†	0.07±0.02†	0.04±0.01	0.03±0.01	0.2±0.1	0.2±0.1
180	0.40±0.14	0.47±0.10	0.11±0.04	0.22±0.08	0.04±0.01	0.04±0.01	0.2±0.1	0.3±0.1

Values are means ± SE given in mM. FFA, free fatty acid; OGTT, oral glucose tolerance test. *Significantly different from Con, $P < 0.05$. †Significantly different from basal concentration (−30 and 0 min), $P < 0.05$.

3.3 糖代谢关键酶活性

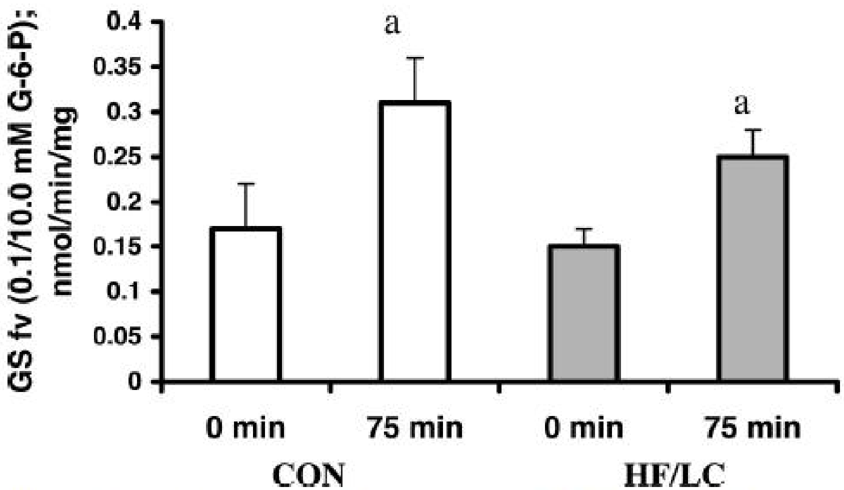


Fig. 3. Fractional velocity of glycogen synthase (GS_{fv}) before (0 min) and during an OGTT (75 min), after a Con diet and a HF/LC diet. Values are means ± SE. GS_{fv}, activity of the glycogen synthase active form [0.1 mM glucose-6-phosphate (G-6-*P*)]/total glycogen synthase activity (10 mM G-6-*P*). [a] Significantly different from 0 min, $P < 0.05$.

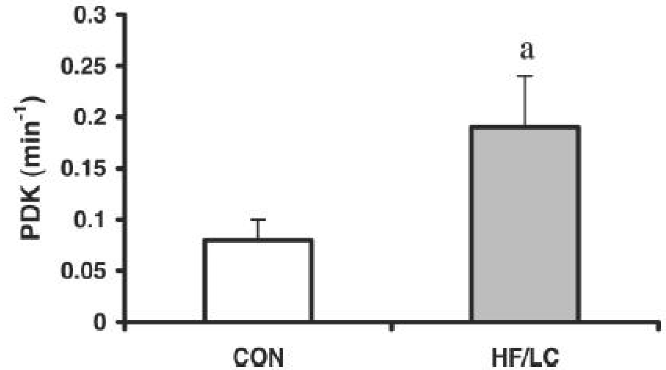


Fig. 4. Pyruvate dehydrogenase kinase (PDK) activity after Con and HF/LC diet. Values are means ± SE. [a] Significantly different from Con, $P < 0.05$.

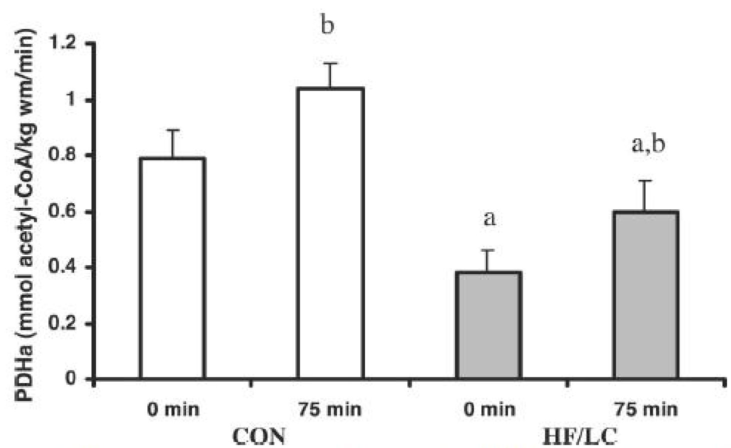


Fig. 5. Pyruvate dehydrogenase in the active form (PDH_a) before (0 min) and during an OGTT (75 min) after Con and HF/LC diets. Values are means ± SE. ww, Wet wt. [a] Significantly different from Con, $P < 0.05$. [b] Significantly different from 0 min, $P < 0.05$.

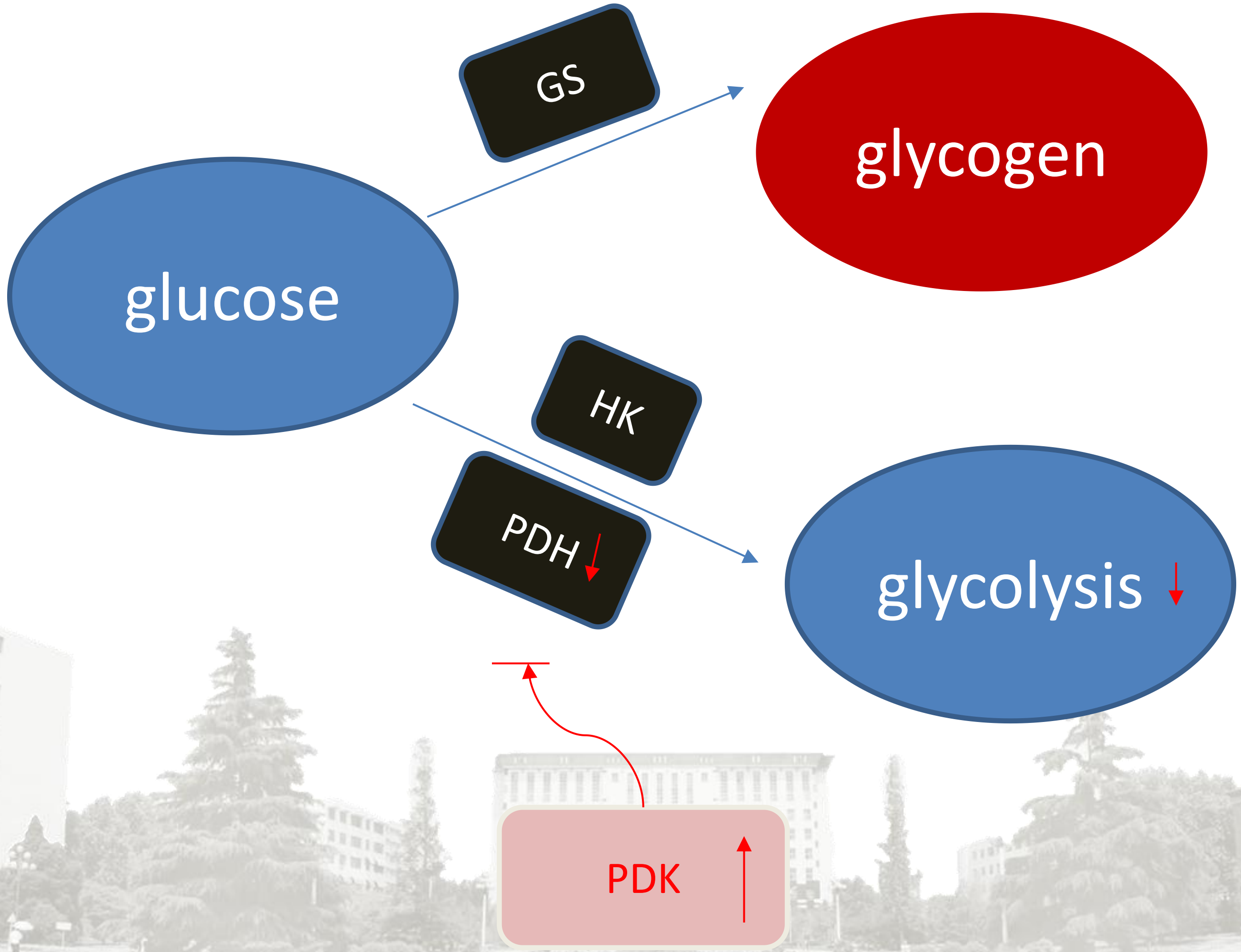
56 h HF/LC diet处理显著提高PDK活性。

3.3 糖代谢关键酶活性

- HK and GS activities. Maximal HK activity was not altered by the 56 h HF/LC diet (Con; 0.42 ± 0.04 vs. HF/LC; 0.36 ± 0.04 mol/kg protein-1 h-1).

- 56 h HF/LC diet处理对HK/GS没有显著影响。

3.4摄食HL/LC饲料对肌肉糖的利用的影响



3.5肥胖对骨骼肌糖摄取的影响

- 肥胖时，骨骼肌糖摄入减少已经是不争的事实，脂肪在骨骼肌组织的异位沉积、骨骼肌线粒体功能降低、慢性炎症、内质网应激等都参与了肥胖时骨骼肌糖代谢的调节过程。

- 上述因素作用于胰岛素受体信号通路，下调葡萄糖转运体4（glucose transporter 4，GLUT4) 的表达、抑制GLUT4 转位，减 少葡萄糖的摄取(Boden 等． 2011) 。

四、碳水化合物再投喂，对肌肉PDK活性的快速扭转作用

Am J Physiol Regul Integr Comp Physiol 297: R885–R891, 2009.
First published July 22, 2009; doi:10.1152/ajpregu.90604.2008.

Carbohydrate refeeding after a high-fat diet rapidly reverses the adaptive increase in human skeletal muscle PDH kinase activity

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Submitted 16 July 2008; accepted in final form 15 July 2009

四、碳水化合物再投喂，对肌肉PDK活性的快速扭转作用

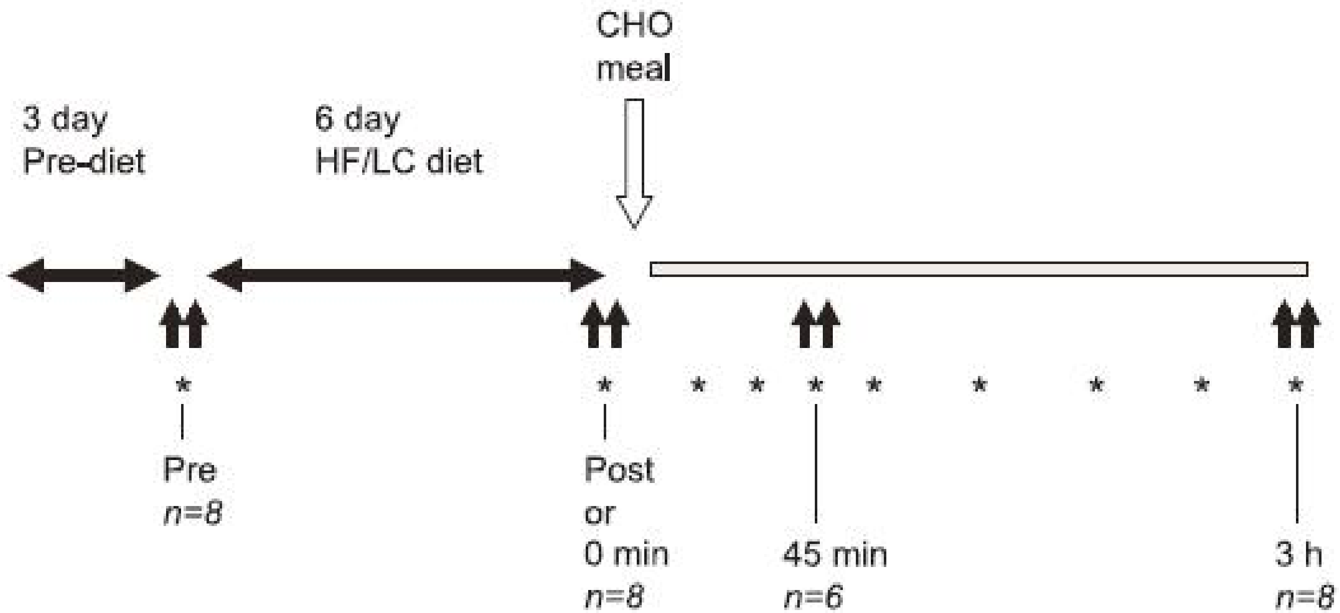

Fig. 1. Experimental protocol. Subjects consumed a standardized Pre-diet for 3 days (~50:30:20% of the energy from carbohydrate/fat/protein) followed by a 6-day high-fat low-carbohydrate (HF/LC) diet (~5:75:20% carbohydrate/fat/protein). Blood samples and muscle biopsies were taken prior to and following the HF diet. A single meal of high-glycemic index mixed carbohydrates (88:5:7% carbohydrate/fat/protein) was given, and muscle biopsies were taken at 45 min and 3 h after refeeding. Blood samples were taken every 15 min for the first hour after refeeding and then every 30 min for the remainder of the 3 h. Muscle biopsies; *blood samples.

4.1 血糖、血浆胰岛素、乳酸含量

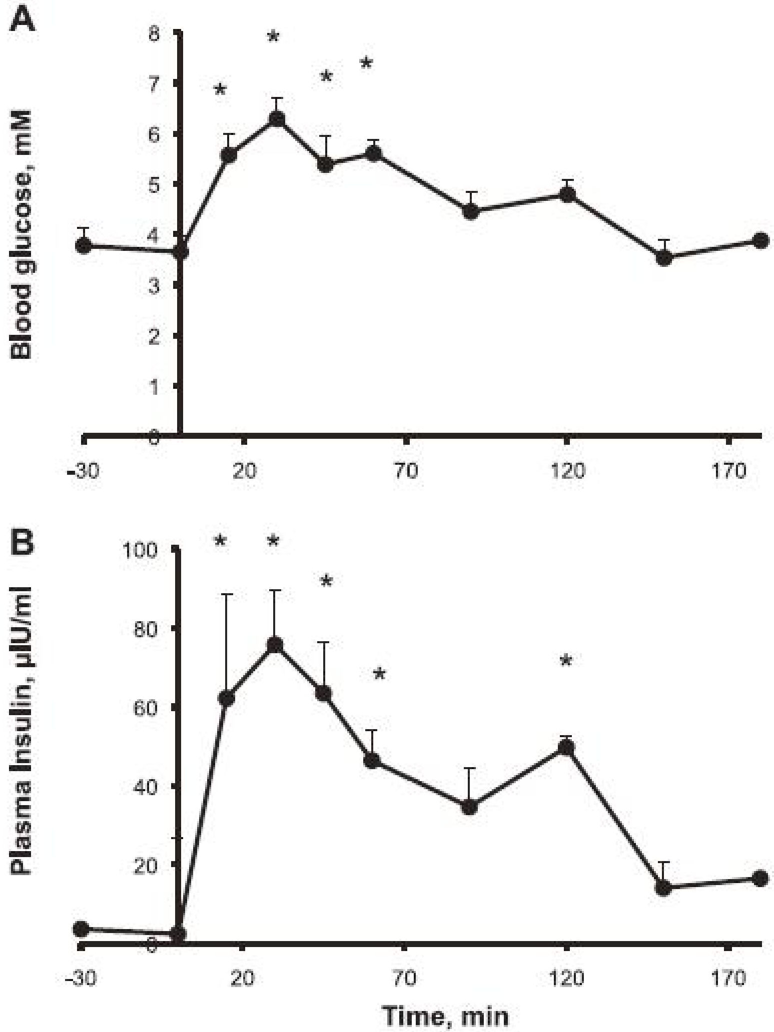

Fig. 2. Blood glucose (mM) and plasma insulin (μIU/ml) for 3 h after refeeding of a high carbohydrate meal. Values are means ± SE (n = 6). *Significantly higher than 0 min ($P < 0.05$).

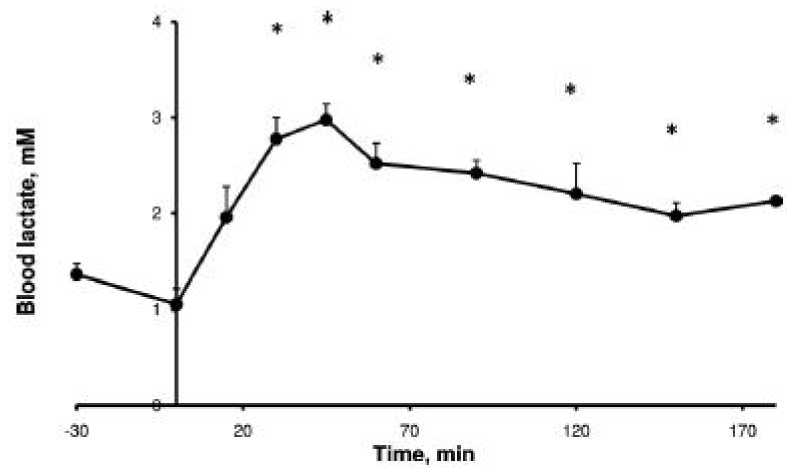

Fig. 3. Blood lactate (mM) for 3 h after refeeding of a high carbohydrate meal. Values are means ± SE (n = 6). *Significantly different from 0 min ($P < 0.05$).

4.2 血甘油、羟基丁酸酯（HB），血浆游离脂肪酸（FFA）等脂代谢相关指标

Table 3. *Blood glycerol, β-hydroxybutyrate (β-HB), and plasma free fatty acids (FFA). Lipid-related blood parameters Pre- and Post-HF diet (0 min) and 180 min after refeeding a high-carbohydrate meal*

	Pre	Post, 0 min	15 min	30 min	45 min	60 min	90 min	120 min	150 min	180 min
Glycerol	0.05±0.01	0.08±0.01	0.05±0.01	0.05±0.01	0.05±0.005	0.043±0.01*	0.04±0.01*	0.04±0.01*	0.04±0.01*	0.04±0.01*
β-HB	0.10±0.05	0.42±0.17†	0.25±0.10	0.16±0.06	0.11±0.04*	0.09±0.03*	0.05±0.02*	0.05±0.02*	0.03±0.01*	0.04±0.01*
FFA	0.52±0.11	0.86±0.10†	0.51±0.05*	0.44±0.05*	0.34±0.04*†	0.27±0.05*†	0.24±0.04*†	0.18±0.03*†	0.23±0.05*†	0.25±0.06*†

Values are means ± SE in mmol/l (mM). Lipid-related blood parameters Pre- and Post-HF diet (0 min) and 180 min after refeeding a high-carbohydrate meal. HF-diet, high-fat low-carbohydrate diet. *Significantly different from 0 min during refeeding; †significantly different from Pre-diet value.

4.3 肌肉PDK及PDHa活性分析

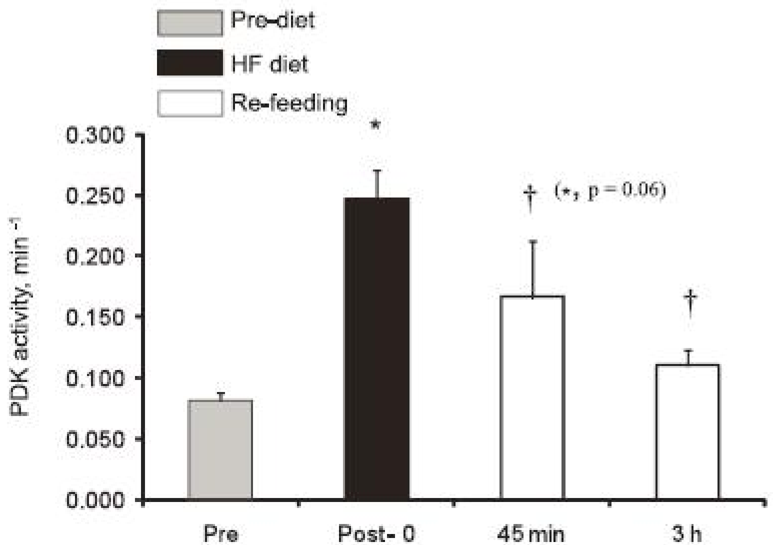

Fig. 4. Skeletal muscle PDH kinase (PDK) activity (min^{-1}) prior to (Pre) and following (Post) HF diet, and 0, 45 min, and 3 h after refeeding carbohydrates. Values are means ± SE (n = 8 for all time points except at 45 min, where n = 6). *Significantly different from Pre ($P < 0.05$, unless otherwise indicated), †significantly different from Post-0 min ($P < 0.05$).

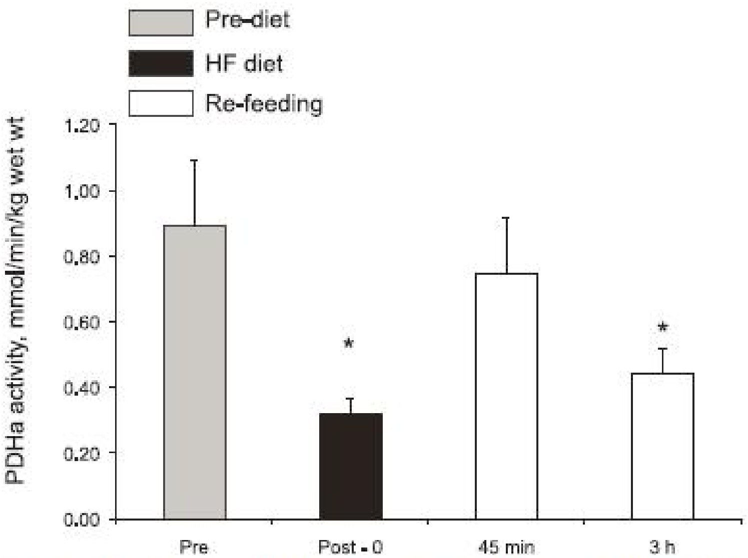

Fig. 5. Skeletal muscle pyruvate dehydrogenase to the active form (PDHa) activity. PDHa activity ($mmol \cdot min^{-1} \cdot kg$ wet wt^{-1}) prior to (Pre) and following (Post) HF diet, and 0, 45 min, and 3 h after refeeding carbohydrates. Values are means ± SE (n = 8 for all time points except at 45 min, where n = 6). *Significantly different from Pre ($P < 0.05$).

4.4 结论

- PDK activity increased Post-HF diet, and decreased with carbohydrate refeeding at 45 min and 3 h, respectively.
- PDHa decreased following the HF diet, and was increased transiently with refeeding at 45 min, but returned to lower values by 3 h (P =0.025 compared with Pre).
- These data demonstrate that in human skeletal muscle, the adaptive increase in PDK activity following an HF diet is rapidly reversed to Pre-diet activity levels within 45 min to 3 h, and this is accompanied by a short-term increase in PDHa activity.

后续报道：HF/LC 对机体糖代谢影响

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Applied Physiology, Nutrition, and Metabolism
Physiologie appliquée, nutrition et métabolisme

Short-term high-fat diet alters postprandial glucose metabolism and circulating vascular cell adhesion molecule-1 in healthy males

The concentrations of plasma glucose, insulin, glucagon-like peptide-1 (GLP-1), intercellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1)

健康男性短期摄入含有高比例的脂肪食物后，导致餐后血糖过度增加和血管细胞粘附分子-1 （VCAM-1）浓度和使得第一阶段胰岛素释放衰减。

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