Fenofibrate prevents high fat diet - induced insulin resistance and 3 month isolation stress - induced obesity

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We tested the ability of fenofibrate (FF), a hypolipidemic drug, to suppress insulin resistancc (IR). Male C57BL/6 mice were given either a standard-diet (C), standard-diet containing 0.15% FF (Cf), high fat- (HF), or HF-diet containing 0.15% FF (HFf). FF reduced plasma insulin, glucose and triglycerides levels, whereby these levels were significantly higher in mice receiving HF-diet. HF mice demonstrated IR, as estimated by HOMA index. SREBP-lc, Fasn and SCD-l genes were elevated in HF mice, whereas FF effectively down- regulated these genes. FF promoted β-oxidation, as evidenced by increased liver EHHADH expression and plasma ketone bodies. The effect of FF on IR was not mediated by PPAR-α Major liver fatty acids were decreased in HF mice. FF maintained the amount of these fatty acids, given rise to levels comparable to control mice. Our results showed that FF prevented IR by correcting the HOME index, and suppressing SREBP-lc target genes. FF consumption did not affect *de novo* fatty acids production in the liver.

On the other hand, two groups of mice were exposed to a l-month and 3-month isolation stress, respectively. One-month isolation stress increased food intake in mice, but did not result in an increase of body weight gain compared to control mice. In the 3-month study, significant increases in body weight, reproductive and visceral fat tissues were observed. A treatment of mice with FF significantly overturned the conditions. Although not statistically significant, both l-month and 3-month isolation stress have up-regulated ACOX, EHHADH, and SREBP-1. FF further enhanced the expression of these genes. The reduced expression of IGFBP-l in l-month stress mice was an indicator of stress, while an identical level of IGFBP-l between the stress and control mice in the 3-month study suggests that recovery has taken place. A significantly high level of fatty acids production was found in stress mice, in accords with the increased body weight gain. FF appeared to have alleviated stress-induced adiposity.