Short term high fat diet evokes long lasting hepatic steatosis

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Adipose tissue inflammation plays an important role in the pathogenesis of obesity-associated insulin resistance and type 2 diabetes. We have previously demonstrated that chronic exposure to high fat diet increases hepatic lipogenesis, leading to hepatic inflammation and, finally, to insulin resistance in mice [1, 2]. Interestingly, we reported that adipose tissue inflammation (i.e. TNF-α expression), glucose intolerance as well as hepatic steatosis may be achieved also by an acute exposure to high fat diet for only 4 days, due to an early dysfunctional adipose tissue-liver cross talk [3]. According to the 'portal theory', increased amounts of free fatty acids (FFA) and pro-inflammatory factors released from visceral fat into portal vein, may directly promote fat accumulation and hepatic insulin resistance [4]. Here we investigated whether short-term HFD induced glucose intolerance and hepatic steatosis are readily reversible or rather persistent. 12 weeks old C57BL/6J mice were fed either a high fat diet (~60% kcal, HFD) for 7 days, followed by regular chow diet for 8 weeks (HFD/Chow group) or received chow diet for the entire 9 weeks (Chow group). Intra-peritoneal glucose tolerance tests (ipGTT) were performed 1, 2, 5 and 9 weeks after the start of the experiment. Thereafter animals were euthanized and systemic and portal blood, liver and fat pads were collected for analysis. Western blots, rtPCR and biochemical assays were performed.
The results confirmed our previous findings showing that one week of high fat feeding deteriorated glucose tolerance. Importantly, glucose tolerance was still impaired after eight weeks of recovery chow diet. Fat pad weight was trendwise increased in the HFD/Chow group, and TNF-α mRNA expression was triplicated in mesenteric fat of HFD/Chow mice. Moreover, total liver lipids were increased in HFD/Chow mice, suggestive of hepatic steatosis. Such finding was paralleled by a significant increase in portal but not systemic FFA levels in HFD/Chow mice
In conclusion, a short-term HFD has long-lasting effects on hepatic lipid accumulation and glucose tolerance.

References

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