Effects of short-term high fat diet on rat liver triglyceride content using in vivo 1H MRS

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Introduction

A high fat diet is associated with the development of insulin resistance. Important characteristics of insulin resistance include fasting hyperglycaemia and disruption of whole-body triglyceride metabolism. Hyperglycaemia may be associated with abnormal levels of hepatic triglycerides since they promote hepatic gluconeogenesis. Both hyperglycemia and elevated hepatic triglyceride content (HTGC) are prevalent in the ZDF rat, an animal model of type 2 diabetes. In a large scale studies, these characteristics were endemic in non-diabetic obese subjects and may reflect a western-style high fat diet. To determine if diet per se as an effect on HTGC we compared hepatic lipids in rats fed with a standard chow with those given a high fat diet. We also performed glucose intolerance test in these animals to determine if HTGC is associated with impaired glucose tolerance.

Animals and methods

200-250 g male Sprague Dawley rats were housed during 20 days at 20ºC and on a 12-h light-dark cycle with ad libitum access to water. One group of animals (n=9) was fed with a standard chow rat diet and the other (n=10) was given a high fat diet (HFD) with 40% of calories from fat. ^{1}H MR spectra were acquired on a 7.0 T Bruker Pharmascan system from liver using a PRESS sequence (TR 1100 ms/ TE 28 ms) without water saturation and with 128 signal averages. Transverse images of the liver were used to ensure accurate positioning of the (5x5x5 mm) voxel in the liver, avoiding blood vessels, the gall bladder, and fatty tissue. Spectra were analysed using an NMR data processing program, MestREC. Peak areas for all resonances were obtained and lipid resonances were quantified with reference to water resonance, after correcting for T_1 and T_2. On day 21, animals were sacrificed after 6h fasting and serum free fatty acids (FFA) and triglycerides were measured using commercial available kits. A parallel group of animals (Controls, n=13 and HFD, n=5) were subjected on day 21 to an i.p. glucose tolerance test (1.5mg glucose/g body weight). Blood glucose concentrations were determined at specific time points with a standard glucometer.

Results

At day 8, HTGC, represented as the percentage of fat relative to water, is increased in the group of animals fed with the high fat diet relative to the controls (4.87 ± 0.56 *vs.* 1.62 ± 0.75, $p<0.01$). On day 1 values of HTGC are similar between the two different groups studied. **Figure 1** shows the i.p. glucose tolerance test profile for the groups studied. 60 min after the glucose load, blood glucose levels had returned to basal levels in control animals while HFD animals were hyperglycaemic (>200 mg/dL). Serum FFA (9.23 ± 0.81 *vs.* 12.31 ± 1.19 mg/dL), and triglycerides (76.4 ± 5.0 *vs.* 70.4 ± 7.3 mg/dL) determined on the last experiment day, were not significantly different between both groups.

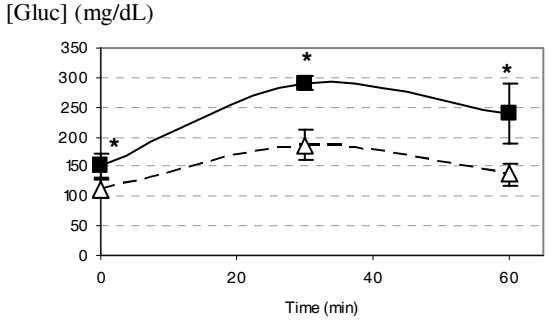

Figure 1: i.p. glucose tolerance test profile. ■ Group of animals fed with the high fat diet (n=5) and △ group of control animals (n=13). * $p<0.01$, relative to controls.

Discussion and Conclusions

Our results show that in healthy rats, a high fat diet is responsible for a rapid increase in HTGC and that this is associated with the onset of glucose intolerance. Importantly, serum lipids were not significantly increased in this setting. Therefore, HTGC is a more sensitive marker of disturbed lipid and glucose states than serum FFA and triglycerides levels.