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What and When to Eat? Role of Chrono Nutrition in Disease Prevention

SK Verma[1]* and Riya Pareek[2]

[1]*Professor Emeritus, Department of Medicine, Pacific Medical College and Hospital, Udaipur, Rajasthan, India*

[2]*Graduate Student in Public Health, Schulich School of Medicine & Dentistry, University of Western Ontario*

***Corresponding Author:** Dr. SK Verma, Professor Emeritus, Department of Medicine, Pacific Medical College & Hospital, Udaipur, Rajasthan, India.

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Abstract

Human biology is extremely complex. It is in fact a real reflection of vast Cosmic Mind`s creation. Every bodily system is running cyclically and orderly like a systemic bodily clock. This biological clock is the human circadian system which has a period of 24 hours. Recent studies on circadian rhythm and on the consequences of its disruption- "Chronodisruption" have been expanded to a great extent. Modern life-style and environmental factors can disrupt the circadian system of the body and may lead to adverse effects on individual`s health. Furthermore, complex reciprocal relationship between metabolism and the circadian system of the body have been demonstrated. Current research evidences also provide the impact of the interaction between the circadian system and nutrition and the way this link can influence the epigenome and microbiome. Based on this whole concept, it is possible to develop nutritional strategies to manage circadian-aligned feeding that is what and when to eat in order to reduce the prevalence and burden of chronic diseases.

Keywords: Chronodisruption; Epigenetic; Nutrigenetics; Nutrimicromics

Introduction

The term circadian rhythm has come from *circa* -around and *dies* -one day. These rhythms occur at central and local levels in several peripheral tissues and regulate many behavioral and biochemical processes through day/night cycle [1]. In addition to these, the core circadian clock machinery can be modulated by energy/nutrient input, pointing towards the role of energy metabolism [2, 3]. In this regard, a reciprocal and complex interconnectivity between the circadian system and metabolism has been identified. Circadian desynchrony typical of modern living and triggered by several chronodysruptions such as night shift work, stress, sleep disruption, social jet lag etc. can have adverse effect on human health, resulting in an increased risk of metabolic diseases. It has also been demonstrated that diet is one of the synchronizers of the human circadian clock mechanisms and therefore abnormal feeding times can lead to unhealthy consequences [4].

Looking from the point of nutrigenetics, several genetic variants in circadian-related genes, interacting with dietary intakes and obesogenic behaviors, can influence the individual response to diet; stressing that chronobiology should be taken into consideration when thinking in nutritional practices [5-7].

Epigenomes and gut microbiomas also show diurnal rhythms. Epigenome is the collection of all the epigenetic markers on the DNA in a single cell. The epigenetic mechanisms also play an important role in the regulation of the molecular clock machinery transcription, and clock -controlled genes, gut microbiota and microbial metabolism are known to mediate the effects of disruptions of circadian rhythms on human health. New opportunities have risen from recent findings on a dynamic crosstalk among diet-biological rhythm-omics [8, 9].

The effect of dietary components on human health outcomes has been widely explored. However, the complex relationship between meal timings and the circadian machinery is still undergoing investigations. Interestingly, chrono-nutrition has emerged as a new area of research which is involved in studying the impact of the timing of eating on the well-being of an organism. The modification of the cycle between periods of eating and fasting has been associated with predisposition to nutrition-related diseases including obesity, type 2 diabetes and cardiovascular disease [4].

Circadian Rhythms

The circadian system is composed of a set of interconnected clock oscillators which are located in the suprachiasmatic nuclei (SCN) of the hypothalamus and in some metabolically active peripheral organs. This system regulates the physiological daily rhythms of sleep/wake, fasting/feeding and catabolic/anabolic cycles, body temperature and endocrine functions [10].

Several factors are expressed are expressed and secreted following circadian stimuli such as glucose tolerance peaks during daylight and is lower the night, melatonin drops at 7.00 and rises at 20.00, cortisol rises at 8.00, sleep deepens at 1.00 and body temperature rises at 3.00 [11].

Chronotype

Circadian system is entrained to an external light-dark cycle with a period of 24 hours, even then there are interindividual circadian preferences influencing behavior patterns, defined as chronotypes. Chronotype is a biological characteristic leading to interindividual differences in the circadian phase relative to the light-dark cycle.

Categories of chronotypes [12]

(i) "Morning" types.
(ii) "Evening" types.
(iii) "Intermediate" types.

Morning types prefer activities at the beginning of the day and evening types prefer main activities in the late afternoon or evening [13]. The intermediate chronotype occupies an intermediate position between the morning and evening types. Several studies have described the different features between extreme groups in circadian rhythmicity [13, 14].

Morning chronotype verses evening chronotype

Morning chronotypes are characterized by a phase advance in the peak of body temperature and alertness in the sleep-wake cycle, and in the performance compared with evening types [15].

Evening chronotype is associated with irregular eating and meal skipping especially breakfast skipping as well as being related to a lower intake of fruits and vegetables and a higher intake of energy drinks and fat, suggesting long-term consequences on cardio metabolic health [16]. The evening chronotypes therefore have been correlated with the risk of a variety of conditions including metabolic dysfunction, diabetes, gastrointestinal disorders, psychiatric symptoms and some cardiovascular risk factors such as higher rate of smoking and obesity when compared with the morning chronotype [13, 17].

Evening chronotypes have also been associated with poor glycemic control in type 2 diabetes patients [18] as well as increased risk of all-cause mortality over 6.5 years [17]. These data suggest that chronotype may be predictive of disease out-comes, highlighting the role of circadian system in metabolic regulation. Eating schedule, in fact, is a key to reduce the risk of diabetes. A recent prospective cohort study published online in Diabetes Care has shown that consuming foods with a more glycemic load and having more calories in the late morning is associated with reduced risk of developing type 2 diabetes.

Circadian misalignment in adolescence

Circadian misalignment and metabolic disease in adolescence, which is considered a vulnerable period for obesity, have also been investigated. It has been reported that adolescents sleeping less than eight hours consumed a higher proportion of calories from fats compared to those with a nocturnal sleep of more than eight hours [19]. These young adolescents are at risk of increased BMI and poorer dietary behaviors with a higher frequency of consuming unhealthy snacks, night time caffeine consumption, and inadequate daily intake of fruits and vegetables [20].

Chronodisruptions

Past few years have witnessed growing amount of attention on the role of circadian disruption in the susceptibility to non-communicable diseases. Chronodisruption as defined by Erren et al. is a "disturbance of the circadian organization of physiology, endocrinology, metabolism, and behavior" [21]. Escalating chronodisruption is resulting from the adaptation of modern life styles, especially including excessive energy consumption, irregular times of food consumption, sleep disturbances a night shift work [4].

Researchers have reported that prolonged short sleep durations and /or poor sleep quality with circadian misalignment are correlated with metabolic dysfunctions, including obesity, type 2 diabetes and hypertension [22-24] as well as with decreased leptin, increased appetite and insulin resistance [24, 25].

Chrono-Nutrition

The concept of chrono-nutrition was developed by Alain Delabos in 1986 [26]. It is in fact a nutritional regimen that follows our biological clock, which in turn is marked by changes in metabolism that occur throughout the day. Late meal timings and irregular eating are the factors which are not in line with biological clock and therefore associated with increased adiposity, T2DM and cardio-metabolic risk factors [27, 28]. The concept of chrono-nutrition is based on three different dimensions of eating behavior including timing, frequency and regularity [29-31].

Analysis of modern lifestyle habits reveal that this is characterized by being more often in a postprandial state with exposure to unhealthy diets, prolonged sitting times (sedentary habitus), irregular eating, skipping meals, chronic psychological stress, emotional eating and food consumption late at night [32, 33]. This triggers a vicious cycle where obesity -causing unhealthy lifestyle results in disrupted circadian rhythms, which in turn leads to obesity.

Several studies have shown a beneficial effect of dietary regimens which are based on an availability of food only at discrete windows of time within the daily cycle [11]. These strategies can delay and often reverse the symptoms associated with metabolic disorders, reducing insulin resistance and increasing glucose tolerance [34-37].

Clock Genes Variants

The effect of chronotype combined with the genotypes of several clock genes through eating time has also been investigated. Several single nucleotide polymorphisms (SNPs) in circadian-related genes have been associated with the susceptibility to obesity, cardiovascular disease and metabolic syndrome, as well as gene-diet interactions being described for some of these genetic variants [38-40].

Nutrigenetics

Nutrigenetic, a branch of nutritional genomics, focuses on the role of genetic susceptibility to diseases as well as on the link between genetic variants and response to diet [41, 41]. It is noteworthy that by changing our eating habits it is possible to reduce or even eliminate the deleterious effect induced by a specific allele risk. The interplay between gene variants in circadian machinery and diet may help to design effective, personalized nutritional strategies based on the identification of specific allele carriers [4].

Epigenetic alterations

DNA methylation, micro-RNAs and histone modifications are the epigenetic mechanisms, that can regulate gene expression and control many physiological processes [41-43]. These epigenetic alterations are considered as potential contributors to the development of health and disease [44]. Different dietary patterns, lifestyle alterations, and environmental insults have potential to modulate the DNA methylation and can influence circadian rhythm [45].

It has been suggested that for future research, nutrimiromics, the science that studies the influence of the diet on the modification of gene expression due to micro RNAs and chronobiology should be merged to evaluate the circadian-related micro RNAs and their modulation by dietary compounds in order to understand if this relationship may affect the risk of chronic diseases [4].

Gut Microbiome and circadian rhythm

Gut microbiome (GM) is a complex and dynamic population of microorganisms living in the human gut. It is considered as an auxiliary metabolic organ [46, 47]. The GM plays a crucial role in the preservation of mucosal integrity of the intestinal epithelial barrier and in the digestion, metabolism as well as in regulation oh many hormones levels [48]. The main bacterial phyla in healthy individuals are Bacteroidetes and Firmicutes [49]. They have symbiotic relationship with the host. The bacterial rhythms also have a period of 24 hours with variation of bacteria during light and dark periods regulated by melatonin and temperature [50, 51].

There are many factors such as dietary regimen, food additives, pre and probiotic supplements, food processing and cooking methods that can contribute to shaping the GM [52, 53]. High-fat diet affects the composition of the GM. Interestingly, it has also been observed that the establishment of a persons GM, which are essential for metabolic processes and immune function is influenced not only by the factors described above but also on the mode of delivery [54]. Infants born via cesarian section, do not pass through the birth canal and are , therefore, not exposed to maternal microbiota. As a result, their initial GM composition may differ from those born vaginally. GM plays an important role in immune system development and oveall health [55]. Data are emerging that demonstrate that the disruption of the circadian system from the host can influence the composition of GM. Not only this, the gut microbial community can regulate host circadian and metabolic homeostasis and also exhibit diurnal oscillations [56, 57].

It is obvious that nutrients and bioactive compounds of food can modify gut-microbial composition and functions. Several recent strategies based on manipulation of GM may at least partially consolidate host circadian rhythms. Plant-food-derived fiber and polyphenols can generate bioactive short chain fatty acids, vitamins, bioamines might help in resynchronization of circadian rhythms, mitigating some of the modern-life style associated metabolic change [58-60].

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