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Commentary:

Intermittent Fasting Induces Weight Loss but the Effects on Cardiometabolic Health Are Modulated by Energy Balance

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Keywords

intermittent fasting; weight loss; insulin sensitivity; energy balance

COMMENTARY

Intermittent fasting (IF) encompasses a wide range of practices that alternate eating and extended periods of fasting. Most studies report that IF improves body weight and cardiometabolic health (1). However, the underlying mechanisms are unclear: some studies suggest that IF's effects arise solely from calorie restriction (CR) (2), while other studies implicate "metabolic switching" between "fed" and fasting states (1, 3), rather than weight loss per se.

To test these competing hypotheses and investigate the effects of metabolic switching, Hutchison et al. recently performed an 8-week feeding study comparing IF (three non-consecutive 24-hour fasts per week) versus continuous food intake (control groups) at two different energy intakes: 30% CR (IF70) and neutral energy balance (IF100) (4). Interestingly, both IF groups lost more weight than their respective control groups. The IF70 group also had improvements in fasting glucose and insulin following "fast" days and in total cholesterol, LDL cholesterol, triglycerides, and free fatty acids following fed days. However, the IF100 group had no improvements in any endpoints, and fasting insulin transiently increased following fed days. After pooling the data, IF also transiently increased free fatty acid levels and impaired insulin sensitivity as measured by clamp following fast days.

These are important findings. First, they demonstrate that IF is more effective than traditional CR for weight loss when prescribed at identical calorie intake—due to reduced hunger and food intake on fed days. Second, metabolic switching induces differential cardiometabolic states between fed and fast days. Third, according to the authors, the data suggest that IF does not improve cardiometabolic health in the absence of CR.

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The authors' third conclusion deserves some caveats. First, these data should not be generalized to all types of IF, as a form of IF called *time-restricted feeding* involving shorter fasts (typically 14–18-hour fasts) can improve insulin sensitivity even in the absence of CR (3). Since insulin sensitivity progressively declines with the duration of fasting, there may be an optimal duration for periodic fasting. Another plausible explanation for why this form of IF did not improve cardiometabolic health in the absence of CR is that the IF100 group alternated fasting and gorging (45% overfeeding). IF interventions involving overeating on "feast days" may partially or wholly negate the benefits of periodic fasting.

Other caveats include the small sample size, the short duration of the intervention (8 weeks), and that only women were included in this study. At least one prior study found dichotomous effects by biological sex, with glycemic indicators improving in men but worsening in women (5). Moreover, the impairment in insulin sensitivity following a fast day may be only temporary and may not be representative of the whole 24-hour day, underscoring the need to measure endpoints over a 24-hour period in future studies.

Despite these caveats, this is an important seminal study. It suggests that IF may be superior to daily CR for weight loss and that the cardiometabolic effects of IF are likely modulated by energy balance.

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