Impact of intermittent Fasting on Glucose Metabolism

Authors

1. **Monalisa Khuntia**
MSW, NDEP, PhD Scholar (Rural Management)
a. School of Rural Management, KIIT University, Bhubaneswar, India
b. Sevayan Diabetes Centre, Puri, India

2. **Ramaballav Mahapatra**
MSW, MTA, PGDYM, NDEP, PhD Scholar
a. Utkal University of Culture, Bhubaneswar, India
b. Sevayan Diabetes Centre, Puri, India

3. **Sanjay Chand**
MA in Phil, NDEP
a. Sevayan Diabetes Centre, Puri, India
b. Government Women's College, Puri, India

4. **Dr. Soumya Sucharita**
BHMS
Sevayan Diabetes Centre, Puri, India

5. **Dr. Santosh Kumar Swain**
MBBS, MD
Associate Professor, Department of Medicine , Shri Jagannath Medical College, Puri India

6. **Prof. Abhay Sahoo**
MBBS, MD, DM
Dept. of Endocrinology, Apollo Hospitals, Bhubaneswar, India

7. **Dr. Hariballav Mahapatra**
MBBS, MHSc, PGD in Endo, Dip Diab, FDRC, PhD Scholar (Endocrinology)
a. Dept. of Endocrinology, IMS & SUM Hospital, SOA University,Bhubaneswar, India
b. Shree Hospitals, Bhubaneswar, India
c. Sevayan Diabetes Centre, Puri, India

Corsponding Author
Dr. Hariballav Mahapatra
401, Iris Prakash, D-7 BJB Nagar
Bhubanswar, India
Mob: +919438667798
Email: nullandzero@gmail.com

Abstract:

The obesity pandemic has had a lasting impact on public health outcomes, thus effective and novel approaches to weight management are urgently needed. Intermittent fasting encompasses a wide variety of timetables for short-term food avoidance, such as "fasting every other day,""fasting for the whole day," and "time-restricted feeding," in which all of the day's food is ingested within a 6-hour window, resulting in 18 hours of fasting. Weight loss and metabolic health may be aided by intermittent fasting. These eating schedules are effective because they trigger the body to manufacture healthy ketones by intermittently inducing the conversion of fatty acids. Overall, the regimens result in reduced body mass index (BMI) and have been associated to better control of dyslipidemia and blood pressure. They cause a loss of body fat as an added benefit. While, more study is needed on longer-term effects, and this technique should be avoided in some health situations, intermittent fasting should be regarded as a realistic alternative for persons who have a record of unhealthy weight gain when adopting regular eating habits. Also, in some health circumstances, intermittent fasting is not recommended.

Keywords: intermittent fasting, diabetes, metabolic effects, health conditions, ketones

DOINumber:10.48047/nq.2022.20.22.NQ10408 NeuroQuantology2022;20(22):4087-4096

Introduction

Glucose metabolism is the process by which the body breaks down and uses glucose. It is an important part of maintaining a healthy body and is closely related to intermittent fasting, which is a dietary pattern that involves alternating periods of eating and fasting. The health advantages of intermittent fasting include better metabolic health, weight reduction, and lower inflammation(Vasim et al., 2022). By controlling glucose metabolism, intermittent fasting can help to regulate blood glucose levels, which is important for managing diabetes and other metabolic diseases. Additionally, intermittent fasting has been linked to improved energy levels, mental clarity, and mood. Therefore, understanding the impact of glucose metabolism on intermittent fasting is important for optimizing health and well-being(de Cabo & Mattson, 2019). The major goal of this study is to evaluate the effects of intermittent fasting regimens and offer an overview of the evidence for the health advantages of intermittent fasting, with a special emphasis on studies involving human intervention. We highlight important rodent research and reviews since they comprise the bulk of the available data on intermittent fasting. Alterations in body mass index as well as metabolic parameters related to diabetes, cardiovascular disease, and cancer treatments are of particular importance as health consequences(Gudden et al., 2021).

Recently, intermittent fasting has gained favour as a method for enhancing both the composition of one's body and the health of one's metabolism. The term "intermittent fasting" is used to describe eating schedules that revolve on the principle of ingesting little or no calories over intervals of time that may range from 12 hours to several days. These time intervals may be done in a pattern(Malinowski et al., 2019). The practice of intermittent fasting may be carried out in a variety of ways. One such method is called "alternate day fasting," and it consists of alternating days of abstaining from food intake with days of eating anything they want. Periodic fasting is still another strategy, in which people abstain from eating for either one or two days each week (this practice is also known as 5:2 or 6:1 fasting). Time-restricted feeding is the third method, and it involves limiting eating to a certain window of the day, usually between 16 and 20 hours. This is the method that is used the most frequently(Park et al., 2020). A graphical illustration of the most popular types of intermittent fasting schedules may be seen in below Figure.

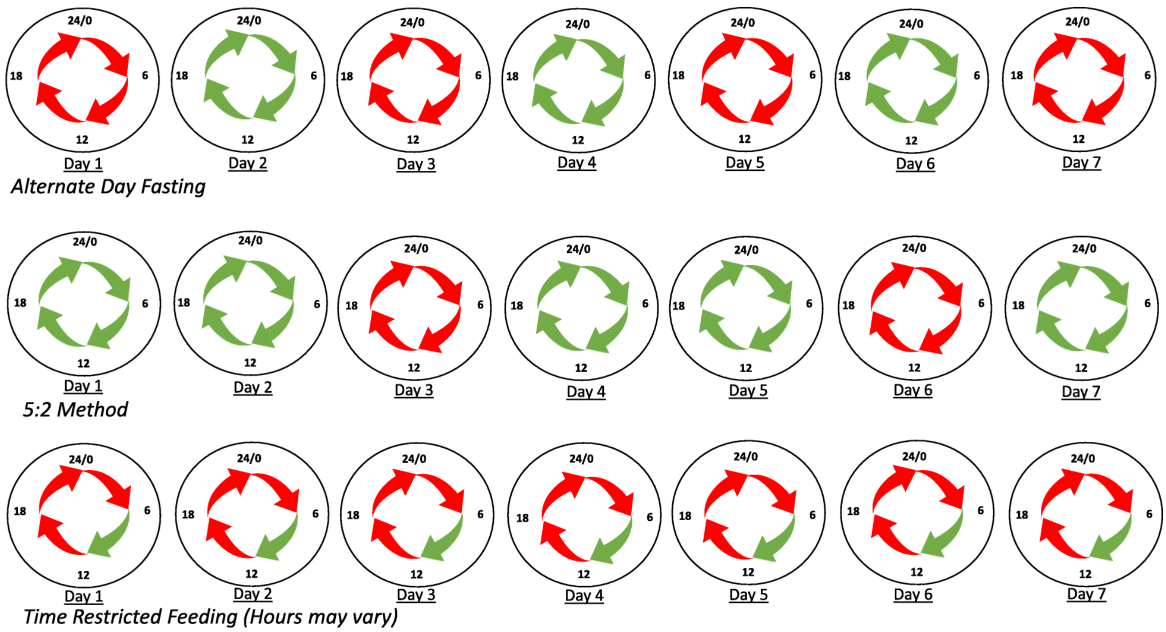

Figure 1Intermittent Fasting Regimens

Complete Alternate Day Fasting	Fasting days (during which no food or drink containing calories is taken) are alternated with eating days in these plans (foods and beverages consumed ad-libitum).
Modified fasting regimens	On days when the patient is scheduled to fast, modified regimens permit the ingestion of 20–25% of the required daily calories. This practice serves as the foundation for the well-known 5:2 diet, which calls for extreme calorie restriction on two days of the week that are not consecutive and ad libitum eating on the other five days of the week.
Time-restricted feeding	These protocols enable people to eat an unlimited amount of energy within predetermined windows, which results in the induction of periodic bouts of fasting on a regular basis. Indirect tests of a protracted daily or overnight fasting period are those that take place in studies with less than three meals per day.
Religious feeding	Several different types of fasting schedules are followed by those who are doing it for religious or spiritual reasons.
Ramadan fasting	A fast that is observed throughout the holy months of Ramadan from sunrise till sundown each day. The most typical pattern of eating involves having one substantial meal after the sun goes down and another meal that is somewhat lighter in the early hours of the morning. As a result, both the feast and the fasting periods in the month of Ramadan last around 12 hours each.
Other religious fasts	Fasting is a common practice among members of the Church of Jesus Christ of Latter-day Saints. A prolonged time of fasting occurs throughout the night for some Seventh-day Adventists since they have their second and last meal of the day during the afternoon. This prolonged period of fasting may be physiologically significant.

Intermittent Fasting and Metabolic Switching

The primary sources of energy that are used by cells are glucose and fatty acids. After meals, glucose is converted into an energy source, and adipose tissue is employed to store fat in the form of triglycerides(Patikorn et al., 2021). When an individual goes without food for an extended length of time, the body converts the stored triglycerides into energy-rich fatty acids and glycerol. During periods of fasting, the liver is responsible for converting fatty acids into ketone bodies, which are then

used by many different tissues, most notably the brain, as a significant source of energy(M. A. I. Faris et al., 2020a). Blood levels of ketone bodies are low while the body is fed, but they start to increase within 8 to 12 hours following the start of a fast in humans, eventually reaching levels as high as 2 to 5 mM after 24 hours. An increase in plasma ketone levels begins anywhere from four to eight hours after the start of fasting in rodents, and it reaches millimolar levels within twenty-four hours after the start of the fast. In regimens of intermittent fasting, The timing of this response gives us clues about how often we should fast. (Clifton et al., 2021).
Alternate-day fasting, 5:2 intermittent fasting (which entails abstaining from food for two days per week), and daily time-restricted eating are the three forms of intermittent fasting that have been examined the most extensively in humans(Haupt et al., 2021). Increased amounts of ketone bodies occur on days when a person follows a diet that severely restricts caloric intake (for example, reducing to 500 to 700 calories per day). The ability of the organism to convert from using glucose as a fuel source to using fatty acids and ketone bodies is reflected in a drop in the respiratory-exchange ratio (the ratio of carbon dioxide created to oxygen absorbed). The ratio of carbon dioxide exhaled to oxygen inhaled is known as the respiratory-exchange ratio. (M. A. I. E. Faris et al., 2020).

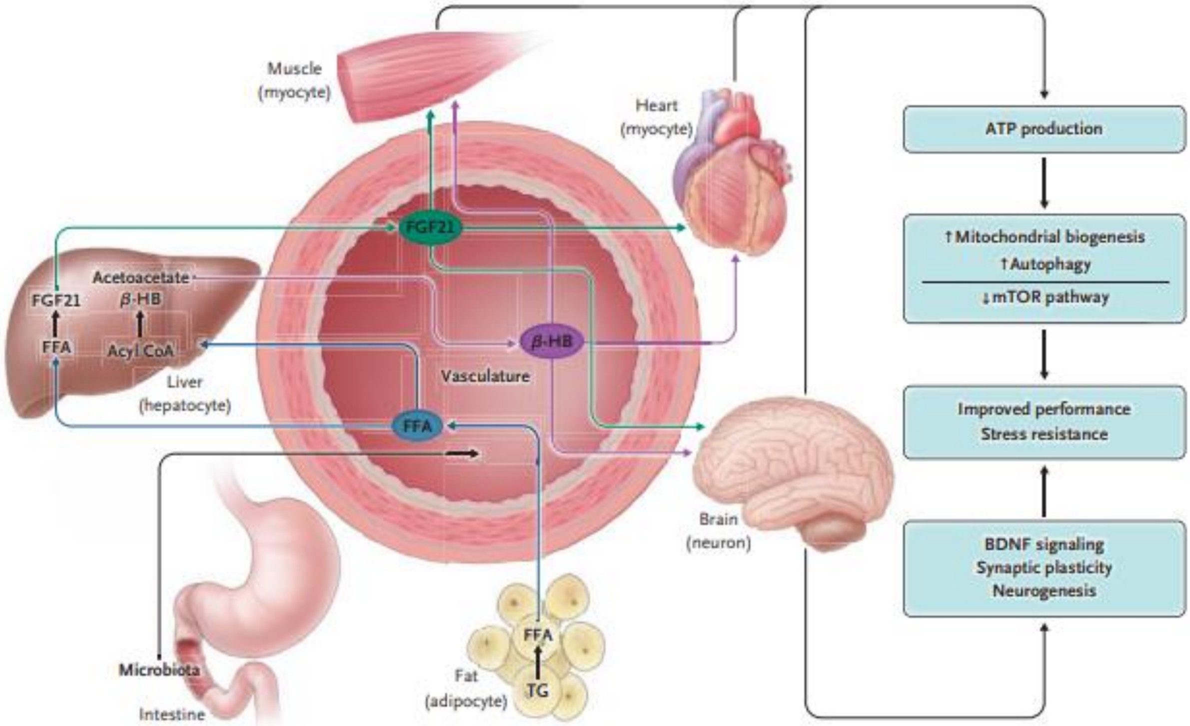

Figure 2 Metabolic Adaptations to Intermittent Fasting

Physiology of Glucose Metabolism

Glucose is the primary source of energy for the body, and its metabolism is regulated by a number of hormones. As blood glucose levels rise, the hormone insulin is secreted as a major regulator of glucose metabolism. Glucose is stored as glycogen when insulin is present, and glucose absorption into cells is facilitated. (Templeman et al., 2020). When blood sugar drops too low, the hormone glucagon is secreted to speed up the breakdown of glycogen stores and release glucose into the circulation. Glucose metabolism is regulated in part by the stress hormones cortisol and adrenaline, which promote the breakdown of glycogen as well as the release of glucose into circulation(Freire, 2020).

Intermittent fasting and insulin sensitivity

Because of the impact it has in stimulating the storage and use of glucose, insulin plays an important part in maintaining normal glucose levels in the body. On the other hand, the actions of insulin are not restricted to the homeostasis of glucose (Haupt et al., 2021). Insulin's effects extend beyond those on lipid metabolism, since it also promotes DNA and RNA synthesis, cell development and differentiation, amino acid uptake, protein synthesis, and suppression of protein breakdown. These are the two most important functions that insulin performs(M. A. I. E. Faris et al., 2020).

It is generally accepted that insulin resistance is the root cause of type 2 diabetes. Insulin resistance is defined as the need for greater circulating insulin levels to induce a glucose-lowering response. To induce a glucose-lowering response, greater insulin levels are required in those with insulin resistance(Templeman et al., 2020). Insulin mainly acts on receptors in skeletal muscle, the liver, and white adipose tissue to fulfill its goal of managing glucose levels and maintaining homeostasis. In a nutshell, researchers have put out a number of different hypotheses concerning the genesis of insulin resistance. One of the most well-known hypotheses put up to explain this phenomena is the link between insulin resistance in tissues is on the increase due to rising obesity and the chronic inflammation it causes. (Freire, 2020).

Impact of Intermittent Fasting on Glucose Metabolism

Several studies have investigated the impact of intermittent fasting on glucose metabolism. The results of these studies suggest that intermittent fasting may have beneficial effects on glucose regulation. (Correia et al., 2020) shown that intermittent fasting may improve insulin sensitivity. This is thought to be due to the reduction in caloric intake, which can result in lower levels of circulating insulin. In addition, intermittent fasting has been shown to increase the activity of insulin receptors and decrease insulin resistance. (Lee et al., 2020) Intermittent fasting have been shown to have an effect on glucagon levels. Evidence suggests that it does this via stimulating the glucagon receptors, which in turn causes more glucagon to be secreted. Increased glycogen breakdown and glucose release into the blood may result from this. (Harney et al., 2019) Intermittent fasting has also been shown to have an effect on cortisol and epinephrine levels. It has been demonstrated to lower cortisol levels, which in turn increases glycogen breakdown and glucose release into the blood. The breakdown of glycogen stores as well as the release of glucose into the blood are both accelerated by intermittent fasting, which has also been demonstrated to boost the activation of epinephrine receptors.

(Grajower & Horne, 2019) Effect on Glucose Production and Utilization Intermittent fasting can also affect glucose production and utilization. It has been shown to reduce the production of glucose by the liver, which can lead to a decrease in the amount of glucose available in the blood. Fasting at irregular intervals provides additional benefits, including enhanced glucose absorption and utilization. (Zouhal et al., 2020) Health The effects of intermittent fasting on glucose metabolism have potential implications for health. Improved insulin sensitivity, increased glucagon levels, and increased glucose utilization can lead to improved metabolic health and a decreased risk of developing diabetes. In addition, the reduction in glucose production may be beneficial for those with obesity or other metabolic diseases.

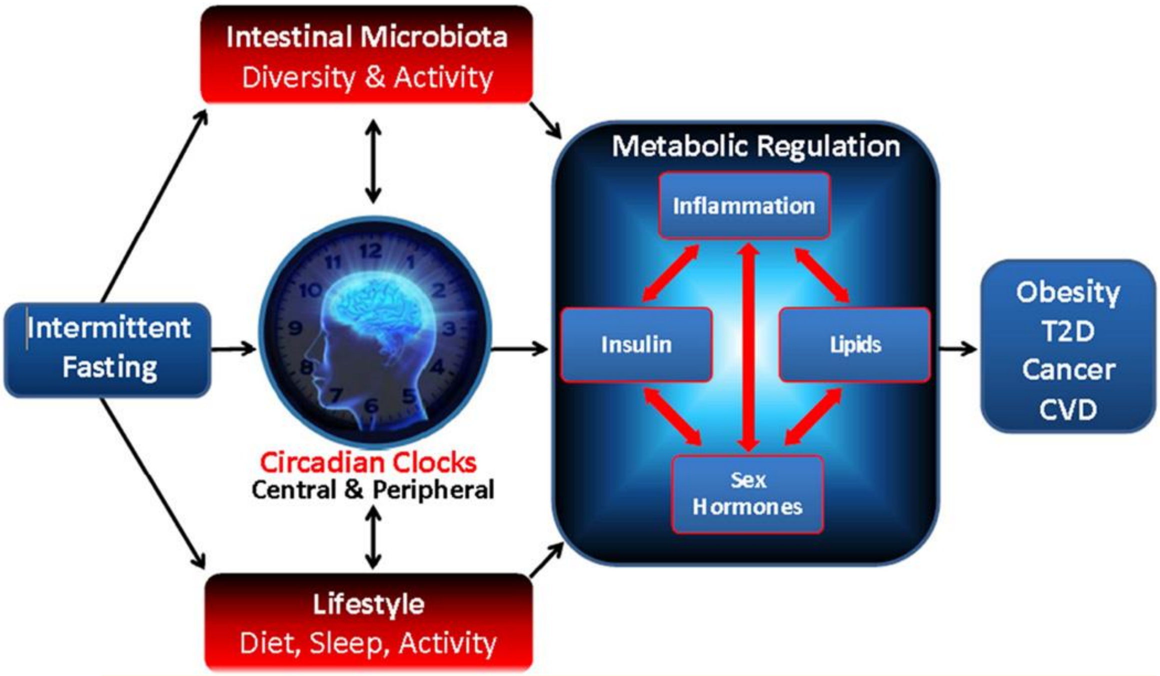

Figure 3Intermittent fasting and the gut microbiome, sleep, and circadian rhythms: a prospective study

The accompanying diagram shows the hypothesized connections between variables that link intermittent fasting with health benefits. Overall, the impacts on (1) circadian biology, (2) gut flora, as well as (3) modifiable lifestyle behaviors of intermittent fasting regimens are hypothesized to influence metabolic control. Alterations in these systems may set up an unfavorable metabolic climate, making individuals more susceptible to conditions including obesity, diabetes, cardiovascular disease, as well as cancer(Munhoz et al., 2020).

Obesity and Diabetes Mellitus

In studies conducted on animal models, intermittent fasting has been shown to increase insulin sensitivity, prevent obesity brought on by a diet heavy in fat, and improve diabetic retinopathy. In the island of Okinawa, the indigenous people traditionally practice a method known as intermittent fasting(M. A. I. E. Faris et al., 2020). As a result, they have very low rates of obesity and diabetes mellitus, in addition to an exceptionally high life expectancy. In general, Okinawans enjoy a diet that is low in calories and high in nutrients, including Okinawan sweet potatoes, various vegetables, and legumes. Okinawan fish is also a common component of the Okinawan diet. Low levels of insulin-like growth factor 1, growth hormone, inflammatory markers, as well as oxidative stress indicators were also seen among CRON (Calorie Restriction with Optimal Nutrition) dieters (members of the Calorie Restriction Society)(Park et al., 2020).

Cardiovascular Disease

Intermittent fasting has been shown to improve a variety of cardiovascular health markers in both animals and humans, including blood pressure, resting heart rate, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, glucose, insulin, as well as insulin resistance. Moreover, atherosclerosis-related markers including systemic oxidative stress and inflammatory processes are decreased by intermittent fasting(Gudden et al., 2021). In humans, the variability of heart rate may be increased by the enhancement of parasympathetic tone during intermittent fasting, as shown by analyses of electrocardiographic recordings. Comprehensive Evaluation of Long-Term Effects of Energy-Reduction Interventions (CALERIE) study indicated revealed several cardiovascular risk variables were decreased by 12% after 2 years of calorie restriction in people who were not fat (Wilhelmi de Toledo et al., 2020).

Cancer

There have been or are now being conducted clinical studies examining the effects of intermittent fasting on cancer patients. The majority of the early clinical tests have concentrated on assessing adherence, identifying adverse effects, and defining biomarkers(Parvaresh et al., 2019). One study found that males with prostate cancer who participated in a daily calorie restriction trial had a very high adherence rate (95%) and had no side effects. It has been shown in a number of case studies involving individuals who have glioblastoma that intermittent fasting may inhibit the development of tumors and increase survival rates. Patients who have malignancies of the breast, ovary, prostate, endometrium, colon, and digestive tract, as well as glioblastoma, are participating in ongoing research studies that examine the effects of intermittent fasting. Studies use a variety of different regimens for intermittent fasting, but they all need patients to fast at regular intervals while they are receiving chemotherapy. There have been no studies done on people to assess whether or not intermittent fasting has an effect on the recurrence of cancer(Cherkas et al., 2020).

Effects of Intermittent Fasting on Health and Aging

Calorie restriction and intermittent fasting have both been the focus of several research on the effects of aging and lifespan. Following over a century of study on the effects of caloric restriction on animal subjects, the overarching finding was that lower calorie intake significantly lengthens the life span of the subjects. Good Rick and colleagues did one of the early research on intermittent fasting (M. A. I. Faris et al., 2020b). When rats are young adults, they benefit most from an alternate-day feeding schedule, which has been shown to enhance their lifespan by as much as 80%. This was a striking discovery from the research. While calorie restriction has been shown to improve health and longevity, the magnitude of its benefits varies across individuals and may be influenced by factors like sex, diet, age, as well as genetics. Caloric restriction may also have an influence on the life span(Hutchison et al., 2019). A meta-analysis of studies published between 1934 and 2012 found that caloric restriction increased median lifespan in rats by 14 to 45% but only in mice by 4 to 27%. It has been found that the longevity of recombinant inbred mouse strains varies substantially depending on the strain and the sex of the mouse. The study, however, only used one form of calorie restriction (a limitation of 40% of calories), and then it didn't investigate any death rates, health indicators, or processes. Adiposity loss was shown to be inversely proportional to life expectancy, suggesting that shorter-lived animals responded to severe caloric restriction by losing more weight and entering a state of famine more quickly than their longer-lived counterparts. Also, shorter-lived animals made the starving transition more rapidly when placed under such extreme calorie restriction(Levy & Chu, 2019).

Physical and Cognitive Effects of Intermittent Fasting

In both animals as well as humans, intermittent fasting has been found to improve physical performance. For instance, mice maintained on an alternate-day fasting diet exhibit greater sprinting endurance than mice with free access to food, while being of similar body weights(Hwangbo et al., 2020). Animals who are fed at a limited period each day or who fast every other day see improvements in their balance and coordination as a result of these dietary regimes. 35 Teenage males who fast for 16 hours a day and do strength exercise for two months lose fat but maintain muscle mass. Alternate-day fasting and daily calorie restriction may ameliorate the impairments in spatial memory and learning brought on by obesity, diabetes, and neuroinflammation. (Arciero et al., 2023). Experimental research on animals shows that intermittent fasting boosts cognitive abilities across the board.

Older people who took part in a clinical investigation and were allocated a short-term program of calorie restriction showed an increase in verbal memory. A calorie restriction program that lasted for a year resulted in improvements in verbal memory, executive function, as well as global cognition in a study that included adults who were overweight and had minor cognitive impairment(Mirmiran et al., 2019). Caloric restriction over a period of two years led to a considerable improvement in working memory, according to findings from a major, multi-centre, randomized clinical study that was conducted more recently. There is a clear and present necessity to conduct additional research on intermittent fasting and how it affects cognition in older people. Given that no pharmacological treatments exist to alter the normal course of neurodegenerative disorders or the aging process in the brain, this is particularly so. (Corley et al., 2018).

Conclusion:

Fasting for a single period of time (e.g., overnight) can decrease the resting levels of insulin and glucose, two metabolic indicators linked to chronic disease, in humans. In order to get steady-state fasting readings for a wide variety of metabolic substrates and hormones, including insulin, patients must fast for 8-12 hours prior to blood collection. The clinical and scientific community has yet to reach a consensus on whether or not intermittent fasting can be used effectively to improve metabolic health on a population scale. To determine whether intermittent fasting regimes may give long-term metabolic benefits and body weight management, more adequately powered, controlled clinical research is required.

In addition, the goal of intermittent fasting routines is to reduce the risk of chronic illness in humans by adopting the same eating patterns that have been shown to be effective in mice and other species. Under "Future Issues," we provide some recommendations for where future studies on intermittent fasting as well as metabolic health could go. This study provides support for the use of intermittent fasting regimens for weight loss and metabolic health in those who are able to refrain from eating at certain times of the day, night, or week. There are several potential public health benefits from adopting one of these diets if it is shown to be effective at improving population health.

References:

Arciero, P. J., Poe, M., Mohr, A. E., Ives, S. J., Arciero, A., Sweazea, K. L., Gumpricht, E., & Arciero, K. M. (2023). Intermittent fasting and protein pacing are superior to caloric restriction for weight and visceral fat loss. *Obesity*, *31*(S1), 139–149. https://doi.org/10.1002/oby.23660

Cherkas, A., Holota, S., Mdzinarashvili, T., Gabbianelli, R., & Zarkovic, N. (2020). Glucose as a major antioxidant: When, what for and why it fails? *Antioxidants*, *9*(2), 1–20. https://doi.org/10.3390/antiox9020140

Clifton, K. K., Ma, C. X., Fontana, L., & Peterson, L. L. (2021). Intermittent fasting in the prevention and treatment of cancer. *CA: A Cancer Journal for Clinicians*, *71*(6), 527–546. https://doi.org/10.3322/caac.21694

Corley, B. T., Carroll, R. W., Hall, R. M., Weatherall, M., Parry-Strong, A., & Krebs, J. D. (2018). Intermittent fasting in Type 2 diabetes mellitus and the risk of hypoglycaemia: a randomized controlled trial. *Diabetic Medicine*, *35*(5), 588–594. https://doi.org/10.1111/dme.13595

Correia, J. M., Santos, I., Pezarat-Correia, P., Minderico, C., & Mendonca, G. V. (2020). Effects of intermittent fasting on specific exercise performance outcomes: A systematic review including meta-analysis. *Nutrients*, *12*(5). https://doi.org/10.3390/nu12051390

de Cabo, R., & Mattson, M. P. (2019). Effects of Intermittent Fasting on Health, Aging, and Disease. *New England Journal of Medicine*, *381*(26), 2541–2551. https://doi.org/10.1056/nejmra1905136

Faris, M. A. I. E., Alsibai, J., Jahrami, H. A., Obaideen, A. A., Jahrami, H. A., & Obaideen, A. A. (2020). Impact of Ramadan diurnal intermittent fasting on the metabolic syndrome components in healthy, non-athletic Muslim people aged over 15 years: A systematic review and meta-analysis. *British Journal of Nutrition*, *123*(1), 1–22. https://doi.org/10.1017/S000711451900254X

Faris, M. A. I., Jahrami, H., BaHammam, A., Kalaji, Z., Madkour, M., & Hassanein, M. (2020a). A systematic review, meta-analysis, and meta-regression of the impact of diurnal intermittent fasting during Ramadan on glucometabolic markers in healthy subjects.

Diabetes Research and Clinical Practice, *165*. https://doi.org/10.1016/j.diabres.2020.108226

Faris, M. A. I., Jahrami, H., BaHammam, A., Kalaji, Z., Madkour, M., & Hassanein, M. (2020b). A systematic review, meta-analysis, and meta-regression of the impact of diurnal intermittent fasting during Ramadan on glucometabolic markers in healthy subjects. *Diabetes Research and Clinical Practice*, *165*. https://doi.org/10.1016/j.diabres.2020.108226

Freire, R. (2020). Scientific evidence of diets for weight loss: Different macronutrient composition, intermittent fasting, and popular diets. *Nutrition*, *69*, 110549. https://doi.org/10.1016/j.nut.2019.07.001

Grajower, M. M., & Horne, B. D. (2019). Clinical management of intermittent fasting in patients with diabetes mellitus. *Nutrients*, *11*(4), 1–11. https://doi.org/10.3390/nu11040873

Gudden, J., Arias Vasquez, A., & Bloemendaal, M. (2021). The effects of intermittent fasting on brain and cognitive function. *Nutrients*, *13*(9), 1–25. https://doi.org/10.3390/nu13093166

Harney, D. J., Hutchison, A. T., Hatchwell, L., Humphrey, S. J., James, D. E., Hocking, S., Heilbronn, L. K., & Larance, M. (2019). Proteomic Analysis of Human Plasma during Intermittent Fasting. *Journal of Proteome Research*, *18*(5), 2228–2240. https://doi.org/10.1021/acs.jproteome.9b00090

Haupt, S., Eckstein, M. L., Wolf, A., Zimmer, R. T., Wachsmuth, N. B., & Moser, O. (2021). Eat, train, sleep—retreat? Hormonal interactions of intermittent fasting, exercise and circadian rhythm. *Biomolecules*, *11*(4), 1–19. https://doi.org/10.3390/biom11040516

Hutchison, A. T., Liu, B., Wood, R. E., Vincent, A. D., Thompson, C. H., O'Callaghan, N. J., Wittert, G. A., & Heilbronn, L. K. (2019). Effects of Intermittent Versus Continuous Energy Intakes on Insulin Sensitivity and Metabolic Risk in Women with Overweight. *Obesity*, *27*(1), 50–58. https://doi.org/10.1002/oby.22345

Hwangbo, D.-S., Lee, H.-Y., Abozaid, L. S., & Min, K.-J. (2020). Mechanisms of Lifespan Regulation by Calorie. *Nutrients*, *12*(4), 1194.

Lee, J. H., Verma, N., Thakkar, N., Yeung, C., & Sung, H. K. (2020). Intermittent fasting: Physiological implications on outcomes in mice and men. *Physiology*, *35*(3), 185–195. https://doi.org/10.1152/physiol.00030.2019

Levy, E., & Chu, T. (2019). Intermittent fasting and its effects on athletic performance: A review. *Current Sports Medicine Reports*, *18*(7), 266–269. https://doi.org/10.1249/JSR.0000000000000614

Malinowski, B., Zalewska, K., Węsierska, A., Sokołowska, M. M., Socha, M., Liczner, G., Pawlak-Osińska, K., & Wiciński, M. (2019). Intermittent fasting in cardiovascular disorders—an overview. *Nutrients*, *11*(3), 1–18. https://doi.org/10.3390/nu11030673

Mirmiran, P., Bahadoran, Z., Gaeini, Z., Moslehi, N., & Azizi, F. (2019). Effects of Ramadan intermittent fasting on lipid and lipoprotein parameters: An updated meta-analysis. *Nutrition, Metabolism and Cardiovascular Diseases*, *29*(9), 906–915. https://doi.org/10.1016/j.numecd.2019.05.056

Munhoz, A. C., Vilas-boas, E. A., Panveloski-costa, A. C., Santos, J., Leite, M., Lucena, C. F., Emilio, H., & Carpinelli, A. R. (2020). Munhoz-2020-Intermittent-fasting& fat mass & Hyperinsulinemia. *Nutrients*, *12*, 1029.

Park, S., Zhang, T., Wu, X., & Yi Qiu, J. (2020). Ketone production by ketogenic diet and by intermittent fasting has different effects on the gut microbiota and disease progression in an Alzheimer's disease rat model. *Journal of Clinical Biochemistry and Nutrition*, *67*(2), 188–198. https://doi.org/10.3164/jcbn.19-87

Parvaresh, A., Razavi, R., Abbasi, B., Yaghoobloo, K., Hassanzadeh, A., Mohammadifard, N., Safavi, S. M., Hadi, A., & Clark, C. C. T. (2019). Modified alternate-day fasting vs. calorie restriction in the treatment of patients with metabolic syndrome: A randomized clinical trial. *Complementary Therapies in Medicine*, *47*. https://doi.org/10.1016/j.ctim.2019.08.021

Patikorn, C., Roubal, K., Veettil, S. K., Chandran, V., Pham, T., Lee, Y. Y., Giovannucci, E. L., Varady, K. A., & Chaiyakunapruk, N. (2021). Intermittent Fasting and Obesity-

Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials. *JAMA Network Open*, *4*(12), 1–12. https://doi.org/10.1001/jamanetworkopen.2021.39558

Templeman, I., Gonzalez, J. T., Thompson, D., & Betts, J. A. (2020). The role of intermittent fasting and meal timing in weight management and metabolic health. *Proceedings of the Nutrition Society*, *79*(1), 76–87. https://doi.org/10.1017/S0029665119000636

Vasim, I., Majeed, C. N., & DeBoer, M. D. (2022). Intermittent Fasting and Metabolic Health. *Nutrients*, *14*(3), 1–15. https://doi.org/10.3390/nu14030631

Wilhelmi de Toledo, F., Grundler, F., Sirtori, C. R., & 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), 147–161. https://doi.org/10.1080/07853890.2020.1770849

Zouhal, H., Saeidi, A., Salhi, A., Li, H., Essop, M. F., Laher, I., Rhibi, F., Amani-Shalamzari, S., & Ben Abderrahman, A. (2020). <p>Exercise Training and Fasting: Current Insights</p>. *Open Access Journal of Sports Medicine*, *Volume 11*, 1–28. https://doi.org/10.2147/oajsm.s224919