

## **Can Intermittent Fasting Change How Your DNA Works?**

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#### STORY AT-A-GLANCE

- A 2023 animal study showed how limiting food to the hours of the day when you are most active may alter up to 80% of genetic expression in multiple organ systems
- > Activation of these pathways may help explain how fasting improves health and longevity. Roughly 40% of genetic expression in the hypothalamus, pancreas and adrenal glands was affected, which may affect hormone regulation
- > Data show restricted eating patterns have a neuroprotective effect and are associated with better cognitive and heart health; data also find it reduces the ability of cancer cells to adapt and survive and may help improve the effectiveness of cancer treatments
- > Fasting promotes pancreatic beta-cell growth in animal studies, which may be another pathway in which it helps markedly improve blood sugar control and affect metabolic health
- Most people find it easier to skip breakfast instead of dinner to limit the number of hours they consume food, but take care to restrict eating at least three hours before bed. Skipping breakfast before your workout may offer additional benefits throughout the day

Obesity rates are climbing, along with associated health conditions, such as Type 2 diabetes, metabolic syndrome and cardiovascular disease. According to the CDC,<sup>1</sup> the rate of obesity in adults rose from 30.5% in 1999-2000 to 41.9% in 2017-2020, and the estimated annual medical costs were \$173 billion in 2019 dollars.

There are a variety of reasons that contribute to these rising numbers, including a sedentary lifestyle,<sup>2</sup> increased consumption of highly processed food,<sup>3</sup> medications<sup>4</sup> and psychological triggers.<sup>5</sup> One beneficial strategy to lower weight gain and improve insulin resistance associated with obesity and Type 2 diabetes is intermittent fasting. A 2023 animal study<sup>6</sup> demonstrated that restricted feeding schedules affected 80% of how genes were expressed.

Resistance to insulin and leptin signaling drives your blood glucose level high, which is a hallmark symptom of Type 2 diabetes. Conventional medicine treats the symptoms of the condition, which is in fact preventable and in most cases reversible by simply changing your diet and lifestyle habits.

A significant risk factor for insulin resistance is overeating carbohydrates and added sugars, which spike your insulin level and gradually increase cellular resistance to insulin. Overeating carbohydrates and sugar are the primary causes of obesity.

The featured animal study in Cell Metabolism helps explain how fasting benefits these health conditions. Shaunak Deota is the first author of the study and a postdoctoral fellow at the Salk Institute for Biological Studies in San Diego. He is encouraged by the data, saying:<sup>7</sup>

"Molecularly speaking, we saw a lot of pathways which are activated by (the time-restricted diet) in multiple organ systems. And a lot of these pathways actually have been implicated in improving health and leading to a longer, healthy life."

## Intermittent Fasting Affects 80% of Genetic Expression

The results from the 2023 study demonstrated that it's not only about what you eat, but also about when you eat it. The researchers tested time-restricted feeding in mice. Deota defined the researcher's use of the term "time-restricted feeding" as "eating consistently in a narrow window of eight to 10 hours" when a person or animal is most active and fasting during the rest of the day.

Intermittent fasting is one form of time-restricted feeding according to the definitions used by the researchers. The researchers placed two groups of mice on the same high-calorie diet. One group was allowed to eat only during a nine-hour window and the other had free access to food whenever they wanted it.

The researchers found that after seven weeks, the time-restricted fed animals gained less weight than the other group and biopsies showed that the genetic expression of the mice in the intervention group was synchronized to their feeding schedules.

Interestingly, the paper reported that nearly 80% of the animal's "genes show differential expression or rhythmicity under TRF [time restricted feeding] in at least one tissue." Deota explained the importance of this finding, saying, "... these genes will get translated into proteins. Those proteins are helping our body to anticipate that there is food coming." 10

The data from the study supports past research that demonstrated the benefits of restricting the number of hours during the day in which you're allowed to eat. This has included increasing lifespan in animal studies.<sup>11</sup> The featured study sought to determine how fasting affects multiple organ systems and genetic expression.

The researchers looked at more than 22 areas of the body and brain, finding that by changing what time food was given, the genetic expression in an animal's body could also be changed. Time-restricted feeding affected nearly 40% of genetic expression in the pancreas, hypothalamus and adrenal glands. This in turn may affect hormone regulation.

It is possible that since hormones coordinate functions throughout the body, and hormonal imbalance is associated with many diseases, fasting may help to improve health along several pathways. The researchers also found that restricting food supply to the most active time of the day helped align circadian rhythms in multiple organ systems. Satchidananda Panda, Ph.D., from the Salk Institute and senior writer of the study, told World Pharma News:<sup>12</sup>

"Circadian rhythms are everywhere in every cell. We found that time-restricted eating synchronized the circadian rhythms to have two major waves: one during fasting, and another just after eating. We suspect this allows the body to coordinate different processes."

## **Periodic Feast and Famine Improve Health**

In this short three-minute clip from BBC studios, Michael Mosley discusses the effects of feast or famine feeding with professor Mark Mattson from the National Institute on Aging. Mattson describes the results of their intervention with mice in relation to cognitive impairment and memory loss.

The researchers used mice that were bred to develop Alzheimer-type symptoms. Mattson described one study in which one group was offered food intermittently and the others were fed a diet that resembled fast food. The group that ate intermittently lived significantly longer without memory impairment, in one study by six months to one year. Mosley notes that this is the difference in human life between developing Alzheimer's at age 50 or age 80.

Researchers have also noted that eating a high-fat, low-carbohydrate diet has a fasting-like effect on the body and the brain.<sup>13</sup> During fat metabolism, ketone bodies are produced which have a neuroprotective impact on the brain. This could help enhance mitochondrial function and reduce inflammation.

Eating a high-fat diet has been analyzed as a potential adjunctive therapy for neurodegenerative conditions, like Alzheimer's disease. One paper<sup>14</sup> reported that some studies have shown modest functional improvement in people with Parkinson's disease and cognitive benefits in people with Alzheimer's disease.

Limiting the hours of the day in which you eat also has a beneficial effect on your cardiovascular system. One paper<sup>15</sup> theorized that the effect may be exhibited through multiple pathways, including optimizing your circadian rhythms and reducing oxidative stress.

An umbrella review<sup>16</sup> of 11 meta-analyses totaling 130 random controlled trials found a beneficial association between intermittent fasting and cardiometabolic outcomes that was supported by moderate to high-quality evidence. Fasting has also been shown to have a pronounced impact on longevity.

One narrative review of the literature<sup>17</sup> summarized the impact of restricting calories and protein, and the effect on biomarkers of healthy aging. They predicted that periodic use of low-calorie, fasting-mimicking diets (FMD) and low protein intake could promote health benefits while minimizing the difficulty associated with chronic calorie restriction.

Researchers have also discovered that an FMD influences growth factors and reduces the capacity of cancer cells to adapt and survive. They propose that "combining an FMD with chemotherapy or other cancer treatments is a promising strategy to increase treatment efficacy, prevent resistance acquisition and reduce side effects."<sup>18</sup>

### **Fasting May Promote Pancreatic Beta-Cell Growth**

Research has demonstrated that fasting can improve insulin sensitivity,<sup>19</sup> reverse Type 2 diabetes<sup>20</sup> and support your weight management efforts when it's combined with exercise.<sup>21</sup> Interestingly, an editorial in the BMJ<sup>22</sup> by noted research scientist James DiNicolantonio, Pharm.D., discusses the results of several studies that found repeated episodes of fasting may induce cell growth of pancreatic beta cells in an animal model.

The growth was associated with an increased expression of Ngn3,<sup>23</sup> a protein involved in converting DNA into RNA critical for endocrine cells in the pancreatic islet of Langerhans, the cells responsible for producing insulin. The increase in islet beta cells induced through intermittent fasting was accompanied by a marked improvement in blood sugar control in the animal studies.<sup>24</sup>

This observation is of great interest to individuals who suffer from Type 1 diabetes since they often experience near-complete inflammatory destruction of the islet beta cells. In the latter stages of severe Type 2 diabetes, the same destruction of islet of beta cells can occur.

DiNicolantonio believes these findings may be replicated clinically, which opens the path to reversing Type 2 diabetes in those with "enough discipline and commitment to adopt a lifestyle that would have prevented diabetes in the first place."<sup>25</sup>

He first recommends practicing a diabetes-preventive lifestyle by eating a diet primarily of whole foods and complemented with regular exercise. This helps to improve insulin sensitivity and may be sufficient for those with a recent diagnosis of diabetes to reduce their condition over time.

In those who fail to respond, he recommends an intermittent fasting protocol and using supplemental measures during the transition back to a health-protective diet to shield the beta cells from toxicity so they retain functional capacity. Reducing oxidative stress may be accomplished using spirulina, NAC and or berberine.<sup>26</sup> The goal is to achieve normal blood sugar control without drugs and maintain compliance with a diabetic preventive diet and lifestyle.

# **Skipping Breakfast Before Your Workout May Add Benefits**

For many people, restricting food intake to the hours between lunch and dinner feels easier than skipping dinner. A 2019 study<sup>27</sup> in The Journal of Nutrition found that omitting a meal before your workout increases the effectiveness of your weight loss efforts. Researchers enrolled 12 healthy, physically active young men who completed all three stages of the study in a randomized order separated by over one week.

During the first stage, the men ate a breakfast of oats and milk followed by rest. In the second stage, they ate the same breakfast and then exercised for 60 minutes, and during the third stage, they fasted overnight and exercised in the morning before eating. The researchers then monitored the following 24 hours of calorie intake.

They found that those who fasted and then exercised had a negative 400-calorie intake during the following 24 hours as compared to those who ate and rested or those who

ate breakfast before exercising. Javier Gonzalez, Ph.D., from the University of Bath, oversaw the study and suggested working out on an empty stomach will not likely trigger overeating but, instead, may lead to a calorie deficit.<sup>28</sup>

The study was limited in that there was a small number of participants who were all fit young men. There is some question if those results would be comparable in a group of older, overweight, out-of-shape or female participants. The data could not explain why the men who skipped eating before exercise did not continue to eat the rest of the day. Gonzalez hopes to continue work to study these questions.

## Take Care to Restrict Eating Three Hours Before Bed

While it may be easier to skip breakfast as you practice intermittent fasting, it's also necessary to avoid eating at least three hours before bed. For most Americans, the evening meal is often the largest of the day and usually consists of heavily processed foods. Under the best of circumstances, it takes your stomach several hours to empty after you've eaten.

However, as you age, the process can take even longer. As you lie down to sleep, this increases the risk that acid can enter your esophagus and lead to acid reflux. Even if you do not have heartburn, symptoms like hoarseness, chronic throat clearing and even asthma can indicate acid reflux. Additionally, as the featured study demonstrates, eating outside of your most active times of the day can throw off your body's circadian rhythm.

This in turn has a detrimental effect on your mitochondria as they are "highly regulated by the body's biological, or circadian, clocks."<sup>29</sup> As described in an article in Neuroscience News, offsetting your circadian clock increases your risk of developing metabolic syndrome, obesity and diabetes.

In a follow-up paper,<sup>30</sup> the same researcher describes how the circadian clocks in your cells respond to a variety of metabolic cues and play a principal role in metabolic control. In the review of the literature, he finds diurnal changes affect mitochondrial

biology in mammals. Dysfunction of these little powerhouses located in most of your body cells is a foundational cause of many degenerative diseases.

When the mitochondria receive inappropriate amounts of fuel at the wrong time of the day they can deteriorate and malfunction, laying the groundwork for the subsequent breakdown in a variety of bodily symptoms. As a featured study shows, you can take control of your health through fasting. It is a profoundly effective intervention that can help stimulate mitochondrial biosynthesis.

It is important to understand that as you're fasting, you may experience symptoms of low salt intake and your body will automatically begin to liberate toxins from your fat stores. It's recommended to consume some high-quality unprocessed salt each day and use an infrared sauna to help your body rid itself of these toxins.

Binders like modified citrus pectin, cilantro, chlorella or activated charcoal can help eliminate these toxins as well, and prevent their reabsorption. Although it's highly beneficial for most, fasting is not for everyone. You should not do any type of extended fasting if you're underweight, pregnant, breastfeeding or have an eating disorder.

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