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Intermittent fasting and dietary supplementation with 2-deoxy-D-glucose improve functional and metabolic cardiovascular risk factors in rats[1]

RUIQIAN WAN, SIMONETTA CAMANDOLA and MARK P. MATTSON[2]

+ Author Affiliations

Correspondence: [2]Correspondence: National Institute on Aging, GRC 4F01, 5600 Nathan Shock Dr., Baltimore, MD 21224, USA. E-mail: mattsonm@grc.nia.nih.gov

SPECIFIC AIMS

Experiments were designed to test the hypothesis that intermittent fasting (IF) can improve cardiovascular risk factors in adult rats and that such effects can be mimicked by dietary supplementation with 2-deoxy-D-glucose (2DG), an analog of glucose that inhibits glycolysis. The studies were based on the concept that intermittent fasting is a metabolic stress that can improve cardiovascular function and enhance glucose metabolism.

PRINCIPAL FINDINGS

1. Rats maintained on an intermittent fasting feeding regimen exhibit reduced body weight and decreased body temperature, blood pressure (BP), and heart rate (HR) compared with rats fed ad libitum (**Fig. 1**⇓)

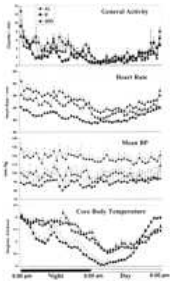

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Figure 1.

IF and dietary supplementation with 2DG decrease BP and HR in rats. Values are the mean and SE of determinations made in 5-8 rats. IF significantly reduced HR ($P<0.01$), mean BP ($P<0.01$), general activity ($P<0.05$), and body temperature ($P<0.01$). 2DG supplementation significantly reduced HR ($P<0.05$), mean BP ($P<0.01$), but had no significant effects on general activity or body temperature.

2. Rats maintained on a diet supplemented with 2DG did not reduce their food intake nor lose body weight but did exhibit significant decreases in blood pressure and heart rate (Fig. 1)⇓

3. Blood glucose and insulin levels were significantly reduced in rats maintained on IF and 2DG-supplemented diets compared with rats fed ad libitum (Table 1)⇓

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Table 1.

Effects of IF and 2DG supplementation on plasma

concentrations of glucose, insulin, and IGF-1[a]

4. The beneficial effects of IF and 2DG supplementation on cardiovascular risk parameters were associated with a stress response, suggesting that periodic metabolic stress results in adaptive beneficial responses of cells in the cardiovascular system

5. The magnitudes of the decreases in BP and HR and in insulin and glucose levels in rats maintained on IF or 2DG-supplemented diets were as great as or greater than those previously reported to be achieved with regular aerobic exercise programs

CONCLUSIONS AND SIGNIFICANCE

Even though overeating is a major cause of cardiovascular disease and its associated morbidity and mortality, it has proved difficult for many people to reduce their food intake. The present study was aimed at understanding how dietary restriction improves cardiovascular health and to determine whether such beneficial effects might be mimicked without a reduction in food intake. We documented striking improvements in cardiovascular risk factors in rats maintained on an IF regimen; generally, similar changes occurred in rats fed a diet supplemented with 2DG. The reductions in BP and HR and in plasma levels of insulin and glucose in rats on the IF diet were even greater than those achieved with regular physical exercise programs in previous studies. Because increased BP and insulin levels are risk factors for cardiovascular disease and stroke, the ability of IF to reduce BP and insulin levels suggests that IF may reduce the risk of these diseases.

The present findings also provide novel insight into the mechanism whereby dietary restriction increases life span and reduces the incidence of various age-related diseases. We found that IF and 2DG supplementation each induced a neuroendocrine stress response (**Fig. 2**⇓). Because previous studies have shown that IF induces cellular stress responses in a variety of tissues throughout the body, it seems likely that such a stress responses increase the resistance of cells to disease. The latter mechanism of action of IF therefore appears to be similar to the mechanism whereby physical exercise improves the function (and resistance to damage and disease) of skeletal muscle, the heart, and blood vessels. IF and caloric restriction are known to decrease levels of oxidative damage to cells; oxidative damage is believed to contribute to the pathogenesis of a variety of disorders, including cardiovascular disease, cancers, diabetes, and neurodegenerative disorders. The present findings provide a scientific basis for tests of the effects of IF and dietary supplements that mimic IF in humans and for the development of novel approaches for preventing and treating cardiovascular disease and diabetes.

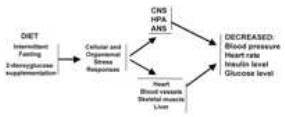

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Figure 2.

Proposed mechanisms whereby IF and dietary supplementation with 2DG improve functional and metabolic cardiovascular risk factors. IF and 2DG supplementation induce both a neuroendocrine stress response involving the central nervous system (CNS), hypothalamic-pituitary-adrenal axis (HPA), and autonomic nervous system (ANS) and a cellular stress response in cells of the heart, blood vessels, skeletal muscle, and liver. Cardiovascular adaptations occur that result in decreased blood pressure and heart rate, and metabolic adaptations occur that involve increased insulin sensitivity with associated reductions in plasma insulin and glucose levels.

Footnotes

↵[1] To read the full text of this article, go to http://www.fasebj.org/cgi/doi/10.1096/fj.02-0996fje; to cite this article, use *FASEB J.* (April

22, 2003) 10.1096/fj.02-0996fje

Articles citing this article

Mitochondrial Substrate Availability and Its Role in Lipid-Induced Insulin Resistance and Proinflammatory Signaling in Skeletal Muscle
Diabetes October 1, 2013 62:3426-3436
Abstract **Full Text** **Full Text (PDF)**

Intermittent fasting: a dietary intervention for prevention of diabetes and cardiovascular disease?
British Journal of Diabetes & Vascular Disease March 1, 2013 13:68-72
Abstract **Full Text** **Full Text (PDF)**

Caloric Restriction Mimetic 2-Deoxyglucose Antagonizes Doxorubicin-induced Cardiomyocyte Death by Multiple Mechanisms
J Biol Chem June 24, 2011 286:21993-22006
Abstract **Full Text** **Full Text (PDF)**

Dietary Interventions to Extend Life Span and Health Span Based on Calorie Restriction
J Gerontol A Biol Sci Med Sci July 1, 2010 65A:695-703
Abstract **Full Text** **Full Text (PDF)**

Effect of acute and chronic caloric restriction and metabolic glucoprivation on spontaneous physical activity in obesity-prone and obesity-resistant rats
Am. J. Physiol. Regul. Integr. Comp. Physiol. July 1, 2009 297:R176-R184
Abstract **Full Text** **Full Text (PDF)**

Effects of modified alternate-day fasting regimens on adipocyte size, triglyceride metabolism, and plasma adiponectin levels in mice
J. Lipid Res. October 1, 2007 48:2212-2219
Abstract **Full Text** **Full Text (PDF)**

Dose effects of modified alternate-day fasting regimens on in vivo cell proliferation and plasma insulin-like growth factor-1 in mice
J. Appl. Physiol. August 1, 2007 103:547-551
Abstract **Full Text** **Full Text (PDF)**

Alternate-day fasting and chronic disease prevention: a review of human and animal trials
Am J Clin Nutr July 1, 2007 86:7-13
Abstract **Full Text** **Full Text (PDF)**

A controlled trial of reduced meal frequency without caloric restriction in healthy, normal-weight, middle-aged adults
Am J Clin Nutr April 1, 2007 85:981-988
Abstract **Full Text** **Full Text (PDF)**

Caloric restriction and intermittent fasting alter spectral measures of heart rate and blood pressure variability in rats
FASEB J. April 1, 2006 20:631-637
Abstract **Full Text** **Full Text (PDF)**

Cardioprotection by Intermittent Fasting in Rats
Circulation November 15, 2005 112:3115-3121
Abstract **Full Text** **Full Text (PDF)**

2-Deoxyglucose as an Energy Restriction Mimetic Agent: Effects on Mammary Carcinogenesis and on Mammary Tumor Cell Growth In vitro
Cancer Res. August 1, 2005 65:7023-7030
Abstract **Full Text** **Full Text (PDF)**

Dietary supplementation with 2-deoxy-D-glucose improves cardiovascular and neuroendocrine stress adaptation in rats
Am. J. Physiol. Heart Circ. Physiol. September 1, 2004 287:H1186-H1193
Abstract **Full Text** **Full Text (PDF)**