Suppression of Hepatic Fatty Acid Oxidation and Food Intake in Men

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We investigated the effects of the fatty acid oxidation inhibitor etomoxir (ETO) on food intake and on fat and carbohydrate metabolism in two double-blind crossover studies in male, normal-weight subjects. In study 1, ETO (75 mg [1]-racemate) or placebo was given orally 30 min after completion of a standardized, fat-enriched (total energy: 2698 kJ, 40% from fat) lunch. The subjects (*n* 5 15) were isolated from external time cues and free to choose when to eat dinner from an oversized serving (total energy: 6656 kJ, 60% from fat). In study 2, subjects (*n* 5 13) were selected for habitually high fat intake (mean: 44% of energy intake). ETO (150 mg) or placebo was given after an overnight fast, 2.5 h before offering an oversized high fat breakfast (6960 kJ, 72% from fat). In both studies, blood samples were taken and the respiratory quotient (RQ) was measured several times during each test period. In study 1, ETO (75 mg) did not affect the timing and size of the dinner or subjective feelings of hunger and satiety. Although ETO (75 mg) did not affect the RQ, it decreased plasma b-hydroxybutyrate (BHB) and increased plasma lactate compared with placebo. Plasma triacylglycerols (TG), free fatty acids (FFA), glucose, and insulin were not affected by ETO. In study 2, ETO (150 mg) enhanced hunger feelings and increased the size of the breakfast by 22.7%. ETO did not affect the RQ, but baseline RQ was lower in study 2 than in study 1 (0.83 versus 0.89, *P* , 0.01). Compared with placebo, ETO (150 mg) decreased plasma BHB and increased plasma FFA and plasma lactate. Baseline plasma concentrations of BHB, FFA, and lactate were higher in study 2 than in study 1 (BHB: 242 versus 81 mmol/L, *P* , 0.001; FFA: 0.674 versus 0.406 mmol/L, *P* , 0.01; lactate: 1.08 versus 0.74 mmol/L, *P* , 0.05). Plasma concentrations of TG, glucose, and insulin were not affected by ETO. The results suggest that inhibition of hepatic fatty acid oxidation stimulates eating in men when baseline fatty acid oxidation is sufficiently high and markedly suppressed by the treatment.

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