



Fatty liver and insulin resistance in obese Zucker rats: No role for mitochondrial dysfunction

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Résumé en anglais

The relationship between insulin resistance and mitochondrial function is of increasing interest. Studies looking for such interactions are usually made in muscle and only a few studies have been done in liver, which is known to be a crucial partner in whole body insulin action. Recent studies have revealed a similar mechanism to that of muscle for fat-induced insulin resistance in liver. However, the exact mechanism of lipid metabolites accumulation in liver leading to insulin resistance is far from being elucidated. One of the hypothetical mechanisms for liver steatosis development is an impairment of mitochondrial function. We examined mitochondrial function in fatty liver and insulin resistance state using isolated mitochondria from obese Zucker rats. We determined the relationship between ATP synthesis and oxygen consumption as well as the relationship between mitochondrial membrane potential and oxygen consumption. In order to evaluate the quantity of mitochondria and the oxidative capacity we measured citrate synthase and cytochrome c oxidase activities. Results showed that despite significant fatty liver and hyperinsulinemia, isolated liver mitochondria from obese Zucker rats display no difference in oxygen consumption, ATP synthesis, and membrane potential compared with lean Zucker rats. There was no difference in citrate synthase and cytochrome c oxidase activities between obese and lean Zucker rats in isolated mitochondria as well as in liver homogenate, indicating a similar relative amount of hepatic mitochondria and a similar oxidative capacity. Adiponectin, which is involved in bioenergetic homeostasis, was increased two-fold in obese Zucker rats despite insulin resistance. In conclusion, isolated liver mitochondria from lean and obese insulin-resistant Zucker rats showed strictly the same mitochondrial function. It remains to be elucidated whether adiponectin increase is involved in these results.

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