

Journal Club

 METABOLISM



INTERMITTENT FASTING IS GAINING INTEREST FAST

The term intermittent fasting encompasses various dietary regimens that include extended periods without any caloric intake. When I started studying intermittent fasting 15 years ago, there was virtually no awareness of this regimen, and only a handful of studies had been performed.

My interest in intermittent fasting was piqued by two key articles. In 1990, a pivotal study by Goodrick et al. demonstrated that mice fed every other day experienced significant extensions in lifespan. Following this study, Anson et al. sparked renewed interest in fasting by showing that mice on an alternate day fasting diet had greater resistance to endotoxic stress and improved glycemic control, versus animals fed the same amount of energy, but on a daily basis. Since then, hundreds of studies of intermittent fasting in animals and humans have been published. These studies demonstrate that fasting is

generally effective for the prevention and treatment of many chronic conditions, including diabetes, cardiovascular disease, cancer and neurodegenerative disorders, and in delaying ageing.

Although the precise mechanisms responsible for these health benefits are still unclear, several hypotheses have been proposed. The most prominent is the metabolic switching hypothesis. During periods of fasting, the liver converts fatty acids to ketone bodies. Ketones act as fuel during periods of fasting, but also as potent signalling molecules, controlling the expression and activity of many factors, including various regulators of systemic metabolism. Another, more recently discovered mechanism, involves the upregulation of autophagy. Reductions in circulating glucose and amino acids during fasting result in the decreased activity of the mammalian target of rapamycin (mTOR) protein synthesis pathway,

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which stimulates autophagy and induces the removal of damaged proteins and mitochondria to prevent their accumulation. Collectively, these adaptive cellular responses improve glucose regulation, suppress inflammation and reduce oxidative and metabolic stress.

Thirty years after the ground-breaking study by Goodrick et al., interest in intermittent fasting has flourished in the scientific community and in the general public. Though dozens of papers in this field are now published every month, much more remains to be explored. In particular, data from long-term, randomized controlled trials in humans are desperately needed to secure a place for intermittent fasting in clinical treatment guidelines.

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ORIGINAL ARTICLES Goodrick, C. L. et al. Effects of intermittent feeding upon body weight and lifespan in inbred mice: interaction of genotype and age. *Mech. Ageing Dev.* **55**, 69–87 (1990) | Anson, R. M. et al. Intermittent fasting dissociates beneficial effects of dietary restriction on glucose metabolism and neuronal resistance to injury from calorie intake. *Proc. Natl Acad. Sci. USA* **100**, 6216–20 (2003)