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Fasting–mimicking diet prevents high–fat diet effect on cardiometabolic risk and lifespan

Amrendra Mishra ^{# 1}, Hamed Mirzaei ^{# 1}, Novella Guidi ^{# 1}, Manlio Vinciguerra ², Alice Mouton ³, Marina Linardic ⁴, Francesca Rappa ⁵, Rosario Barone ⁵, Gerardo Navarrete ¹, Min Wei ¹, Sebastian Brandhorst ¹, Stefano Di Biase ¹, Todd E Morgan ¹, S Ram Kumar ⁶, Peter S Conti ⁷, Matteo Pellegrini ⁴, Michel Bernier ⁸, Rafael de Cabo ⁸, Valter D Longo ^{9 10}

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Abstract

Diet-induced obesity is a major risk factor for metabolic syndrome, diabetes and cardiovascular disease. Here, we show that a 5–d fasting–mimicking diet (FMD), administered every 4 weeks for a period of 2 years, ameliorates the detrimental changes caused by consumption of a high–fat, high–calorie diet (HFCD) in female mice. We demonstrate that monthly FMD cycles inhibit HFCD–mediated obesity by reducing the accumulation of visceral and subcutaneous fat without causing loss of lean body mass. FMD cycles increase cardiac vascularity and function and resistance to cardiotoxins, prevent HFCD–dependent hyperglycaemia, hypercholesterolaemia and hyperleptinaemia and ameliorate impaired glucose and insulin tolerance. The effect of monthly FMD cycles on gene expression associated with mitochondrial metabolism and biogenesis in adipocytes and the sustained ketogenesis in HFCD–fed mice indicate a role for fat cell reprogramming in obesity prevention. These effects of an FMD on adiposity and cardiac ageing could explain the protection from HFCD–dependent early mortality.

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