

## **Intermittent Fasting on Human Health and Disease**

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Chronic non-communicable diseases (NCDs) are the leading cause of morbidity and mortality worldwide, but most of all in industrialized countries, and are fundamentally correlated to improper nutrition and impaired lifestyle behaviours [1]. Also, the ageing process, with all its associated chronic disparities, is accelerated by imbalanced nutrition, altered feeding behaviour and lifestyle in general, benefiting from changes in these factors [2,3]. The brain cellular network is highly dependent on the bioenergetics homeostasis, as it is negatively influenced by sedentary and imbalanced food intake; under such conditions, decreased neuroplasticity and impaired calcium homeostasis are reported, changes that make the subjects more susceptible to neurodegeneration and stroke [4].

Over-nutrition is an important risk factor for various human diseases, including neurodegenerative diseases, metabolic disorders, and cancers; diet, one of the most important lifestyle factors, is strongly correlated either with a good health status or with the development of many chronic conditions such as obesity, cardiovascular disease, hypertension, stroke, type 2 diabetes, metabolic syndrome, some cancers, and some neurological diseases [5–7]. In this context, changes in dietary patterns are highly discussed in recent research in the quest for discovering some kind of *magic bullet* against all the above-mentioned health impairment issues which represent a heavy burden on the quality of life all over the world [3,4,6–10]. In the framework of changes in dietary patterns, there are two main approaches: either a reductive shift of the caloric intake/change in food quality or an important modification of feeding behaviour in regard to the timeline of eating. Regarding food composition, research shows that enriching human diet in polyunsaturated fatty acids as well as natural antioxidants leads to an improvement of cardio-metabolic risk [3,6,11–19].

The second approach is represented by intermittent fasting, comprising eating programs of individuals that undergo long time periods (16–48 h) with very reduced/no energy/food intake, alternating with periods of normal food consumption; under the "umbrella" of intermittent fasting, several forms are encountered—temporary food avoidance or time-restricted feeding or other similar fasting patterns; studies, either on animal models or human ones (most of which include the Ramadan model) show that intermittent fasting improves the metabolic outcome, diminish inflammation, improve weight management, increase insulin sensitivity and even counteract ageing in both normal-weight and overweight subjects [2,4,5,8,18–25].

Studies show that this kind of approach has beneficial metabolic effects, improving mitochondrial function and stimulating fatty acid oxidation as well as increased clearance of cellular lipids, regulating glucose homeostasis, activating adaptive cellular stress responses, reducing oxidative stress and diminishing inflammatory responses, inducing DNA repair and autophagy, etc. [5–7,18,26,27]. Intermittent fasting regimens are able to regulate metabolic routes by influencing the target of rapamycin (TOR) pathway and circadian clock, profoundly changing the gut microbiota composition, influencing the sleep quality and other lifestyle factors [10,28].

All these acute changes in cellular and metabolic pathways are associated with a decrease in chronic disease burden as well as the increase in protective molecule levels [12].



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**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Intermittent fasting has been shown to have important health benefits in the prevention and management of chronic diseases and in the process of biological aging. The effect of intermittent fasting on hormonal circadian rhythms has also received particular attention, mainly due to the tremendous importance of circadian hormonal impact on normal physiology and its pathophysiological involvement in clinical endocrinology [10,21,22,29,30]. However, more profound research is needed to determine the efficacy and safety of intermittent fasting in humans, and to fully understand the underlying mechanisms by which this nutritional approach exerts its effects in human health and disease.

In this context, the current Special Issue "Intermittent Fasting on Human Health and Disease" is aiming to gather current knowledge in the field and to update the information regarding the clinical relevance of this dietary pattern, to further collect arguments in support of already available data regarding the potential of intermittent fasting regimens to be efficacious and offer a certain non-pharmacological approach to improving health at the population level, and induce public health benefits.

This Special Issue welcomes contributions from researchers and nutrition experts in all related fields; specialists are invited to submit their original work, review articles and communications, clinical, preclinical and experimental studies that are linked to the interplay between nutrition, all forms of restricted eating and their effects on chronic disease.

These findings will support health professionals and nutritional practitioners in the shaping of new ideas and coach their patients to embrace improved eating behaviours.

Conflicts of Interest: The authors declare no conflict of interest.

## References

- Global Burden of Disease Study, C. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015, 386, 743–800. [CrossRef]
- Lee, M.B.; Hill, C.M.; Bitto, A.; Kaeberlein, M. Antiaging diets: Separating fact from fiction. Science 2021, 374, eabe7365. [CrossRef] [PubMed]
- Patikorn, C.; Roubal, K.; Veettil, S.K.; Chandran, V.; Pham, T.; Lee, Y.Y.; Giovannucci, E.L.; Varady, K.A.; Chaiyakunapruk, N. Intermittent Fasting and Obesity-Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials. JAMA Netw. Open 2021, 4, e2139558. [CrossRef] [PubMed]
- 4. Mattson, M.P.; Longo, V.D.; Harvie, M. Impact of intermittent fasting on health and disease processes. *Ageing Res. Rev.* 2017, 39, 46–58. [CrossRef]
- 5. Tang, D.; Tang, Q.; Huang, W.; Zhang, Y.; Tian, Y.; Fu, X. Fasting: From Physiology to Pathology. *Adv. Sci.* 2023, *10*, e2204487. [CrossRef]
- 6. Malinowski, B.; Zalewska, K.; Wesierska, A.; Sokolowska, M.M.; Socha, M.; Liczner, G.; Pawlak-Osinska, K.; Wicinski, M. Intermittent Fasting in Cardiovascular Disorders—An Overview. *Nutrients* **2019**, *11*, 673. [CrossRef]
- Dong, T.A.; Sandesara, P.B.; Dhindsa, D.S.; Mehta, A.; Arneson, L.C.; Dollar, A.L.; Taub, P.R.; Sperling, L.S. Intermittent Fasting: A Heart Healthy Dietary Pattern? Am. J. Med. 2020, 133, 901–907. [CrossRef]
- 8. Vasim, I.; Majeed, C.N.; DeBoer, M.D. Intermittent Fasting and Metabolic Health. Nutrients 2022, 14, 631. [CrossRef]
- Hoddy, K.K.; Marlatt, K.L.; Cetinkaya, H.; Ravussin, E. Intermittent Fasting and Metabolic Health: From Religious Fast to Time-Restricted Feeding. *Obesity* 2020, 28 (Suppl. S1), S29–S37. [CrossRef]
- 10. Patterson, R.E.; Sears, D.D. Metabolic Effects of Intermittent Fasting. Annu. Rev. Nutr. 2017, 37, 371–393. [CrossRef]
- Margina, D.; Ungurianu, A.; Purdel, C.; Nitulescu, G.M.; Tsoukalas, D.; Sarandi, E.; Thanasoula, M.; Burykina, T.I.; Tekos, F.; Buha, A.; et al. Analysis of the intricate effects of polyunsaturated fatty acids and polyphenols on inflammatory pathways in health and disease. *Food Chem. Toxicol.* 2020, 143, 111558. [CrossRef] [PubMed]
- Purdel, C.; Ungurianu, A.; Margina, D. Metabolic and Metabolomic Insights Regarding the Omega-3 PUFAs Intake in Type 1 Diabetes Mellitus. *Front. Mol. Biosci.* 2021, *8*, 783065. [CrossRef] [PubMed]
- Margina, D.; Ilie, M.; Gradinaru, D. Quercetin and epigallocatechin gallate induce in vitro a dose-dependent stiffening and hyperpolarizing effect on the cell membrane of human mononuclear blood cells. *Int. J. Mol. Sci.* 2012, *13*, 4839–4859. [CrossRef] [PubMed]
- Ungurianu, A.; Zanfirescu, A.; Margina, D. Regulation of Gene Expression through Food-Curcumin as a Sirtuin Activity Modulator. *Plants* 2022, 11, 1741. [CrossRef] [PubMed]
- 15. Ungurianu, A.; Zanfirescu, A.; Margina, D. Sirtuins, resveratrol and the intertwining cellular pathways connecting them. *Ageing Res. Rev.* **2023**, *88*, 101936. [CrossRef]

- 16. Ungurianu, A.; Zanfirescu, A.; Nitulescu, G.; Margina, D. Vitamin E beyond Its Antioxidant Label. *Antioxidants* **2021**, *10*, 634. [CrossRef]
- Nicolae, A.C.; Dumitrescu, I.-B.; Diaconu, C.C.; Ritivoiu, M.E.; Sirbu, C.A.; Drăgoi, C.M. Chronotherapy Advances in the Management of Chronic Neurological and Cardiovascular Diseases: Complex Interactions of Circadian Rhythm Environmental Inputs, Nutrition and Drug Administration and Their Impact on Human Health. In *Circadian Rhythm—New Insights into Physiological and Pathological Implications*; IntechOpen: London, UK, 2022.
- Ooi, T.; Meramat, A.; Rajab, N.; Shahar, S.; Sharif, R. Antioxidant Potential, DNA Damage, Inflammation, Glycemic Control and Lipid Metabolism Alteration: A Mediation Analysis of Islamic Sunnah Intermittent Fasting on Cognitive Function among Older Adults with Mild Cognitive Impairment. J. Nutr. Health Aging 2022, 26, 272–281. [CrossRef]
- 19. Zairi, I.; Bejar, M.A.; Mrad, I.B.; Mzoughi, K.; Kraiem, S. Effect of intermittent fasting and chronotherapy on blood pressure control in hypertensive patients during Ramadan. *Arter. Hypertens.* 2022, *26*, 67–72. [CrossRef]
- 20. Ezzati, A.; Rosenkranz, S.K.; Horne, B.D. Importance of Intermittent Fasting Regimens and Selection of Adequate Therapy on Inflammation and Oxidative Stress in SARS-CoV-2 Infection. *Nutrients* **2022**, *14*, 4299. [CrossRef]
- Al-Rawi, N.; Madkour, M.; Jahrami, H.; Salahat, D.; Alhasan, F.; BaHammam, A.; Al-Islam Faris, M.e. Effect of diurnal intermittent fasting during Ramadan on ghrelin, leptin, melatonin, and cortisol levels among overweight and obese subjects: A prospective observational study. *PLoS ONE* 2020, 15, e0237922. [CrossRef]
- 22. Gaeini, Z.; Mirmiran, P.; Bahadoran, Z. Effects of Ramadan intermittent fasting on leptin and adiponectin: A systematic review and meta-analysis. *Hormones* **2021**, *20*, 237–246. [CrossRef] [PubMed]
- Drăgoi, C.M.; Mitrea, N.; Arsene, A.L.; Nicolae, A.C.; Ilie, M. In vitro effects of some bio-indoles on the transmembrane potential of Jurkat E6. 1 limphoblasts. *Farmácia* 2012, 60, 240–248.
- 24. Drăgoi, C.M.; Mitrea, N.; Arsene, A.L.; Ilie, M.; Nicolae, A.C. Jurkat E6. 1 cell line studies regarding the effects of some bio-indoles on the membrane fluidity. *Farmácia* 2012, *60*, 13–20.
- Frank, J.; Gupta, A.; Osadchiy, V.; Mayer, E. Brain–Gut–Microbiome Interactions and Intermittent Fasting in Obesity. *Nutrients* 2021, 13, 584. [CrossRef] [PubMed]
- 26. Mindikoglu, A.L.; Abdulsada, M.M.; Jain, A.; Choi, J.M.; Jalal, P.K.; Devaraj, S.; Mezzari, M.P.; Petrosino, J.F.; Opekun, A.R.; Jung, S.Y. Intermittent fasting from dawn to sunset for 30 consecutive days is associated with anticancer proteomic signature and upregulates key regulatory proteins of glucose and lipid metabolism, circadian clock, DNA repair, cytoskeleton remodeling, immune system and cognitive function in healthy subjects. J. Proteom. 2020, 217, 103645.
- 27. Drăgoi, C.; Nicolae, A.C.; Dumitrescu, I.-B.; Popa, D.E.; Ritivoiu, M.; Arsene, A.L. Dna targeting as a molecular mechanism underlying endogenous indoles biological effects. *Farmacia* **2019**, *67*, 367–377. [CrossRef]
- Drăgoi, C.; Moroşan, E.; Dumitrescu, I.-B.; Nicolae, A.C.; Arsene, A.L.; Drăgănescu, D.; Lupuliasa, D.; Ioniță, A.C.; Stoian, A.P.; Nicolae, C. Insights into chrononutrition: The innermost interplay amongst nutrition, metabolism and the circadian clock, in the context of epigenetic reprogramming. *Farmacia* 2019, 67, 557–571. [CrossRef]
- 29. Chawla, S.; Beretoulis, S.; Deere, A.; Radenkovic, D. The window matters: A systematic review of time restricted eating strategies in relation to cortisol and melatonin secretion. *Nutrients* **2021**, *13*, 2525. [CrossRef]
- Kim, B.H.; Joo, Y.; Kim, M.-S.; Choe, H.K.; Tong, Q.; Kwon, O. Effects of intermittent fasting on the circulating levels and circadian rhythms of hormones. *Endocrinol. Metab.* 2021, *36*, 745–756. [CrossRef]

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