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Is Intermittent Fasting a Better Option than Continuous Calorie Restriction?

Joseph J Cynamon

Joseph Cynamon will graduate with a Bachelor of Science degree in Biology in the Fall of 2023

Abstract

Intermittent fasting has become an increasingly popular diet for weight loss in the United States in the past ten years. Proponents of intermittent fasting claim that restricting calories via a fasting period yields more significant weight loss and better improvements in biomarkers for longevity than restricting calories continuously. The goal of this paper is to determine whether intermittent fasting leads to weight loss and is more beneficial than continuous calorie restriction. The paper first details the physiological processes which can occur during fasting that are theorized to render fasting advantageous. It then reviews the limited available research that experimentally compares intermittent fasting with continuous calorie restriction. Based on the review, it concludes that intermittent fasting is just as effective as continuous calorie restriction in causing weight loss and other health improvements. Intermittent fasting also does not lead to any short-term detrimental effects. There is not enough substantial evidence to assume other than these conclusions. The work also details some risks associated with intermittent fasting. More, higher-quality studies are necessary to confirm the findings of this review.

Introduction

Plutarch, an ancient Greek writer once wrote, "Instead of using medicine, better fast today". Fasting, the abstinence from all or some kinds of food, has been practiced for spiritual reasons for centuries. It remains a part of almost every major religion today. Fasting has long been theorized to induce an improvement in health, slowing of aging, and the delayed onset of disease. Paracelsus, one of three fathers of modern Western medicine wrote, "Fasting is the greatest remedy—the physician within" (Vasim et al., 2022). Recently, fasting has become more common as a method for weight loss. Maintaining a healthy body weight is essential to living a long, healthy life because being obese or even overweight increases a person's risk of heart disease, stroke, type 2 diabetes, certain types of cancer, and mental illness (Centers for Disease Control and Prevention, 2022). Unfortunately, obesity and overweight in the United States are as prevalent as it has ever been. According to 2017–2018 data from the National Health and Nutrition Examination Survey (NHANES), almost one-third of American adults (30.7%) are overweight and more than 2 in 5 adults (42.4%) are obese (U.S. Department of Health and Human Services). This creates the need for effective, safe, and maintainable diet and weight loss programs. One effective and safe technique to help people lose body fat is a continuous daily calorie restriction. Current recommendations for the treatment of overweight and obesity is a daily consumption of only 70-80% of daily weight maintenance requirements. Over a 6-month period, this approach normally yields a modest weight loss of 5-10% (Das et al. 2017). However, many people find it too difficult to constantly count calories. Because of this problem, a new fad called Intermittent Fasting has become increasingly popular. Intermittent fasting refers to a diet regimen in which a person has consistent periods of extremely limited caloric intake followed by an eating window. It can involve a fast on 2 nonconsecutive days each week, a 24-hour fast on alternate days, or a daily fast for 16 hours. The advantage of intermittent fasting is that the program does not restrict one's calorie intake during the eating window (Cienfuegos, et al. 2020). The goal is to yield a net calorie deficit in a more sustainable way. Proponents of intermittent fasting allege that the program is not only more effective than a continuous calorie restriction program in facilitating weight loss, but that it also improves biomarkers related to longevity (Anton et al., 2018). Is intermittent fasting more advantageous than a moderate continuous calorie restriction? This paper will discuss if there is sufficient scientific evidence to determine whether intermittent fasting is more effective than continuous calorie restriction in helping achieve a healthy weight, and whether fasting provides other health benefits beyond energy deficit and weight loss.

Methods

Data was collected using ProQuest, Google Scholar, and PubMed databases through Touro College's online library. Among the key phrases used were "intermittent fasting," "calorie restriction," "time restriction eating," and "weight loss."

Discussion

It is well known that restricted calorie intake is an effective way to lose body fat (Das, et al. 2017). This means reducing the intake of average daily calories, while still getting the nutrition that the body needs. Beyond weight loss, restricted calorie intake also has been linked to slower aging, longer lifespans, and better health biomarkers in animals (Masaro, 2000). For example, caloric restriction has been shown in animals to slow cancer formationl, reduce the likelihood of stroke, and increase the brain's ability to resist neuron deterioration and dysfunction in models of Alzheimer's and Parkinson's (Bruce-Keller et al., 1999; Mukherjee et al., 2002).

Research has suggested that dietary restriction facilitates health benefits for humans as well. For example, in a long-term study with normal and slightly overweight adults, Das, et al. (2017) found that a 25% calorie restriction led to a loss of fat mass and better overall markers

for heart and metabolic health. These indicators included LDL, cholesterol, insulin sensitivity and blood pressure. Intermittent fasting is a diet technique designed to allow one to restrict their average calorie intake more easily than one that continuously restricts calories.

There are some issues involving the effectiveness of intermittent fasting for weight loss that must be investigated. One issue is that fasting may cause the participant to engage in less physical activity and calorie expenditure ,as one feels weak while fasting. Also, periods of fasting may cause the body to hold on to fat in preparation for continued malnutrition. Furthermore, intermittent fasting may not lead to an average calorie intake deficit at all. When one can only eat at certain times, they may compensate for this energy deficit by eating more during the eating window. Additionally, people also tend to indulge more with the knowledge that they will be restrained soon. Critics of intermittent fasting use these arguments to claim that the diet may lead to an overall calorie surplus and weight gain (Templeman et al., 2021).

This discussion will first detail the potential theories behind the belief that intermittent fasting is more advantageous than continuous calorie restriction. It will then examine if an intermittent fasting regimen facilitates a net calorie restriction and weight loss in people. Then, the claim that the fasting period component of intermittent fasting offers an advantage will be reviewed, with a focus on weight loss and cardiovascular and metabolic disease risk factors. When reviewing this last claim, any evidence being cited must have produced results that are independent of calorie restriction. This way, it can be determined that the fasting period alone is responsible for the observed differences. Any studies that fail to make this distinction will not be discussed.

The Theories Behind the Advantage of Intermittent Fasting

There are two components of intermittent fasting - a net calorie deficit and a fasting period. Advocates of intermittent fasting insist that intermittent fasting naturally will lead to a decrease in net calorie intake, as there is a period in which one cannot consume food (Vasim et al., 2022). There are different theories to explain why the second component, the fasting period, which does not exist in continuous calorie restriction, may be more effective in causing weight loss and other health biomarkers beyond calorie deficit.

Intermittent fasting may more effectively flip the "metabolic switch" than continuous calorie restriction (Anton et al., 2018). This switch is when the body uses stored fat for energy instead of glucose. The idea behind this is that by restricting food for extended periods of time, glucose levels in the blood drop, forcing the body to use fat stores more quickly and efficiently for energy (Puchalska & Crawford, 2017). This shift from the use of glucose from glycogenolysis to the use of fatty acids and fatty acid-derived ketones is what leads to weight loss. After long periods of food deprivation, the body stops lipid synthesis and fat storage. Instead, the body utilizes fat in the form of free fatty acids and fatty-acid-derived ketones. The metabolic switch happens during fasting because glycogen stores in hepatocytes are low and subsequent adipose tissue lipolysis generates fatty acids and glycerol (Cahil, 2006). The time it takes for the switch to happen depends on liver glycogen content and on the amount of energy used while fasting. Yet, the metabolic switch usually happens between 12 to 36 hours after a fast starts. First, fats (triacylglycerol and diacylglycerol) are broken down into free fatty acids. After they are released into the blood, the free fatty acids are then transferred into the liver's hepatocytes where they are metabolized to produce ketones (Gano et al., 2014). At the same time, other cell types, including astrocytes in the brain, may also start producing ketones. The ketones are taken into cells where they are processed to make acetyl coenzyme A, which then enters the Krebs cycle to produce ATP. By way of these physiological processes, ketones are the energy source for muscle and brain cells during fasting (Cahil, 2006). This means that during fasting, the major energy source the body utilizes is ketones instead of glucose. Because research indicates that ketones are the preferred fuel for both the body and brain (Puchalska & Crawford, 2017; Volek et al., 2015), this can mean that fasting can be beneficial to the body.

Another theory states that autophagy is greatly enhanced during fasting. Autophagy is defined as "a process by which a cell breaks down and destroys old, damaged, or abnormal proteins and other substances in its cytoplasm" (Koutouroushis & Sarkar, 2021). Fasting, by providing a short nutrient deprivation, forces cells to focus on maintenance and to be more efficient with less. This causes cells to become more adept at cleaning themselves and recycling components. The effects of this upkeep bolster mental and physical performance in the fed state as well. Some researchers, such as Kanasaki et al. (2019), suggest that it affects the hormones that control hunger, such as ghrelin, insulin, and glucagon. In a study involving fruit flies, Ulgherait et al. (2021) found that maintenance of a 20-hour daily fasting diet for 30 days, without net calorie restriction, resulted in greater autophagy and consistent, significant lifespan extension in fruit flies.

Finally, studies show that intermittent fasting tends to

improve the gut microbiome which is linked to the improvement of many age-related diseases (Zarrinpar et al., 2014). A healthy gut microbiome helps with digestion, destroys harmful bacteria, and helps control one's immune system (How Your Gut Microbiome Impacts Your Health, 2022). These show potential benefits which include reduced inflammation, higher microbial diversity, and the making of favorable microbial compounds in the form of fatty acids (Liu et al., 2020). These compounds affect the expression of the circadian rhythm genes in the liver. In this way, intermittent fasting is believed to restore the body's normal circadian clock. This has been shown in studies involving mice (Zarrinpar et al., 2014). This reset of the body's internal clock is theorized to allow the body to effectively manage metabolism, sleep, and behavior. With the set schedule that intermittent fasting provides, the dieter is able to take advantage of this reset internal clock by eating consistently when the body is ready for it.

Intermittent fasting has also been shown to decrease measures of assumed obesogenic microflora while increasing the amounts of assumed obesity-protective microflora (Zarrinpar et al., 2014). Ozkul et al. (2020) found that nine people had higher levels of beneficial gut bacteria, including Akkermansia, Faecalibacterium , and Roseburia, after Ramadan. Ramadan is the Muslim holy month in which individuals fast from dawn to sunset. However, this study was limited in sample size and was unable to determine the impact of weight loss and diet on these changes, thus leaving the effects of potential contributing factors unclear.

The extent of the occurrence of the mechanisms mentioned here may vary based on duration of the fast. However, due to limited research available, all types of intermittent fasting will be grouped together to review if fasting has been shown to yield any beneficial results.

Intermittent Fasting For Weight Loss

Many studies have shown that an intermittent fasting diet regimen is effective in decreasing calorie intake causing weight loss. One study found that a 36-hour fast did not lead to compensation of energy the following day in 24 lean adults (Johnstone et al., 2002). Although it was only one fast period, it shows evidence against the claim that fasting leads to subsequent overeating. However, the fact that these were lean adults might have influenced these results. People who are overweight are more likely to overindulge during the eating window.

In another study, researchers set out to determine whether intermittent fasting successfully leads to calorie deficit without calorie counting, and whether it is a worthwhile option for weight loss. The study explored the effects of eight-hour time-restricted feeding on body weight and metabolic disease risk factors in obese adults. For over 12 weeks, 23 obese subjects participated in a daily 8-hour time-restricted feeding intervention. The subjects ate whatever they wanted during their eating window. Controls (n=23) were told not to change their eating habits and to maintain their weight. The intermittent fasting group had a decrease in body weight by ~3% and energy intake by 341 kc/d compared to controls. This study shows that intermittent fasting produces a mild caloric restriction and weight loss without calorie counting (Gabel et al., 2018).

Similarly, others also concluded that intermittent fasting is an effective diet approach for the reduction of HbA1c and is similar to continuous calorie restriction in its ability to help one lose weight. Researchers compared the effect of intermittent fasting with continuous calorie restriction on glycemic control and weight loss in overweight and obese patients with type 2 diabetes. For 12 months, 97 participants with type 2 diabetes either utilized an intermittent fasting diet for 2 nonconsecutive days per week (n=51) or a 30% continuous calorie restriction diet (n=46). Both groups experienced ~5-6 kg in weight loss. Similarly, Cienfuegos et al. (2020) also demonstrated that 35 obese participants on a 4 and 6-hour per day intermittent fasting regimen, yielded a ~550 kcal/d energy restriction and weight loss (~3%) after 8 weeks (Carter et al., 2018).

Those who are opposed to intermittent fasting for weight loss point to a recent study that found that intermittent fasting offers no benefits whatsoever in people. Lowe et al. (2020) set out to determine the effect of 8-hour daily intermittent fasting on weight loss and metabolic risk markers. In this 12-week randomized clinical trial, 116 adults were randomized into two groups. One group was told to eat their daily calorie requirements in three structured meals per day. The intermittent fasting group was instructed to eat ad libitum from 12:00 pm until 8:00 pm and refrain from eating from 8:00 pm until 12:00 pm the next day. There was significant weight loss in the intermittent fasting group; however, there was no difference in weight loss between the two groups. Not only that, but there were also no meaningful observed differences in fat mass, fasting insulin, blood sugar, HbA1C, or blood lipids between the groups. Time-restricted eating did not even result in less energy intake. Moreover, people in the intermittent fasting group also lost on average about 3.5 lbs. of lean mass. Normally, only about 20-30% of total weight loss is lean mass but here, the proportion of lean mass loss was 65%. There are potentially other factors that caused this loss of lean

mass. It is possible the participants did not eat enough protein or engage in enough physical activity. The shift in activity can lead to dwindling lean mass. More research is required to account for these factors.

The researchers conclude that fasting does not lead to an overall calorie deficit and is not more effective in causing weight loss than eating regular meals throughout the day. They claim that the weight loss of the three-meal group indicates that short-term weight loss can result from just participation in a weight loss study alone. However, this conclusion is flawed because perhaps eating three structured meals each day on a set schedule utilizes the body's circadian rhythm to more efficiently metabolize fat as well. Although this study had a relatively large sample size with a wide range of BMI among participants including both men and women, it does conflict with many studies that do show that intermittent fasting does indeed lead to a calorie deficit and weight loss. An earlier, more advantageous eating window, would perhaps lead to compatible results as people tend to eat more at night. This study should be repeated to account for any errors.

Intermittent Calorie Restriction vs Continuous Caloric Restriction

Contrary to widespread belief, most research has found that a fasting period, although not detrimental, does not cause more weight loss than continuous calorie restriction. However, there is a lot of conflicting research about fasting and its ability to offer metabolic benefits beyond weight loss.

In one important study, Anson et al., (2003) showed that a fasting period leads to health benefits similar to continuous calorie restriction, even without overall energy intake deficit or weight loss. C57BL/6 mice were placed in one of three groups: fed ad libitum, alternate-day intermittent fasting, and daily calorie restriction. Throughout the twenty-week trial, mice in the intermittent fasting group ate almost the same amount of food as the mice fed ad libitum. This is because, on feeding days, they ate about twice as much as the fed ad libitum mice ate. However, no application about energy compensation can be made to other animals because researchers point out that this is a specific characteristic of the strain of mice they used and does not occur in other mice. The mice in the daily calorie restriction ate 60% of the energy eaten by the ad-libitum-fed animals and had a 49% lower body weight. In contrast, the mice that intermittently fasted had only slightly lower body weights than those in the ad libitum-fed group. Yet, the intermittent fasting mice did have improvements in glucoregulatory health indicators. In the mice fed ad libitum, the fasting serum concentrations of glucose and insulin averaged 150 mg/dl and 3,400 pg/ml, respectively. In contrast, in the mice of both the daily restriction and intermittent fasting groups, the concentrations of glucose and insulin decreased drastically to 100 mg/dl and 700–1,100 pg/ml, respectively. Increased insulin sensitivity is a key beneficial physiological change that happens in mammals when their calories are restricted. Decreased fasting plasma levels of glucose and insulin reflect this change.

When reviewing this study, however, it is important to note that throughout the twenty weeks, there was some overall energy restriction in the intermittent fasting group. This energy restriction, which may have led to the group's slight weight loss, may have contributed to the favorable results. However, the negligible difference in energy consumption, although it perhaps contributed, could not have been solely responsible for the very favorable insulin resistance data. This animal study indicates that although the fasting period itself does not cause weight loss, it can still facilitate the beneficial effects of caloric restriction in regard to glucoregulatory health.

Harvie et al. (2010) also found that intermittent fasting is better for cardiovascular and glucoregulatory health in humans. Over a 6-month period, two groups of obese premenopausal women were instructed to, every week, consume only 75% of the weekly calories required for weight maintenance. However, the two groups accomplished this with two different eating schedules. One group (n=47) did so by consuming only 75% of their daily calorie needs each day. The other group (n= 42) did so with an intermittent energy diet by consuming only 25% of their daily energy needs on two nonconsecutive days while eating the rest of their allowed weekly calories on the other days. Importantly, intermittent energy did not lead to overeating on the other five days and weight loss was similar between the groups. In the intermittent fasting group, weight reduced from a mean of 81.5 kg to 75 kg compared to a decline from 84.4 kg to 78.7 kg in the continuous calorie restriction group. The two groups had similar drops in body fat, hip, bust, and thigh circumference, and composition of weight loss. Both groups experienced mild reductions in fasting serum insulin and improvements in insulin sensitivity. However, these reductions were greater in the intermittent fasting group. Correspondingly, there was a moderate rise in adiponectin levels in the intermittent fasting group, but not in the continuous calorie restriction group. Adiponectin is a hormone that helps with insulin sensitivity and inflammation. Adiponectin is important because its anti-inflammatory properties protect the vascular system, heart, lungs, and colon (Adiponectin: What It Is, Function & Levels). Also, slow-acting AOPP (Advanced Oxidation Protein Product), which is a protein product that promotes oxidative stress, the imbalance of

free radicals and antioxidants, (Advanced Oxidation Protein Product - an overview), decreased in the intermittent fasting group and had a slight increase in the continuous energy restriction group. Both diets yielded similar reductions in total and LDL cholesterol, triglycerides, and blood pressure. This study demonstrates that in humans, a fasting period may be more effective in increasing insulin sensitivity and adiponectin while reducing oxidative stress and inflammation. However, a few things should be taken into account when reviewing this study. The study only included women. Also, energy intake records were based on self-reporting, which means that they were not entirely accurate. On the other hand, in contrast to traditional intermittent fasting, subjects were allowed to eat 25% of average daily calories on "fasting" days. It is possible that completely fasting on those days would result in even more drastic health improvements than observed in this study.

Gabel et al. (2019) found similar results. The first 6 months of the year-long trial consisted of weight loss followed by 6 months of weight maintenance. Subjects with insulin resistance were grouped into an intermittent fasting group and a continuous calorie restriction group. Both groups achieved a 25% calorie restriction per day during the first 6 months. The intermittent fasting group (n=11) participants consumed 25% of their daily calorie requirements on fast days, and 125% on alternating feast days. Continuous calorie restriction participants (n=17) consumed 75% of their energy needs every day. During the next 6 months, participants were instructed to consume an additional 25% every day to reach the energy intake required for weight maintenance. Controls (n=15) did not change their eating habits throughout the twelve months. At the end of the year, reductions in weight were similar (~6-8 kg) between the intermittent fasting group and the continuous calorie restriction group. However, the intermittent fasting group had a bigger reduction in fasting insulin by month 12 (−52%) than the continuous calorie restriction group (-12%). Intermittent fasting also yielded a greater decrease in HOMA-IR (a marker of insulin resistance) by month 12 (−53%) when compared to continuous calorie restriction (-10%). However, there were no significant differences detected between the two groups regarding other metabolic disease risk factors, including blood pressure, plasma lipids, and inflammatory mediators. This study is very limited by its sample size.

Sutton et al. (2018) also found that intermittent fasting can improve glucoregulatory health and blood pressure. In this 5-week randomized trial, eight overweight, prediabetic men were split into two groups. One group adopted an intermittent fast schedule with a 6-hr daily eating period while the other group had a 12-hr daily eating window. The two groups followed diets that were designed to maintain their weight and participants were required to eat only the food provided. All meals were monitored by study staff to account for potential differences in food intake or meal frequency. At the end of a 7-week washout period, intermittent fasting did not alter glucose levels; however, it did lower fasting insulin by 3.4 – 1.6 mU/L. and insulin resistance by 36 – 10 U/mg. The intermittent fasting also lowered blood pressure but had no effect on arterial stiffness or cholesterol. Researchers say the effect of the lowered blood pressure was similar in effectiveness to anti-hypertensive medications such as angiotensin-converting enzyme (ACE) inhibitors. Intermittent fasting also reduced oxidative stress but did not affect inflammatory markers. The study also found that intermittent fasting reduced hunger in the evenings. This study suggests that intermittent fasting, even when there is no calorie deficit or weight loss, can improve insulin levels, blood pressure, insulin sensitivity, and oxidative stress levels. This study was specifically well done because it did not rely on self-reporting for calorie intake. However, this trial was extremely small and must be repeated in a larger trial that includes women.

There are many stronger studies, however, that find that a fasting period offers no health benefits.

In the study conducted by Carter et al. (2018) detailed above, weight loss and HbA1c levels between the continuous and intermittent fasting restriction groups were similar. Trepanowski et al. (2017) also found that intermittent fasting is not more advantageous than daily calorie restriction in aiding with weight loss and health biomarkers. Over a one year period, 46 obese participants spent 6 months on a weight loss regimen followed by 6 months on a weight maintenance regimen. For all participants, the weight loss regimen involved a 25% overall average calorie restriction, while the weight maintenance regimen involved no overall calorie restriction. However, the 46 participants who completed the study were in one of two groups. The alternate-day fasting group (n=21) was instructed to consume an average 75% of their daily calorie requirements using alternate-day fast (25% on fast days, 125% on eating days). The other group (n=25) used a daily 25% calorie restriction. During the 6 months of weight maintenance participants in both groups were to consume 100% of their requirements by adding 25% daily from the previous six months. An additional 23 participants made up the control group. Based on the data, both experimental groups experienced similar physical activity and consumed equal amounts of energy throughout the year. However, weight loss was similar between the intermittent fasting group and the daily calorie restriction group at months six (~-6.8%) and twelve

(-~5-6%). Weight regain from months 6 to 12 was also not substantially different between the alternate-day fasting group and the daily calorie restriction group. At months 6 and 12, there were no statistically significant differences between the intermittent fasting group and the daily calorie restriction group for blood pressure, heart rate, total cholesterol levels, triglyceride levels, high-sensitivity C-reactive protein, homocysteine levels, fasting insulin, fasting plasma glucose, fat mass, lean mass, or visceral fat mass. The results of this randomized clinical trial revealed that intermittent fasting did not lead to greater adherence, weight loss, or weight maintenance than continuous calorie restriction. It also did not show any improvement in indicators of cardiovascular or metabolic disease risk factors compared with continuous calorie restriction. This study is especially critical because of its sample size and because it compares intermittent fasting and continuous calorie restriction in the context of consuming the same amount of calories. It also backs the claim that intermittent fasting does not cause lean mass loss or less physical activity.

However, this study has a slight limitation. Researchers point out that the intermittent fasting group ate more than prescribed on fast days, and less than prescribed on feast days. This means the "fast days" were not actual fast days. Failing to adhere to restrictions on fast days, in essence, transforms an intermittent fasting diet into a continuous calorie restriction diet. It, therefore, becomes more difficult to draw any conclusion from this study about a subject who will actually adhere to an intermittent fasting diet by consuming very little on fast days.

However, another well-done recent study, Liu et al., (2022), found similar results. 139 Chinese overweight and obese adults were randomly assigned to either restrict calories by 75% using a daily intermittent fast, eating from 8am-4pm, (n=70) or a daily-calorie-restriction regimen (n=69) for 6 months. This time frame was chosen to coincide with the Chinese participant's biggest meal. This weight loss program was followed by 6 months of weight maintenance. By the end of 12 months, physical activity and average caloric deficit were similar in the two groups, although these were based on self-reporting. However, weight loss (6-8kg), fat mass and lean mass loss, and reductions in waist circumference were similar between the groups. There was also no difference in fasting glucose, lipids, and insulin levels along with blood pressure. Additionally, side effects including fatigue, dizziness and headaches were similar between groups.

These results back the last study and show that although fasting does not affect physical activity or lead to higher calorie intake, it does not facilitate weight loss beyond calorie deficit. This study also demonstrates that an intermittent fasting regimen does not lead to a greater loss of lean mass or weakness if followed with a proper diet. The strengths of this study, including sample size and duration of the diet, show that intermittent fasting is essentially the same when considering all potential effects of dieting.

Although most studies show that intermittent fasting is as effective as continuous calorie restriction, there are two that suggest otherwise.

Templeman et al. (2021) concluded that that a calorie deficit achieved while fasting can be less effective than continuous calorie restriction for weight loss. For 3 weeks, 6 lean, healthy adults were equally divided into three groups of 12. The first two groups consumed a net 75% of the required calorie requirements. Group 1, the continuous calorie restriction group, did so by consuming 75% of their usual daily calorie intake every day. Group 2 fasted on alternate days and consumed 150% of their usual calorie intake on other days. The third group, Group 3, did not undergo any overall calorie restriction and only utilized a fasting period. Although they fasted on alternate days, they ate 200% of their normal calorie intake on eating days. This design allowed researchers to determine if fasting itself without a change in energy intake contributes to weight loss. At the end of the study, those in Group 1, lost an average of 1.91 kilograms of body mass almost entirely due to fat loss while those in Group 2 lost an average of 1.60 kg with only half of the reduction due to loss of body fat. Group 3 lost an average of 0.52 kg with a minimal loss of body fat. All metabolic health levels such as blood sugar levels, cholesterol, and blood pressure or fat tissue gene expression remained constant among the study participants. This study is especially important in determining whether the fasting period itself can aid in weight loss. On one hand, Group 1 lost 1 kg more body fat than Group 2. This would suggest that consuming the same calorie amounts while fasting leads to less fat mass loss. However, the third group that only used intermittent fasting as a means of weight loss, managed to lose a minimal amount of fat mass over the three weeks. This indicates that the fasting period doesn't negatively affect fat mass loss. Researchers suggest that the difference between Group 1 and Group 2 is partly due to a reduction in physical activity in Group 2. They also determined that intermittent fasting does not lead to beneficial cardiovascular or metabolic effects. This is an invalid conclusion because the weight loss also did not either improve the metabolic and cardiovascular health of the participants. The researchers themselves say that there were no improvements because the participants were lean at the start of the trial.

Although this study was brilliantly designed, it was

extremely short in duration and small in sample size. This study involved only lean healthy participants, which may be the reason fasting did not result in significant weight loss. The body of a lean person may not switch to ketosis as readily as the body of an overweight or obese one. It is likely because of this reason that this study conflicts with the others. However, this study, demonstrates that fasting is not more effective in causing weight loss than continuous calorie restriction in lean individuals. The weight loss from Group 3 is too insignificant to support that fasting itself is a means of weight loss. Additionally, this weight loss can be attributed to participating in a weight loss study. This trial should be repeated with a longer experimental period and a larger sample size.

Another study (Catenacci et al., 2016) suggests that utilizing intermittent fasting may be less beneficial than continuous calorie restriction when it comes to weight loss, but more beneficial when it comes to weight regain. Twenty-six obese adults completed a diet of either a zero-calorie alternate-day fast or continuous calorie restriction for 8 weeks. The continuous calorie restriction group was given a regimen, with meals, designed to create a 14% deficit from estimated daily energy requirements. The intermittent fasting group was not allowed to eat on fast days but was allowed to consume as much as they wanted on the other days. Results were reviewed at the end of the 8-week intervention and after 24 weeks of follow-up. Importantly, over the 8 weeks, self-reported average daily energy deficits were considerably higher in the intermittent fasting compared to the continuous calorie restriction, 47 and 28%, respectively. However, absolute weight loss was similar between the groups. To explain the lack of correlation between energy deficit and weight loss in the intermittent fasting group, researchers suppose that the groups underreported food intake. Additionally, fasting may have led to less physical activity and energy expenditure than in the continuous energy restriction group. There were no differences in weight regain between the 8-week intervention and the 24-week follow-up; however, the intermittent fasting group gained more lean mass and less fat mass than the continuous calorie restriction group. These results suggest that intermittent fasting may have generated metabolic or hormonal changes that resulted in a favorable pattern of weight regain. This study also demonstrates that intermittent fasting is effective for weight loss.

At first glance, the study supports intermittent fasting over continuous calorie restriction. However, an application can only be made to compare an alternate-day fast vs. a continuous calorie restriction diet regimen initially aimed to facilitate just a 14% daily calorie deficit. In fact, something the researchers fail to point out is that the continuous restriction group doubled the original 14% goal of energy deficit throughout the eight weeks. This is significant and indicates that a more ambitious 25% daily restriction goal can be more advantageous than intermittent fasting. However, the continuous energy restriction group in this study was not burdened with making healthy food choices, choosing appropriate portion sizes, and most importantly ,counting calories. These factors may have led to more favorable results than those which would occur in a real-life situation. This study should be repeated with a bigger sample size and with controls to account for these factors. For the purposes of this work, this study shows that an intermittent fasting regimen is safe and leads to a major overall energy deficit. It conflicts with other studies by suggesting that intermittent fasting may lead to less weight loss than would be expected based on reported energy deficits.

Intermittent Fasting and the Brain

Although there are many studies indicating that intermittent fasting can lead to improved brain health and resistance to neurological disorders in animals (de Cabo & Mattson, 2019), most of them do not control for calorie restriction to isolate the effects of fasting. However, in one study, Baik et al., (2020) determined that intermittent fasting increased markers for neurogenesis in the hippocampus of groups of mice that intermittently fasted for three months. The hippocampus is responsible for learning and memory. Mice that were grouped into intermittent fasting groups were deprived of food every other day for either 12 or 16 hours. The other group had no calorie restriction and ate ad libitum. The fasting mice showed higher amounts of specific protein markers than the ad libitum mice did. This indicates that the mice that fasted were creating new neurons at a faster rate and more efficiently. Researchers claim that the data indicated that there was no significant difference in the overall energy intake between groups. This means that the markers for neurogenesis were detected due to fasting alone. However, the researchers fail to include this data, which is unfortunate considering the significance of this claim. More animal studies like this must be carried out to further explore these findings.

Intermittent Fasting- Mood, Sleep and Alertness

Roky et al. (2000) explored how Ramadan intermittent fasting affected daytime alertness, mood and oral temperature in ten healthy subjects. Ramadan is the month in which Muslims do not drink and eat daily between sunrise and sunset. Researchers found that daytime oral

temperature, alertness, and mood decreased during fasting. However, it is fair to assume that this negative consequence was not a result of the fasting itself but rather a consequence of poor sleep habits during Ramadan. Eating and drinking only at night is disruptive to sleep patterns and the maintenance of a healthy circadian rhythm. Therefore, an intermittent fasting regimen that encourages healthy sleep habits, like an eating window between 12 AM and 8 PM, may not result in such negative effects. One review (McStay et al., 2021) looking at the influence of intermittent fasting on sleep found no overall negative effects. More research that accounts for sleep deprivation is required before any conclusions about alertness and mood can be made.

Risks of Intermittent Fasting

While there may be benefits to intermittent fasting, one must consider some possible negative ramifications. One of the topmost risks associated with intermittent fasting is dehydration. This still holds true even when one consumes non-caloric beverages during their fasting periods. Intermittent fasting can also put someone in a state of ketoacidosis which presents substantial health risks and can lead to hypoglycemia. Hypoglycemic symptoms include anxiety, irritability, low energy, and sleep disturbances. Furthermore, intermittent fasting may play a role in the development of AFRID (Avoidant/Restrictive Food Intake Disorder), especially if one starts intermittent fasting as a child or adolescent. In such cases, individuals will show a lack of interest in food consumption (Harding, 2021). Anybody with underlying health conditions should therefore consult with a doctor before starting an intermittent fast regimen.

Conclusion and Further Research

Based on the currently available research, intermittent fasting is on par with continuous calorie restriction in causing weight loss. Although it is not superior to continuous calorie restriction in causing weight loss, it is a safe and effective approach when done with proper diet and physical activity. Yet, there are conflicting studies on whether fasting offers additional benefits beyond weight loss. Most of the studies that suggest advantages in decreased blood pressure, insulin resistance, glucose levels, and stress levels are of low quality. These involve either a small sample size, self-reporting of food totals, or insufficient duration of the study. The stronger studies reviewed here found that although the fasting period does not hurt, it does not help either. They indicate that both regimens yield similar improvements in glucoregulatory, cardiovascular, and inflammatory biomarkers as well as changes in body composition. Therefore, one who feels that intermittent fasting is the easiest weight loss option should go ahead with it, as long as he makes sure to get proper nutrition and hydration. He should also first consult his doctor to make sure that he is aware of all the risks involved and that he is healthy enough to fast on a consistent basis.

Being that the current literature on human intermittent fasting is limited, more well-done research is required to fully validate the findings of this review. Additionally, a lot of questions remain. None of the current literature explores the long-term effects of fasting in humans, and there is a lot more to learn about the effects of different types of intermittent fasting. We also do not confidently know the effect that age and baseline health and weight have on the effects of fasting.

Long-term studies done in the future should be designed like the Templeman et al. (2021) conducted. They should involve sample sizes of at least 100 men and women from different backgrounds and different ages. To ensure accuracy, all calorie intake and physical activity should be recorded by researchers and not the participants themselves. It should also be repeated with participants with and without various cardiovascular and metabolic diseases who are lean, overweight, and obese. This may be very difficult to pull off practically, but these adjustments can go a long way to truly determine the effects of intermittent fasting.

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