Effects of the cannabinoid CB1 antagonist rimonabant on hepatic mitochondrial function in rats fed a high-fat diet

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The aim of this study was to investigate the effect of rimonabant treatment on hepatic mitochondrial function in rats fed a high-fat diet. Sprague-Dawley rats fed a high-fat diet (35% lard) for 13 wk were treated with rimonabant (10 mg·kg⁻¹·day⁻¹) during the last 3 wk and matched with pair-fed controls. Oxygen consumption with various substrates, mitochondrial enzyme activities on isolated liver mitochondria, and mitochondrial DNA quantity were determined. Body weight and fat mass were decreased in rats treated with rimonabant compared with pair-fed controls. Moreover, the serum adiponectin level was increased with rimonabant. Hepatic triglyceride content was increased, while serum triglycerides were decreased. An increase of mitochondrial respiration was observed in rats treated with rimonabant. The increase of mitochondrial respiration with palmitoyl-CoA compared with respiration with palmitoyl-l-carnitine stating that the entry of fatty acids into mitochondria via carnitine palmitoyltransferase I was increased in rats treated with rimonabant. Moreover, rimonabant treatment led to a reduction in the enzymatic activity of ATP synthase, whereas the quantity of mitochondrial DNA and the activity of citrate synthase remained unchanged. To summarize, rimonabant treatment leads to an improvement of hepatic mitochondrial function by increasing substrate oxidation and fatty acid entry into mitochondria for the β-oxidation pathway and by increasing proton leak. However, this increase of mitochondrial oxidation is regulated by a decrease of ATP synthase activity in order to have only ATP required for the cell function.


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