Dietary fat oxidation is elevated in middle-aged type 2 diabetes


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Background and Aims: Older individuals have increased delivery of endogenous fat to skeletal muscle, which may predispose to insulin resistance if fat oxidation is reduced. Likewise, insulin resistance increases the delivery and storage of dietary and endogenous fat in skeletal muscle. The aim of the present study was to investigate the effect of type 2 diabetes (T2D) and age on dietary fat oxidation.

Materials and Methods: Seven middle age (46.0 ± 1.1 y) and seven older (63.4 ± 0.6 y) patients with T2D (metformin and/or diet control for 4.8 ± 1.1 y) were matched with seven middle age (46.1 ± 2.9 y) normoglycemic controls for BMI (31.1 ± 1.5; 29.6 ± 1.1; 29.6 ± 1.3 kg/m2, respectively), % body fat by DXA (28.5 ± 2.3; 28.2 ± 4.0; ± 30.6 ± 1.2 %, respectively), and habitual physical activity (measured and self-reported). Subjects were prescribed a eucaloric diet (Henry equation) for 72 h preceding a fasted oral glucose tolerance test (OGTT). During this time, interstitial glucose was continuously measured using a subcutaneous probe. Twenty-four h before the OGTT, subjects consumed a meal replacement drink (330 kcal: 44g carbohydrate, 11g fat, and 14g protein) containing 15 mg/kg [131H]palmitate and 0.2 g/kg [18O]water and were asked to collect all passed urine for the following 10 h. Indirect calorimetry was performed to determine respiratory exchange ratio (RER) before and at the end of the 120 min OGTT. Blood samples were taken every 15 min throughout the OGTT for measurement of blood glucose, serum insulin and free fatty acid (FFA) concentration. Urine samples were analysed for 2H/H and 18O/16O isotope ratios by infrared spectroscopy in order to determine dietary fat oxidation and total body water, respectively. Two-way and one-way ANOVA was used to detect any differences in the blood and urine measurements, respectively. Data are presented as mean ± SEM.

Results:
Average blood glucose during the OGTT was greater (P<0.001) in T2D (11.9 ± 0.9 and 10.7 ± 0.8 mmol/L for middle age and older, respectively) than control (7.6 ± 0.5 mmol/L), and average serum insulin was almost half (50.3 ± 5.05 mIU/L and 56.0 ± 7.15 mIU/L vs. 93.9 ± 11.5 mIU/L, respectively; P=0.09). Average 24 h interstitial glucose was also higher in T2D (9.9 ± 0.18 and 7.6 ± 0.14 mmol/L for middle age and older, respectively) compared to control (6.4 ± 0.07; P<0.001). There was a trend (P=0.08) for 10 h dietary fat oxidation to be greater in middle age T2D (22.6 ± 1.6 % recovery of dose) than older T2D (13.9 ± 3.3 %) and control (13.4 ± 2.7 %).
Furthermore, fasting plasma FFA in middle age T2D (0.39 ± 0.05 mmol/L) was lower (P=0.05) than older T2D (0.48 ± 0.05 mmol/L) and control (0.49 ± 0.05 mmol/L), but higher (P<0.05) at the end of the OGTT (0.10 ± 0.03 vs. 0.05 ± 0.01 and 0.04 ± 0.01 mmol/L, respectively). RER increased during the OGTT in all groups (P<0.001) from...
similar fasted values (0.74 ± 0.05, 0.75 ± 0.04, and 0.74 ± 0.03 for controls, middle age T2D, and older T2D, respectively) to similar fed values (0.82 ± 0.03, 0.83 ± 0.02, and 0.84 ± 0.03, respectively).

**Conclusion:** Despite similar fasting fat oxidation, dietary fat oxidation was increased in middle age T2D compared to age matched controls. Combined with an inability to suppress plasma FFA with feeding, this suggests excessive postprandial fat delivery to skeletal muscle in T2D. The lower dietary fat oxidation in older T2D does not appear to exacerbate insulin resistance.