January 2002

Effect of Conjugated Linoleic Acid on Insulin Sensitivity

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The ability of insulin to control blood glucose is lost when mice consume conjugated linoleic acid (CLA).

Summary

Mice were fed a mixture of conjugated linoleic acid isomers (CLA) for nine weeks and then underwent an insulin tolerance test. CLA was then removed from the diet and a second insulin tolerance test was conducted following five weeks of recovery. CLA consumption impaired glucose response to insulin. When CLA was removed from the diet, insulin sensitivity of a low heat-loss genetic mouse line returned to normal. However, mice of a high heat-loss line remained insulin resistant for at least 32 days.

Introduction

Conjugated linoleic acid (CLA) provides several health benefits in areas of cancer, cardiovascular disease and body composition. However, there may be an adverse effect of CLA supplementation. A Japanese laboratory has reported increased plasma insulin concentration and impaired glucose response to insulin in CLA-fed mice. This development of insulin resistance with CLA supplementation may overshadow its antiobesity benefit. We hypothesized that if dietary CLA does impair insulin action, this detrimental effect will disappear when CLA is removed from the diet. Therefore the objective of our study was to determine the effect of temporary CLA supplementation and removal on insulin sensitivity. A second objective was to determine if this CLA effect was consistent between two selection lines of mice that differ in metabolic rate.

Procedure

Twenty-seven high heat loss (MH) and 27 low heat loss (ML), 9-wk-old male mice consumed a 7% soy oil control diet (Control) or the control diet with 1% CLA replacing soy oil (CLA) ad libitum, or the control diet at ~65% of ad libitum (Restricted) for 9 wk. The restricted intake treatment was used to determine if reduced insulin sensitivity caused by CLA was due to loss of body fatness. The mice were then subjected to an insulin tolerance test whereby 0.5 mU insulin/g of body weight were injected intraperitoneally and plasma glucose was measured at 0, 30, 60, 90, and 120 min post-injection (day 0 of recovery). Three days later, 18 of the mice were killed and serum, epidymal fat pads and livers were collected. Body composition was also determined by x-ray densitometry. Remaining mice were then provided free access to the control diet and allowed 32 days of recovery. They then underwent another insulin tolerance test and were killed three days later.
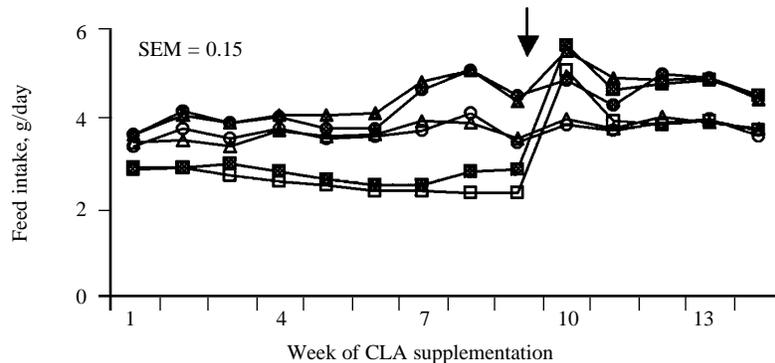

Figure 1. Effect of selection line and dietary treatment on feed intake. MH mice consumed more feed (*P* < 0.01) throughout, regardless of treatment. Prior to wk 9, restricted mice consumed less feed (*P* < 0.01). Filled symbols indicate MH mice and open symbols indicate ML mice. Circles represent the control diet, squares represent the restricted intake, and triangles represent the CLA diet. The arrow indicates when all mice were offered free access to the control diet.
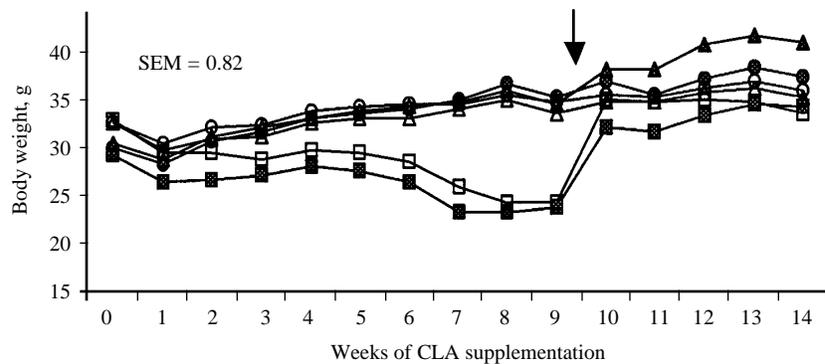

Figure 2. Effect of selection line and dietary treatment on body weight. The only significant effect through wk 9 was reduced (*P* < 0.01) body weight in feed restricted mice. After wk 9, previously restricted mice outgained all others but mice previously fed CLA were heaviest at wk 14. Filled symbols indicate MH mice and open symbols indicate ML mice. Circles represent the control diet, squares represent the restricted intake, and triangles represent the CLA diet. The arrow indicates when all mice were offered free access to the control diet ad libitum.
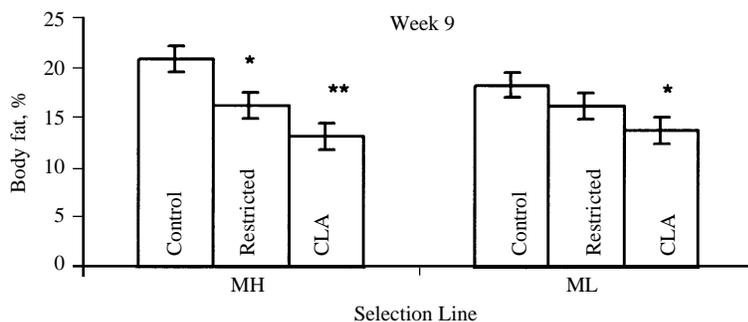
Figure 3. Effect of selection line and dietary treatment on body fat, wk 9 (d 0 recovery). *Means differ from control within selection line ($P < 0.10$). **Means differ from control within selection line ($P < 0.05$). Error bars represent SEM.
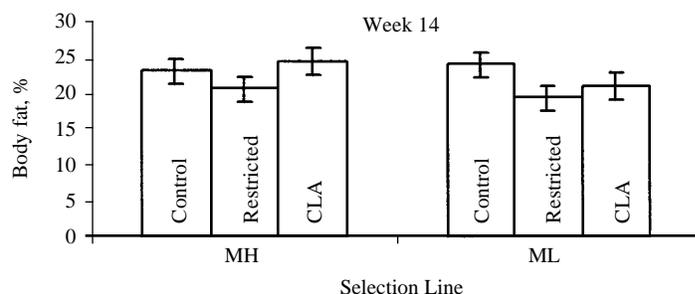

Figure 4. Effect of selection line and dietary treatment on body fat, wk 14 (35 d recovery). No effects of treatment or selection line were detected. Error bars represent SEM.
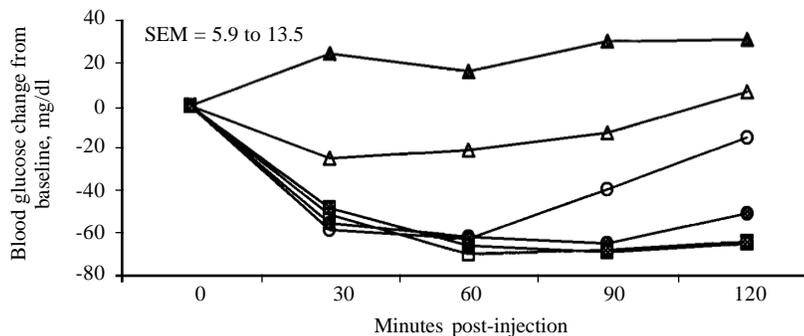

Figure 5. Effect of selection line and dietary treatment on glucose response to insulin, wk 9 (day 0 of recovery). Filled symbols indicate MH mice and open symbols indicate ML mice. Circles represent the control diet, squares represent the restricted intake, and triangles represent the CLA diet.
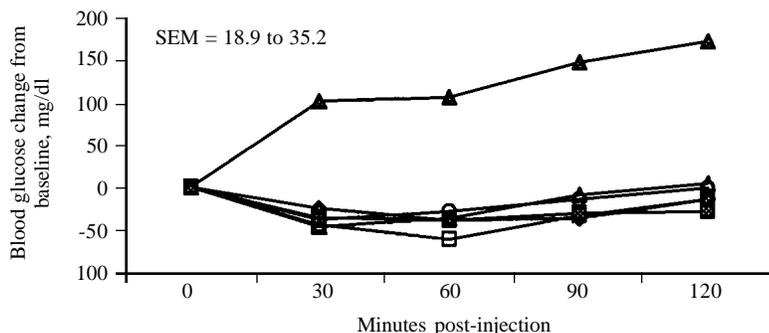

Figure 6. Effect of selection line and dietary treatment on glucose response to insulin, wk 14 (32 days of recovery). Filled symbols indicate MH mice and open symbols indicate ML mice. Circles represent the control diet, squares represent the restricted intake, and triangles represent the CLA diet.

Results

Feed intake was greater in MH mice than in ML mice ($P < 0.01$; Figure 1). Body weight was reduced ($P < 0.01$) in feed intake-restricted mice through wk 9. Following removal of CLA from the diet, MH mice previously fed CLA were the heaviest (Figure 2). There was a reduction ($P < 0.05$) of body fat in MH mice fed CLA vs the MH controls at day 0 of recovery (Figure 3). There was also a trend for a reduction ($P < 0.10$) of body fat in MH mice with restricted intakes and ML mice fed CLA vs their respective controls. Following 32 days of recovery there were no differences in body fat between either selection line or any of the dietary treatments (Figure 4).

Mice fed CLA experienced a lesser drop in blood glucose when injected with insulin, indicating insulin resistance relative to mice not fed CLA (Figure 5). At 11 days after termination of CLA feeding (recovery) the ML mice exhibited insulin sensitivities not different than controls while MH mice remained insulin resistant (data not shown). At 32 days after termination of CLA feeding the ML mice exhibited normal insulin sensitivity but the MH mice remained insulin resistant (Figure 6). Therefore, the effect of CLA on insulin sensitivity does not appear to depend on body fatness.

In conclusion, CLA supplementation did cause insulin resistance. The impaired insulin sensitivity effect of CLA may limit its role in treatment of human obesity or as a livestock feed additive. It is not known which isomer(s) of CLA are responsible for the insulin resistance. However, the sensitivity to CLA seemed to be greater in the MH mice regarding both insulin sensitivity and a loss of body fatness. Because it is known that the C18:2 d10,12 CLA isomer causes the change in body fatness, we can speculate that it may be this isomer that reduces insulin sensitivity (*2002 Nebraska Beef Report,* pp. 92-93). Ruminant products do not contain a relevant amount of C18:2 d10,12 CLA and therefore would not be expected to impact either obesity or insulin sensitivity by a CLA-dependent mechanism.

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