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THE EFFECTS OF INTERMITTENT FASTING ON METABOLISM

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Article ID: 11004

INTRODUCTION

Intermittent fasting, a dietary pattern that involves alternating periods of fasting and eating, has gained significant attention in recent years. Beyond its potential for weight loss, intermittent fasting has also been studied for its impact on metabolism. This practice can trigger various metabolic responses, influencing how the body processes energy and regulates hormones. Intermittent fasting has gained popularity globally, with Western countries leading the trend. While less prevalent in Asia, it's gaining traction, especially in countries like Japan and South Korea. India, with its rich cultural heritage of religious fasting, has embraced modern intermittent fasting for weight loss and health benefits. Obesity and metabolic syndrome (MetS) are escalating global health crises, characterized by a cluster of conditions that significantly increase the risk of cardiovascular disease, type 2 diabetes, and other chronic illnesses. To address these pressing challenges, researchers and healthcare professionals have explored innovative approaches, including dietary interventions.

Intermittent fasting (IF), a dietary pattern involving cyclical periods of abstaining from food and drink, has emerged as a promising strategy. While often associated with weight loss, IF encompasses a broader range of dietary patterns with potential benefits beyond weight management.**[1]**

Throughout human evolution, physiological adaptations such as ability for energy storage and the flexibility of metabolism in relation to food supply were essential for withstanding periodic food shortages. Numerous case studies that show how western lifestyles have been adapted seem to point to obesity as an attribute of modernization **[2, 3].** Over the last ten to fifteen years, intermittent fasting (IF) has gained popularity as an unusual strategy that goes beyond calorie restriction (CR) to potentially lower body weight and enhance metabolic health. Regarding feed-and-fast cycles, meal timing, and calorie intake, there are several IF regimens **[4, 5].** The public has access to a wealth of information about different types of intermittent fasting and their alleged health benefits; in example, a search for "diet fasting intermittent alternate day" on the internet in October 2016 produced more than 210,000 results. Conversely, there is a shortage of data supporting intermittent fasting that may be utilized to inform public health practice recommendations. Periods of voluntarily abstaining from food and liquids, or intermittent fasting, are an age-old practice that people all over the world still adhere to in various forms **[6].** The data supporting the health advantages of intermittent fasting is compiled in this review, which also gives an overview of types of intermittent fasting regimens **[Table1].** The primary goal of research on intermittent fasting (IF) and metabolic health is to investigate its potential benefits in improving overall health and well-being.

TYPES OF INTERMITTENT FASTING REGIMENS

Alternate Day Fasting

It involves alternating days of unrestricted eating with fasting days that include a single meal containing about a quarter of the person's daily calorie needs. This modified fasting approach can vary in duration depending on individual schedules. The fasting period with the small meal can last from 30 to 40 hours. The timing of meals can affect the duration of fasting periods.**[7].** It has also been demonstrated that fasting on alternate days can effectively reduce a number of cardiovascular disease risk factors. Reductions in low-density lipoprotein (LDL) cholesterol, triglycerides, and total cholesterol have been noted, though not always. Two studies **[6,8]** found increases in high-density lipoprotein (HDL); however, one research only found increases in women and did not offer quantitative data. There was no difference in HDL concentrations detected in most investigations. Increasing the size of LDL particles may be considered a way to lower the risk of cardiovascular disease, as small LDL particles have been linked to an elevated risk for the condition. Increased LDL particle size was observed in participants who adhered to the fasting procedure in many alternate-day fasting investigations. **[7,8,9].**

Modified fasting regimens

Energy consumption on regularly scheduled fasting days is often restricted to 20–25% of energy needs, according to modified fasting regimens. In these investigations, periods of extremely restricted energy intake—as opposed to times when no energy is consumed—are referred to as fasting. This kind of plan, also known as intermittent energy restriction, serves as the foundation for the well-known 5:2 diet, which calls for unrestricted eating on the other 5 days of the week and energy restriction on the other 2 non-consecutive days **[10]**. Mouse studies on the effects of modified alternate-day fasting have been conducted by Varady et al. **[11]**. In a study that compared 85% dietary restriction on alternate fasting days to ad libitum chow, the group that experienced energy restriction showed increases in adiponectin and lower levels of visceral fat, resistin, and leptin. Analogous investigations carried out by this team also discovered that similar fasting schedules seem to lower insulin-like growth factor 1 levels, adipocyte size, and cell proliferation in mice **[6]**.

Findings from the small number of modified fasting regimen intervention trials indicate that weight loss is achieved with these eating patterns, whereas glucoregulatory indicators, lipids, and inflammatory markers show modest to mixed effects.

Time restricted feeding (TRF)

Time-restricted feeding is a dietary approach that involves limiting your eating to a specific window of time each day. This means that you fast for a certain number of hours and then eat all of your meals within a designated window. One of the most popular TRF methods is the 16:8 method. In the 16:8 method, you fast for 16 hours and then eat all of your meals within an 8-hour window. The TRF can offer various health benefits, including weight loss, improved blood sugar control, and reduced inflammation. By extending your fasting periods, you allow your body to enter a metabolic state called autophagy, where it repairs damaged cells and tissues. The common 16-hour fasting to 8-hour feeding pattern has not been the subject of any studies, but because of the length of the feeding period, it can be considered a more cautious time-restricted feeding strategy. Compared to other intermittent fasting regimens, the food schedule is far more akin to a regular eating pattern. Since this eating pattern roughly equates to skipping breakfast and not eating after dinner every day, many people even unknowingly follow it.

Religious fasting regimens

Religious fasting regimens are practices within various faiths that involve abstaining from food or drink for a specific period of time. These regimens often hold significant spiritual or symbolic meaning, and their observance can vary widely across different religions and cultures. While the exact rules and practices may differ, the underlying purpose often involves self-discipline, spiritual purification, or seeking a closer connection with a higher power.

1) ***Ramadan***- is a religious fasting regimen observed by Muslims worldwide. During this holy month, which lasts for 29 or 30 days, Muslims abstain from food and drink from dawn until dusk. The fast is broken at dusk with a meal called *iftar*, followed by a light meal called *suhoor* before

dawn. Ramadan is a time for spiritual reflection, prayer, and increased charity. It is believed to foster a sense of community and empathy among Muslims.

2) ***Hindu fasting-*** is a common practice in Hinduism, often undertaken for religious, spiritual, or health reasons. It involves abstaining from food or certain types of food for varying periods.

HEALTHY ADVANTAGES OF INTERMITTENT FASTING ON METABOLISM

Metabolic Switch

The many IF variations vary in how long the fasting phase lasts, and as a result, in how they affect metabolic function **[13]**. But they're all connected by the fact that, if IF is maintained for an extended period of time, a process known as "flipping the metabolic switch" is triggered **[12]**. Depending on the initial hepatic glycogen concentration, the make-up of the last meal, and the quantity of energy expended by the individual throughout the fast, this process takes place 12 to 36 hours after the fasting period starts **[12].** Turning on the metabolic switch means that the body will no longer prefer to obtain energy from the breakdown of glycogen into glucose, or glycogenolysis, but rather from lipolysis, which involves using lipids from adipose tissue that has been stored as fat. Following their release, lipids are broken down into free fatty acids (FFAs) and first undergo β-oxidation to become the intermediate stage acetyl CoA, which is then converted into the ketones acetoacetate (AcAc) and β-hydroxybutyrate (BHB) **[14].**

The metabolic switch's biochemical pathways. Intermittent fasting lowers blood glucose levels and causes fats (triacylglycerols and diacylglycerols) to be converted into free fatty acids (FFAs) through the process of lipolysis. After being transferred to the liver, these lipids undergo β-oxidation, converting into β-hydroxybutyrate (BHB) and acetoacetate (AcAc) via the intermediate steps of acetyl Co Enzyme A and Hydroxymethylglutaryl-Co Enzyme A. Blood carries BHB and AcAc to the brain, where they are subsequently absorbed by neurons. Astrocytes are also able to produce ketones, which may be a significant local supply of beta-hydroxybutyrate (BHB) for neurons in addition to the ketones processed in the liver.

Reduced glucose availability and increased ketones lower the Adenosine monophosphate: Adenosine triphosphate ratio in neurons, activating the kinases AMPK and Calcium/calmodulin-dependent protein kinase II , which in turn induces autophagy through Peroxisome proliferator-activated receptor-γ coactivator 1-α [PGC1α] and Cyclic AMP-responsive element-binding protein [CREB] activation. Furthermore, during a fast, reduced glucose levels trigger autophagy by reducing mTOR pathway activity. Additionally, BHB may enhance mitochondrial biogenesis, synaptic plasticity, and cellular stress resistance by upregulating the expression of brain-derived neurotrophic factor (BDNF). Because IF lowers blood levels of circulating insulin, the insulin/IGF signalling pathway protects against oxidative and metabolic stress and improves neuroplasticity. with a few minor changes, taken from.

These ketones are especially intriguing for cognition because, when fasting occurs, the brain prefers to run on them. Specifically, ketones regulate transcription factors (e.g., CREB or PGC1α) in neurons in addition to their function as an energy source. Brain-derived neurotrophic factors (BDNF) are upregulated as a result of the liver-to-brain transfer of BHB and AcAc, which are then converted back to acetyl CoA and HMG-CoA **[14]**.

By using the mammalian target of rapamycin [mTOR] pathway, neurons can control how much protein is synthesized in response to changes in the availability of nutrients. Protein and lipid synthesis is triggered by the mTOR pathway in a non-fasting state. Conversely, when fasting occurs, the mTOR pathway is less active, which inhibits protein synthesis worldwide and causes autophagy to recycle faulty proteins. Furthermore, as neurodegenerative illnesses progress and age, the body's capacity to withstand oxidative stress—the buildup of damaging free radicals—is largely dependent on autophagy DNA repair, BDNF activation, and antioxidant defenses (molecules that stop free radical oxidation) all improve when the mTOR pathway is inhibited. Furthermore, IF lessens inflammation by lowering blood levels of monocytes, or inflammatory white blood cells, which are the body's overreaction to damage or infection.**[15]**

By increasing insulin sensitivity, intermittent fasting may potentially have a positive indirect impact on the brain **[14]**. Patients with diabetes have reduced insulin sensitivity, which affects how well glucose is absorbed by cells, but this deterioration occurs naturally as people age. Because IF lowers blood levels of circulating insulin, insulin receptor sensitivity is increased and the insulin/IGF-1 signalling (IIS) pathway is upregulated [36], which improves neuron uptake and utilization of glucose **[14]**. Increased neuroplasticity and defense against oxidative stress are linked to upregulated IIS activity, which also lowers the activity of the mTOR pathway

Weight loss

The **Figure 1** depicts the process of intermittent fasting (IF) and its potential benefits for weight loss. IF involves alternating periods of fasting with periods of eating. This can lead to reduced insulin levels, which in turn promotes increased fat oxidation or burning. Additionally, IF often involves caloric restriction, which can further contribute to weight loss. By combining these factors, IF can help preserve lean muscle mass while decreasing body fat, ultimately leading to sustainable weight loss.

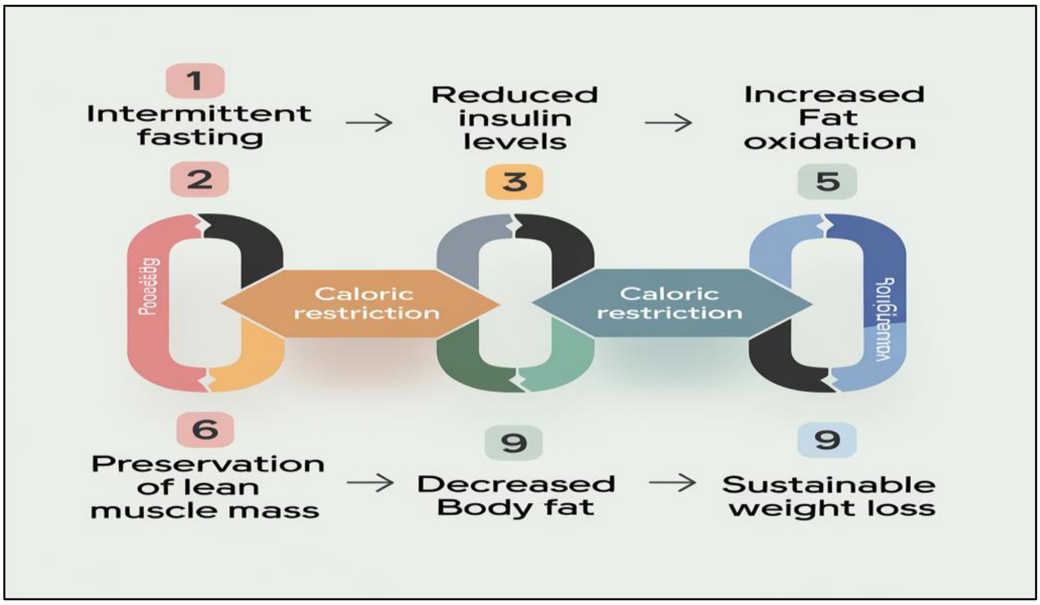

Figure 1: Shows effect of Intermittent fasting on Weight Loss

NEGATIVE EFFECTS OF INTERMITTENT FASTING

Intermittent fasting (IF) can have some side effects, including:

Energy Expenditure

The circadian clock is shown to control locomotion in animals; mice fed an isocaloric diet for a set amount of time showed enhanced motor coordination at the end of the feeding period **[16]** Time-restricted feeding regimens have also been shown to increase locomotion in rats **[16]** and enhance circadian activity rhythms **[16],** which are a measure of overall rhythmicity. In their alternate-day fasting study, Hoddy et al. **[17]** did not find any differences in physical activity as measured by actigraphy at baseline and postintervention. When comparing the 24-hour physical activity of the breakfast-free intervention group to the control group, Chowdhury et al. **[18]** found no differences.

Sleep

Nighttime eating has been linked in a number of observational studies to shorter sleep duration and lower quality sleep. This can result in insulin resistance and a higher risk of obesity, diabetes, cardiovascular disease, and cancer **[19].** In particular, it is theorized that consuming meals at irregular times of day—that is, late at night—causes circadian desynchronization, which in turn disrupts regular sleep cycles. When comparing frequently skipping breakfast (i.e., extending the evening fast) to controls, Chowdhury et al. **[18]** observed no influence on waking time, sleep duration, or sleep time. As far as we are aware, no other research has specifically looked at the relationships between sleep and intermittent fasting in individuals who live independently.

CONCLUSION

A lot of interest has been shown in intermittent fasting (IF) as a possible weight-loss and health-promoting strategy. While research has yielded promising results, it's essential to consider both the potential benefits and limitations. On the positive side, IF has been shown to reduce insulin resistance and promote fat loss. Additionally, some studies suggest that IF may have positive effects on cardiovascular health and longevity. However, it's important to note that IF may not be suitable for everyone, and individual responses can vary. Factors such as underlying health conditions, medication use, and personal preferences should be carefully considered before adopting an IF regimen. It's crucial to properly monitor and only precede or follow medical or dietitian recommendations.

REFERENCES

1. Vasim, I., Majeed, C.N. and DeBoer, M.D., 2022. Intermittent fasting and metabolic health. *Nutrients*, *14*(3), p.631.
2. Mattson, M.P., Allison, D.B., Fontana, L., Harvie, M., Longo, V.D., Malaisse, W.J., Mosley, M., Notterpek, L., Ravussin, E., Scheer, F.A. and Seyfried, T.N., 2014. Meal frequency and timing in health and disease. *Proceedings of the National Academy of Sciences*, *111*(47), pp.16647-16653.
3. Brown, P.J. and Konner, M., 1987. An anthropological perspective on obesity. *Annals of the New York Academy of Sciences*, *499*, pp.29-46.
4. Harris, L., Hamilton, S., Azevedo, L.B., Olajide, J., De Brún, C., Waller, G., Whittaker, V., Sharp, T., Lean, M., Hankey, C. and Ells, L., 2018. Intermittent fasting interventions for treatment of overweight and obesity in adults: a systematic review and meta-analysis. *JBI Evidence Synthesis*, *16*(2), pp.507-547.

5. Harris, L., McGarty, A., Hutchison, L., Ells, L. and Hankey, C., 2018. Short-term intermittent energy restriction interventions for weight management: a systematic review and meta-analysis. *Obesity Reviews*, *19*(1), pp.1-13.
6. Brongers, H.A. ed., 1977. *Instruction and Interpretation: Studies in Hebrew Language, Palestinian Archaeology and Biblical Exegesis: Papers Read at the Joint British-Dutch Old Testament Conference Held at Louvain, 1976, from 30 August to 2 September* (Vol. 20). Brill Archive.
7. Tinsley, G.M. and La Bounty, P.M., 2015. Effects of intermittent fasting on body composition and clinical health markers in humans. *Nutrition reviews*, *73*(10), pp.661-674
8. Heilbronn, L.K., Smith, S.R., Martin, C.K., Anton, S.D. and Ravussin, E., 2005. Alternate-day fasting in nonobese subjects: effects on body weight, body composition, and energy metabolism1, 2. *The American journal of clinical nutrition*, *81*(1), pp.69-73..
9. Johnson, J.B., Summer, W., Cutler, R.G., Martin, B., Hyun, D.H., Dixit, V.D., Pearson, M., Nassar, M., Tellejohan, R., Maudsley, S. and Carlson, O., 2007. Alternate day calorie restriction improves clinical findings and reduces markers of oxidative stress and inflammation in overweight adults with moderate asthma. *Free Radical Biology and Medicine*, *42*(5), pp.665-674
10. Mosley, M. and Spencer, M., 2015. *The FastDiet-revised & updated: lose weight, stay healthy, and live longer with the simple secret of intermittent fasting*. Simon and Schuster.
11. Varady, K.A., Hudak, C.S. and Hellerstein, M.K., 2009. Modified alternate-day fasting and cardioprotection: relation to adipose tissue dynamics and dietary fat intake. *Metabolism*, *58*(6), pp.803-811
12. Wilhelmi de Toledo, F., Grundler, F., Sirtori, C.R. and Ruscica, M., 2020. Unravelling the health effects of fasting: a long road from obesity treatment to healthy life span increase and improved cognition. *Annals of medicine*, *52*(5), pp.147-161.
13. Di Francesco, A., Di Germanio, C., Bernier, M. and De Cabo, R., 2018. A time to fast. *Science*, *362*(6416), pp.770-775.
14. Mattson, M.P., Moehl, K., Ghena, N., Schmaedick, M. and Cheng, A., 2018. Intermittent metabolic switching, neuroplasticity and brain health. *Nature Reviews Neuroscience*, *19*(2), pp.81-94
15. Gudden J, Arias Vasquez A, Bloemendaal M. The Effects of Intermittent Fasting on Brain and Cognitive Function. *Nutrients*. 2021; 13(9):3166.
16. Hatori, M., Vollmers, C., Zarrinpar, A., DiTacchio, L., Bushong, E.A., Gill, S., Leblanc, M., Chaix, A., Joens, M., Fitzpatrick, J.A. and Ellisman, M.H., 2012. Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. *Cell metabolism*, *15*(6), pp.848-860.
17. Hoddy, K.K., Gibbons, C., Kroeger, C.M., Trepanowski, J.F., Barnosky, A., Bhutani, S., Gabel, K., Finlayson, G. and Varady, K.A., 2016. Changes in hunger and fullness in relation to gut peptides before and after 8 weeks of alternate day fasting. *Clinical Nutrition*, *35*(6), pp.1380-1385.
19. Patterson, R.E. and Sears, D.D., 2017. Metabolic effects of intermittent fasting. *Annual review of nutrition*, *37*(1), pp.371-393.