

Glycine supplementation during calorie restriction accelerates fat loss and protects against further muscle loss in obese mice

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Obesity has become one of the leading causes of preventable death. Weight loss is critical to combat the comorbidities which arise from obesity and is generally achieved by increasing daily physical activity and reducing energy intake (through calorie restriction). However, calorie restriction not only results in the loss of fat mass but also reduces lean mass which can predispose people to weight regain. Strategies that can enhance fat loss without compromising muscle mass are needed urgently. High protein diets and exercise have been proposed, but these may not be feasible in patients with a limited exercise capacity and/or problems with digestion. Emerging evidence suggests that the non-essential amino acid glycine may be effective in preserving muscle mass and increasing fat loss. Dietary administration of glycine in a model of cancer cachexia preserved muscle mass and function by almost 50% compared to saline treated tumour bearing mice (Ham *et al.*, 2014), while in sucrose-fed rats, glycine intake decreased adipose cell size and circulating fatty acids (El Hafidi *et al.*, 2004). In this study we investigated the effects of glycine supplementation during calorie restriction in a mouse model of diet-induced obesity and hypothesised that glycine supplementation during calorie restriction would improve fat loss and preserve muscle mass.

All experiments were approved by the Animal Ethics Committee of The University of Melbourne and conducted in accordance with the Australian code of practice for the care and use of animals for scientific purposes (NHMRC). Male C57BL/6 mice were fed a high-fat diet (HFD) or standard chow for 8 weeks. Following this intervention, mice were calorie restricted for 20 days (40% reduced calories) and supplemented with either glycine (1 g/kg/day, n=15) or an isonitrogenous amount of L-alanine (n=15). At day 20 of treatment, body composition was assessed using EchoMRI™ and glucose tolerance tests were performed to determine changes in glucose handling. At the end of treatment, mice were anaesthetized deeply with sodium pentobarbitone (Nembutal, 60 mg/kg, i.p.) and hindlimb skeletal muscles and epididymal fat were excised. Animals were killed by cardiac excision while still anaesthetized deeply.

Eight weeks of a HFD induced obesity (130% greater fat mass; 105% more epididymal fat HFD vs CHOW; $P < 0.001$) and glucose intolerance (basal glucose 5.7 ± 1.0 vs 7.0 ± 1.1 mmol/L; $P < 0.05$). Calorie restriction resulted in rapid weight loss (21%; $P < 0.01$), reducing fat mass (45%; $P < 0.01$), and improving glucose tolerance (AUC 1414.5 ± 49.7 vs 1762.4 ± 75.2 mmol/L \times 120min; $P < 0.001$). Glycine supplementation during calorie restriction increased the percentage of initial fat mass lost by 19% ($P < 0.03$) compared to alanine treatment groups and attenuated the loss of muscle mass in quadriceps (7%; $P < 0.001$), gastrocnemius (3%; $P < 0.03$) and tibialis anterior (4%; $P < 0.04$).

Taken together, these findings suggest that glycine supplementation during calorie restriction may be beneficial for preserving muscle mass and/or stimulating the preferential loss of adipose tissue.

Ham DJ, Murphy KT, Chee A, Lynch GS & Koopman. R(2014) *Clinical Nutrition*, **33**: 448-458.

El Hafidi M1, Pérez I, Zamora J, Soto V, Carvajal-Sandoval G & Baños G. (2004) *American Journal of Physiology – Regulatory Integrative and Comparative Physiology*, **287**: R1387-R1393.

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