Review Articles

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Intermittent fasting and its influence on health

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Abstract

Food addiction is today the major cause of disease and death in our society and other economically developed countries. Hypothetically, this problem could be solved by simply convey the consequences of overeating to professionals and public. In reality though, it has been greatly difficult to successfully execute prolonged dietary restriction regimens. In context of the non-ability of many people to reduce their food intake, research pursuit are in progression to identify ways to alternatively reduce food intake or imitating the beneficial effects of dietary restriction using medical products, dietary supplements and gene therapies. Although all cells in the body require energy to last and perform efficiently, excessive calorie intake over long period of time can modify cell function and promote susceptibility to disease. In this review article we describe evidence suggesting that intermittent fasting (IF), can prolong the health through multiple interactive pathways and molecular mechanisms, all of which help cells cope with stress and resist disease. A better understanding of the impact of IF on the health will likely lead to novel approaches for preventing and treating numerous health disorders.

Keywords: *Dietary restriction, health, aging, animal study, intermittent fasting, overweight*

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INTRODUCTION

Throughout history, number of societies have understand the positive effects on health and general wellbeing of restricting food intake for certain periods of time, either of religious reasons or when food was scarce. Number of recognized scientific studies in the past [1,2,3,4] pointing to restricted diets and their ability to extend life-span. In this review we will attempt to indicate how, with dietary alteration, not only life-span can be extended but also potentially, health-span, that is the time of our lives in which we have a disease-pathology free disposition. In that context we shall as well investigate through which molecular mechanisms the benefits, on the whole organism, of dietary intake modification are derived. Variations of this basic dietary regime, now as caloric restriction (CR), are the most effective way of extending the life-span of mammals without genetically altering them [5]. More recently, another variation, intermittent fasting (IF) or every other day feeding (EODF), has also been shown to extend life-span and have beneficial health effects [6]. The amount by which life-span is extended has been shown to increase progressively as caloric intake is reduced. The time of onset of the dietary restriction (e.g. pre-or post-pubertal) and the duration of the IF regime also determine the amount by which life-span is extended. Research efforts on treating diseases have rapidly expanded in the past decade and those efforts have led to many promising therapeutic interventions to increase both health-span and lifespan. Many people live for eight or more decades and enjoy a well-functioning body through their life span. We therefore know that the human body is capable of aging successfully. We are now at a stage where our knowledge of both genetic and environment factors which have been linked to unsuccessful aging, and their cellular and molecular consequences, can be utilized to provide the general population with advice on aging successfully. In this review, we will discuss IF, dietary strategy, which could potentially be used to mediate successful angina and forestall the onset of number of health disorders.

Rationale behind intermittent fasting

Although biochemical energy production is required to sustain cell survival rate and functions, excessive energy production may cause cells to become impair, and, therefore susceptible to disease. When food supplies are scarce, the cells of organisms are faced with energetic stress that may induce changes that result in adaptive alteration in cellular metabolism and the increased ability of the organism to resist stress [7].

Number of studies [1,8,9] explore the health benefits of IF, which is not a diet, but a more of dieting pattern. Simply, conscious decision to skip certain meals. IF is more about cutting way back on calories for short time periods. That affects hunger and cravings over time. As the body adjusts, it is become satisfied more easily with smaller portions. Moreover, if eating healthier throughout the process, it also reduce craving for unhealthy foods. Intermittent fasting is an umbrella term that covers an array of different fasting schedules. In general, it involves cutting calories in whole or in part, either a couple of days per week, every other day, or even daily. That embraces restricting daily eating to an eating window of 6-8 hours. Compliance is a critical factor in any of these approaches and it seems this is one of the easiest intermittent fasting schedules to implement and maintain, especially once our body has shifted over to burning fat instead of sugar as its primary fuel.

According [10,11,12] on intermittent fasting 90% of the weight we lose is body fat, with only 10% being lean body mass. Be physically active throughout the day and consuming an appropriate amount of high quality protein will help minimize loss of muscle mass [13,14] claim, that splitting the 500 calorie meal up into multiple smaller meals throughout the day was not as successful as eating just one meal, once a day. The rationale behind, when eating tiny amounts

of food multiple times a day, we are far more inclined to want more, so the craving dramatically increases. When IF is combined with exercise in a fasted state, the positive benefits are magnified even further [15]. Exercising on an empty stomach has been shown to have a number of health and fitness benefits as the combination of fasting and exercising maximizes the impact of cellular factors and catalysts that force the breakdown of fat and glycogen for energy, effectively forcing our body to burn fat without sacrificing muscle mass [13].

Intermittent fasting health benefits

Among the major effects of IF relevant to aging and diseases are changes in levels of insulin-like growth factor 1 (IGF-1), insulin like growth factor binding protein 1 (IGFBP1), glucose and insulin [16,17]. IF enhances insulin sensitivity of muscle and liver cells, and alternates IGF-1 production [18,19] study confirmed earlier reports of a reversal of type 2 diabetes through daily calorie restriction, with improvement of pancreatic function and a reduction of occult triglyceride deposition. IF modifies brain neurochemistry and neuronal network activity in ways that optimize brain function and peripheral energy metabolism. Four brain regions that are particularly important in adaptive responses to IF include the hippocampus (cognitive processing), striatum (control of body movements), hypothalamus (control of food intake and body temperature) and brainstem (control of cardiovascular and digestive systems). Data from the animal studies show that neurons in the brain of rats and mice maintained on IF regiment exhibit increased resistance to oxidative, metabolic and excitotoxic insults [20, 21].The neuroprotective mechanism of IF is not fully understand, but it has been reported [22] that IF induces the production of brain-derived neurotrophic factor (BDNF) which was associated with increased hippocampal neurogenesis in rats and mice. This effect consequently promotes the growth and maintenance of dendrites and synapses, and also enhances the production and survival of new neurons from neural stem cells. [5, 8, 23]. IF is known to result in an increased production of ketone bodies, e.g. β-hydroxybutyrate, which can be used by the organism as an energy source in the face of limited glucose availability [24]. This shift to ketogenesis may play a direct role in the cytoprotective effects of IF, because it has been reported that rats fed a ketogenic diet exhibit increased resistance to seizures [25]. Caloric restriction studies have shown improvements in circulating triglycerides concentration, improved blood pressure, and reduced carotid intima-media thickness [26] claim that the energy-restricted diet offered the most positive alteration of lipid profiles through favorable changes in HDL:LDL ratios. Furthermore, improvements in physiological cardiovascular parameters that are associated with IF and survival from myocardial ischemia through pro-angiogenic, anti-apoptotic and anti-remodelling effects [8,19]. Dietary restriction has been shown to decreased infarct size, and increased stress resistance [27]. In above mention [28] allege that, the length of dietary restriction is critical to get beneficial or adverse effects of the restriction.

We recognize health benefits of clean colon and its influence on (immune system, auto-toxemia, clogged colon, constipation, diverticulitis, cancer, chronic fatigue, chrohn's disease). Intermittent fasting increases efficiency of bowel movement, assimilation and absorption that cause many diseases [29]. Fasting has the potential for applications in both cancer prevention and treatment. IF effect on reducing IGF-1, insulin and glucose levels, and increasing IGFBP1 and ketone body levels could generate a protective environment that reduces DNA damage and carcinogenesis. Although depth of understanding of its mechanism is limited, fasting is expected to have cancer preventive effects as indicated by some studies [30, 31]. Thus, fasting may protect from cancer by reducing cellular and DNA damage but also by enhancing the death of pre-cancerous cells.

Obesity comprises multiple genetic, metabolic and behavioral abnormalities that complicate treatment. IF fasting is known to be useful in the treatment of intractable obesity [32] and morbidly in obese individuals [33]. Original treatment regimens were based upon intermittent starving as opposed to restricting calories a harsh regime that must have challenged adherence. Despite the seemingly strict nature of the fasting days IF has a generally good adherence record and can cause significant reductions in body weight in individuals with obesity. Day et al., [34,35] suggesting that IF is a clinically relevant therapeutic approach, therefore offers the potential to improve weight loss.

Table 1. Summarized physiological response to dietary restriction in animal and human sample

Limit inflammation; reduce oxidative stress and cellular damage
Improve circulating glucose
Reduce blood pressure
Alteration in IGF-1 levels
No change in β-hydroxybutyrate
Decrease body temperature
Improve metabolic efficiency and body composition, including significant reduction in body weight in obese individuals
Reduce LDL and total cholesterol levels
Prevent or reverse type 2 diabetes, as well as slow its progression
Improve immune function, and shift stem cells from a dormant state to state of self-renewal
Improve pancreatic function
Improve insulin and leptin levels and insulin/leptin sensitivity
Normalize ghrelin levels
Reproduce some of the cardiovascular benefits associated with physical exercise
Protect against cardiovascular disease
Modulate levels of visceral fat
Boost mitochondrial energy efficiency and protects striatal neurons against mitochondrial toxicity in rat
Helping eliminate sugar cravings as the body adapts to burning fat instead of sugar in rat
Promote human growth hormone production (HGH)
Lower triglyceride levels
Elevate production of brain derived neurotropic factor (BDNF), stimulates neurogenesis and triggering brain chemicals that protect against changes associated with Alzheimer's and Parkinson's disease
Enhance dopamine overflow in striatum in rat
Attenuates age related decrease in cardiac synaptic terminal norepinephrine uptake in rat
Attenuates age related loss of cortical dendritic spines in rat
Protects against seizure-induced hippocampal damage, memory impairment and focal ischemic brain injury in rat
Enhanced learning and motor function in aged mouse
Slow age related loss of spiral ganglion neurons in mouse
Protect thalamic neurons against thiamine deficiency in rat and enhance hippocampal neurogenesis in rat
Amplify changes in energy related genes in mouse
Enhance changes in plasticity related genes in mouse

CONCLUSION

We are approaching a comprehensive understanding of the various molecular mechanisms by which changes in caloric intake can be transferred to an enhanced survival of cells during the various stages in life. However the question remains how does IF will affect us in long term. There are several theories about why fasting provides physiological benefits the one of hypothesis stating that during the fasting period, cells are under a mild stress and they respond to the stress adaptively by enhancing their ability to cope with stress and, therefore, to resist disease. There is considerable similarity between how cells respond to the stress of exercise and how cells respond to intermittent fasting. Possibly as long as we give our body time to recover, it will become more resilient. But perhaps it isn't so much the fasting that produces health benefits, per se, as the resulting overall reduction in calorie intake, that allow the body to keep in the homeostatic balance. Based on the existing evidence from animal and human studies described, we conclude that there is great potential for lifestyle that incorporate periodic or permanent intermittent fasting schedule during adult life and old age to promote optimal health and reduce the risk of diseases. IF can help us how to eat well (a well-balanced way of eating) in addition facilitate incorporation of physical activity into our daily routine. In number of studies, implementation of the IF dietary regime results in an approximately 20-30% reduction in caloric intake over time [36]. We have scientific evidence that maximum lifespan of a range of organisms, animals and humans can be increased by up to 40-50% simply by reducing their calories intake [37,38]. When extrapolated to humans, the data obtained from animal studies described above suggest that a daily calorie intake in the range of 1800–2200 calories for moderately active adults may dramatically reduce the risk of number of diseases and age-related disorders. Lindstrom, Uusitupa [39], indicate that modest weight reduction (>5% of body weight) reduces the incidence and progression of many biomarkers of disease. Foregoing one or two meals a day might be an alternative to reducing meal size. Along eliminating breakfast and not thinking about food until 12pm each day has allowed us to reduce the number of decisions we make in the morning, thus reducing decision fatigue and increasing the willpower we have for the rest of the day. The available data suggest that the nervous system is highly vulnerable to excessive calorie intake, just as is the case with the cardiovascular systems and most other organ systems. Go on to say intermittent fasting could be tailored for specific diseases as stand-alone or adjunct therapies. Results of initial trials of IF (fasting 2 days per week or every other day) in human subjects suggest that there is a critical transition period of 3 – 6 weeks during which time the brain and body adapt to the new eating pattern and mood is enhanced [20,40].

However the main factor that may negate the widespread implementation of IF as an effective therapeutic approach is potentially the modern Western lifestyle of near constant work and persistently high stress levels in favor of constant mental and limited physical activity. In that respect we must not discount the psychological effects of food intake in higher, more introspective, organism such as humans. We possess an almost unique emotional connection with a significant variety of responses to foodstuffs. Therefore removal of this psychological backing, during an IF regime may altogether or partially counteract the physiological benefits of these paradigms. Last but not the least we have to consider that intermittent fasting is not recommended for pregnant women, women who are breast feeding, individuals who need to closely regulate their blood sugar. Also individuals with excessive loss of body fat and followed decline in sex steroids that can lead to menstrual irregularities, amenorrhea, bone thinning and the development of osteoporosis in females. In addition, there has not been research on participants who are underweight, very old, or very young (<18 yrs. old) and these populations could be potentially at higher risk for experiencing negative consequences of intermittent fasting [5].

At the conclusion we should be aware that clinical research studies of intermittent fasting regiment with robust designs and high levels of clinical evidence are sparse in the literature. Moreover we have not much longitudinal studies on IF. Some randomized controlled trials and observational clinical outcomes studies support the existence of a health benefit from fasting, however, substantial further research in humans is needed before the use of fasting as a health intervention can be fully recommended. Nevertheless, the benefits of intermittent fasting do sound incredibly powerful and convincing that is supported by personal experience of the authors of this review. But still there are quite lot of unknown answers that need to be resolved in order to better understand underlying mechanism that are proving to be very complex.

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