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Lipoic acid prevents fructose-induced changes in liver carbohydrate metabolism: role of oxidative stress.

Castro MC[1], Francini F[1], Gagliardino JJ[1], Massa ML[2].

Author information

Abstract

BACKGROUND: Fructose administration rapidly induces oxidative stress that triggers compensatory hepatic metabolic changes. We evaluated the effect of an antioxidant, R/S-α-lipoic acid on fructose-induced oxidative stress and carbohydrate metabolism changes.

METHODS: Wistar rats were fed a standard commercial diet, the same diet plus 10% fructose in drinking water, or injected with R/S-α-lipoic acid (35mg/kg, i.p.) (control+L and fructose+L). Three weeks thereafter, blood samples were drawn to measure glucose, triglycerides, insulin, and the homeostasis model assessment-insulin resistance (HOMA-IR) and Matsuda indices. In the liver, we measured gene expression, protein content and activity of several enzymes, and metabolite concentration.

RESULTS: Comparable body weight changes and calorie intake were recorded in all groups after the treatments. Fructose fed rats had hyperinsulinemia, hypertriglyceridemia, higher HOMA-IR and lower Matsuda indices compared to control animals. Fructose fed rats showed increased fructokinase gene expression, protein content and activity, glucokinase and glucose-6-phosphatase gene expression and activity, glycogen storage, glucose-6-phosphate dehydrogenase mRNA and enzyme activity, NAD(P)H oxidase subunits (gp91(phox) and p22(phox)) gene expression and protein concentration and phosphofructokinase-2 protein content than control rats. All these changes were prevented by R/S-α-lipoic acid co-administration.

CONCLUSIONS: Fructose induces hepatic metabolic changes that presumably begin with increased fructose phosphorylation by fructokinase, followed by adaptive changes that attempt to switch the substrate flow from mitochondrial metabolism to energy storage. These changes can be effectively prevented by R/S-α-lipoic acid co-administration.

GENERAL SIGNIFICANCE: Control of oxidative stress could be a useful strategy to prevent the transition from impaired glucose tolerance to type 2 diabetes.

KEYWORDS: FPG; FPI; Fructokinase; Glucokinase; Glucose metabolism; Glycoxidative stress; HOMA-IR; NAFLD; PFK-2; R/S-α-lipoic acid; fasting plasma glucose; fasting plasma insulin; homeostasis model assessment-insulin resistance; non-alcoholic fatty liver disease; phosphofructokinase 2

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