

Excessive fat intake can throw out the body clock

Dietary factors shown to influence sleep pattern.

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The body's circadian rhythm — the internal 'clock' that regulates physiological processes — can be shifted by eating more fat, say researchers¹(#B1). This surprising finding suggests that a more complex interplay exists between the body clock and metabolism, with implications for disorders such as diabetes and obesity.

The circadian rhythm is a near-24-hour cycle that is known to be modulated by sunlight and eating schedules. Previous studies have shown that a disrupted circadian rhythm leads people to crave high-fat foods. And a study out this week shows that children who lack sleep risk being overweight²(#B2). This is an issue of increasing concern as researchers attempt to elucidate the link between disturbances in circadian rhythm and health conditions such as obesity, heart disease and diabetes³(#B3).



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Joseph Bass, an endocrinologist at Northwestern University in Evanston, Illinois, fed a group of male mice a diet in which 45% of the calories were derived from fat, and monitored their daily wheel-running schedule. Mice given high-fat food had 23.8-hour daily cycles, whereas the body clock in control mice, whose caloric intake included only 16% fat, was 23.6 hours long¹. The internal time change occurred before the mice had gained any weight, although the researchers did not measure changes in body-fat percentage.

"This is the first time that a paper has really shown the impact of feeding on the molecular and behavioural expression of the circadian rhythm," says Eve Van Cauter, a sleep researcher at the University of Chicago in Illinois, who was not affiliated with the study. "In a human, this would mean the person would have increased difficulties going to bed at a reasonable time," she says. "That might result in insomnia or night-eating", which further boost the risk of obesity and diabetes.

The link between circadian rhythm and metabolism is not surprising, says Bass, because the two systems share many molecular signalling pathways. The expression patterns of some genes involved in lipid metabolism change in 24-hour cycles, and several nuclear receptors that are

activated by sterols regulate expression of clock-related genes⁴ (#B4). In addition, mice bearing mutations in the circadian-rhythm gene *Clock* show signs of metabolic dysregulation, including obesity and altered expression of genes involved in appetite regulation⁵ (#B5).

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Precisely how a fatty diet could disturb the circadian clock remains elusive, but the hunt is on. "In discovering these molecular switches that couple metabolic and circadian systems, we might actually uncover new pathways or targets to alter metabolic state," says Bass. Research has shown that the activity of two clock-regulating proteins depends on the nutrient status of the cell⁶ (#B6), providing one possible molecular connection, he says.

Others note that the connection between nutrient status and clock length may be indirect. The eating habits of mice on the high-fat diet also altered — they ate more and consumed more calories during the day, when mice normally sleep. It could be that the change in eating habits, rather than a direct effect of specific nutrients, altered their body clocks, says Hitoshi Ando at Kanazawa University in Japan. Ando has studied the impact of fatty food on the body clock in female mice, but found only a minimal effect⁷ (#B7). The reason for that discrepancy is unclear, he says.

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