

COVID-19 PANDEMIC QUARANTINE AND SOCIAL JETLAG

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Covid-19 pandemic forced the governments to choose the policy to the lockdown the gathering centers, including universities and schools to prevent the rapid spread of the disease, forcing millions of people to stay at home for several weeks and even more. Staying in the home for such long periods is associated with a change in the wake/sleep period (a kind of social jet lag) and the resulting alteration in feeding time and type of food. Moreover, the prevalence of anxiety and depression resulted from the reduction in physical activity and bad news also may help to worsen the social jetlag effect on these parts of society. Possible hazardous changes in this factor are reviewed in this study and some suggestions for better management of this condition are also offered. Pubmed, SCOPUS, WOS, and Google Scholar data banks were searched using the following keyword in combination and/or alone: jetlag, social jetlag, Chronobiology, photoperiod, metabolic disease, cardiovascular, sleep/weak period. Longtime lockdown gathering centers are shown to change the photoperiod cycle in people, and it may induce several consequences, including the effects on cognitive brain function, induce mental illness, metabolic syndrome, insulin resistance, mitochondrial aging, and cardiovascular diseases. Considering these facts, it is important to make rehabilitation programs for all the societies' members for post-pandemic time.

Key words: Covid-19, forced lockdown, social jetlag, depression, metabolic disturbances, anxiety, obesity.

Since October 2019, which the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the new SARS Coronavirus, the rate of infection and also total death from this new virus produced a global horror worldwide and forced the governments to make different and difficult decisions about their societies for saving their societies [1, 2]. These decisions, including a lockdown of economic and instructive activities, forced millions of young people to stay at home for several weeks [3]. These decisions were chosen because there were no solutions for disease cure (no vaccine and/or drug for the treatment of the virus), and it was essential for inhibition of rapid disease transmission [4], which was beyond the capacity of health systems to deal with the growing wave of hospital admissions. For several weeks, staying at home can severely shift the weak/sleep duration

in the youth people [5]. The human is considered to be morning and/or evening activity [6, 7], which is shown to be regulated by the clock genes located in the neurons within the suprachiasmatic nucleus in the hypothalamus [8]. Disruption of photoperiod and/or the time of the work (e.g., shift working in the factories), namely classified as jetlag and social jetlag, respectively [9], can lead to a broad spectrum of metabolism malfunction [10], cardiovascular disease [9], and neural disease [5, 11, 12]. Social jetlag is first mentioned by the factory workers whose shift was changed to the evening, and they must work when they were asleep in their everyday life [5]. However, recently the researchers have considered another type of social jetlag in people. They emphasize that weekend holidays and long-term New Year holidays can influence the photoperiod activity of the youth so that they show a shift in their weak/sleep activity

[5]. The Covid-19 lockdown of the universities and schools led to a long-term holiday-like condition of people, which may induce a severe health condition of this part of the population. In this review, first, we show how social jetlag (a direct result of the so-called stay-at-home policy) may act as a stressor to metabolic, cardiovascular, and neuronal disease induction. Second, the possible ways of overcoming this condition are offered.

Methodological aspects

Data Banks. In this review, several data banks were used. Pubmed, SCOPUS, WOS, and Google Scholar were searched using the following keyword (in combination and/or alone): Jetlag, social jetlag, chronobiology, photoper anxiety iod, metabolic disease, cardiovascular, sleep/weak period. In combination, we use the words 'with, and, or'. Also, we use Systematic Review, Meta-Analysis, and Review, for furthering filtering of the data. At last, the time window was years 2000-2021.

Results. A total of 112 review articles were founded after a comprehensive search of the data banks. Among these articles, 43 articles were considering because of fulfilling our inclusion criteria. Moreover, all the articles considering the psychological effects of Covid-19 and Covid-19 signs and symptoms were considered.

The impact of Covid-19 lockdown on circadian rhythm

There are scanty studies concerning the effects of lockdown on change in circadian rhythm and its hazardous effects on metabolic status. However, in one study, Bagci and colleagues (2020) have emphasized that chronic photoperiod change during lockdown may dramatically affect different organs of the fetus body during its development [13]. According to the previous studies, chronic changes during the daytime photoperiod are enhanced by artificial light during nighttime [8]. Change in photoperiod, as indicated by the longtime light exposure which occurred in lockdown during Covid-19, may alter the function of all body organs, according to Bagic et al. [13]. However, several questions are arising in this regard. First, which hormonal changes occurred during the lockdown in response to photoperiod change? Second, how these hormonal changes can affect the body organs such as the heart, lungs, kidneys, and especially the brain? Tired of these alterations remain for a while? Forth, if there may be some epi-

genetic changes at the cellular level? Moreover, stile other questions also may be existing in this regard.

Social jetlag and metabolic disturbance

Data indicated that some metabolic functions, including blood glucose level and insulin secretion from the pancreatic beta cells, are synchronized with variation in plasma melatonin level [14]. In this regard, data indicated that blood glucose level is under the suprachiasmatic nucleus (SCN) in the hypothalamus and the circadian activity of the pancreas, liver, skeletal muscles, and white adipose tissue [13]. According to these data, social jetlag, most prevalent in modern societies on the metabolic malfunction, is mentioned in several articles in the past few years [15]. On the other hand, there is a strong link between metabolic dysfunction and the severity of Covid-19 [16]. This interrelationship indicated that focus on the metabolic disturbance during Covid-19 a lockdown may play a critical role in reducing the Covid-19 side effects on society's health. In this regard, we will focus on the primary metabolic disturbance induced by photoperiod change, including insulin function, glucose metabolism, obesity, and aging due to insulin resistance and glucose metabolism disturbance.

Social jetlag and insulin resistance

Insulin resistance is defined as a reduction of insulin function in the brain and periphery [17]. Insulin resistance may occur when the photoperiod cycle is removed by shift working [18] or staying in the artificial light, especially at home during nighttime, dramatically changing the normal light/dark cycle [13]. On the other hand, it is shown that increasing the melatonin hormone during the dark phase of the photoperiod cycle has a modulation influence on insulin receptor sensitivity in different organs [19]. According to these data, it is not surprising that changes in photoperiod can influence the hormonal status and induce several metabolic disturbances, including insulin resistance [15]. However, insulin resistance can induce several diseases such as brain cognition deficit, eating behavior and obesity, and anxiety and depression [17]. It must be noticed that the psychological problems associated with Covid-19 lockdown are one of the most frequent signs in home residents [11,20]. In this regard, it is postulated that food composition and amount, physical activity, and fin control of sleep/wake duration during lockdown may help for the metabolic disturbance induced by photoperiod changes [20].

Social jetlag and glucose metabolism

As mentioned above, the change in the photoperiod cycle in the Covid-19 lockdown may influence the melatonin plasma level and induce insulin resistance [17]. One of the most critical signs of insulin resistance is glucose intolerance, defined as the height of plasma glucose level after a glucose tolerance test. Cellular and molecular details of glucose intolerance are suggested elsewhere [21]. In this regard, it is essential to be noticed that glucose entered into the target cells (skeletal muscle cells, liver cells, and white adipose tissue cells) via an insulin receptor-mediated mechanism [8]. Furthermore, as mentioned above, the insulin receptors and insulin function are modulated by the high melatonin level during the dark phase of the photoperiod [19]. Therefore, as predicted, shortening the dark phase of the photoperiod during Covid-19 lockdown may induce and/or enhance the modulation effect of melatonin on insulin function and, at last, induces insulin resistance and glucose intolerance [22].

Social jetlag and obesity

One of the consequences of insulin resistance and glucose intolerance is obesity [22]. Abdominal fat, which is defined as glucose and lipid abnormal metabolism, is the main sign of obesity [23]. This sign is shown to be frequently in the shift workers and other personnel who have to work in the dark phase of the photoperiod [24]. However, no study focuses on the effects of social jetlag induced by lockdown during the Covid-19 pandemic [12]. In other words, because of the importance of obesity as the resulted sign of insulin resistance and glucose intolerance [18], on one hand, and the gap in our knowledge in this regard, on the other hand, the studies dealing with the effects of Covid-19 lockdown on obesity should come into focus as soon as possible [25].

Social jetlag and aging

Aging is considered the malfunction of the hormonal systems, especially those dealing with metabolism [15, 26]. According to the new hypothesis, aging is a reduction in the ability of the cell mitochondria for ATP production because of the damaging effects of stress hormones on its DNA and reduction of mitochondrial DNA for reproduction [27, 28]. As a result, the electron chain system within the mitochondrial wall became dam-

aged [29]. The aged mitochondria cannot produce enough ATP needed for all cellular functions, including protein synthesis, gene duplication, gene and protein expression, and cell regeneration. The result of these failures is defined as aging. As mentioned in the above parts in this section, disrupted photoperiod [30], which is the character of the social jetlag including the Covid-19 lockdown, can increase the hypothalamus-pituitary-adrenal axis (HPA axis) and increase the cortisol plasma level in the stress suffered victims [31]. One of the essential effects of stress-induced aging is that those parts of the brain involved in cognitive function, including the hippocampus, the amygdala, and the frontal cortex, exhibit morphological and functional alterations [32]. The hazardous problem that can occur during the Covid-19 lockdown photoperiod change on aging may also have a high value for the governors [33].

Social jetlag and brain function

The brain is the main organ for the response to stress [34], and chronic stress can damage the brain structures, including the hippocampus and frontal cortex [32]. Since the abnormal change in the photoperiod cycle is considered a negative stressor [35], it is not out of mind that abnormal photoperiod change may affect brain function, especially those categorized as cognitive functions. Several data exist which indicated the importance of the photoperiod phenotype of brain function (for rev see: Correa, et al. 2020 [36]). In addition, it is shown that photoperiod change can induce insulin resistance in the brain [10, 30, 37]. Insulin resistance in the brain is considered one of the leading causes of cognitive deficit [38]. The central brain region which is thought to be responsible for cognitive dysfunction in response to stress is the hippocampus [39, 40].

Although photoperiod cycle change can induce cognitive function deficit, it is also essential that photoperiod change can induce hippocampal shrinkage [41, 42]. Hippocampal shrinkage is also the main basis for several mental diseases, including anxiety and depression [43, 44]. According to previous studies, photoperiod cycle change can induce anxiety and depression in young and older people [45, 46]. Because stress disorders may lead to a failure chain that may end with suicide [47], it is also a hazardous problem that must be resolved in the pandemic lockdown. However, it is not clear if photoperiod change induced by Covid-19 lockdown can influence cognitive function or not? Researches

in this area can help the governors to address the hazards of longtime photoperiod cycle change.

Social jetlag and cardiovascular system function

The cardiovascular system is shown to be affected during the photoperiod cycle change [48]. It is now clear that a shift in the photoperiod cycle can interact with hormonal body pattern, increase the glucose plasma level at the time that the body did not need, and increases several adipokines, including leptin and adiponectin, in the plasma that can impair the lipid metabolism and in turn induce dyslipidemia and vascular diseases including coronary artery disease [10, 12, 49, 50]. Moreover, disruption of the light/dark cycle can interact with peripheral and central clock cells and induce cardiac dysfunction and cardiac arrest [9, 29, 51]. The severity of cardiovascular dysfunction is shown in the mortality of cardiac attacks in shift workers [48]. As mentioned in the above sections, there is no study dealing with the effects of photoperiod cycle change resulting from Covid-19 pandemic lockdown on cardiovascular system dysfunction in young people, and it is also among the most important studies that should be done.

Conclusion remarks. Jetlag and social jetlag are associated with several hazardous consequences on societies [26], which are well discussed in huge research and review articles. For example, the incidence of Covid-19 and its mortality and morbidity has forced governments worldwide to lockdown the gathering centers, including the schools and universities, to reduce the social contact and reduce the number of Covid-19 suffered as a result [13, 52]. However, the longtime lockdown is shown to change the photoperiod cycle in people, and it may induce several consequences, including the effects on cognitive brain function, induce mental illness, metabolic syndrome, insulin resistance, mitochondrial aging, and cardiovascular diseases. Considering these facts, it is essential to make rehabilitation programs for all the societies' members, especially the youth and older people, for post-pandemic time. In addition, studies also needed to clarify the impact of Covid-19 lockdown-induced photoperiod cyclical change in healthy people. Thus, it seems that the effects of the holidays caused by the Covid-19 pandemic may lead to metabolic problems and even obesity, which may increase the risk of severe Covid-19 disease if a person becomes infected. To reduce such a problem,

health policy-makers and planners should consider strategies for creating physical activity at home or in the quarantine area, nutrition control programs, and provide programs to regulate the sleep-wake cycle.

Conflict of interest. Authors have completed the Unified Conflicts of Interest form at http://ukr-biochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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ПАНДЕМІЯ COVID-19 ТА СОЦІАЛЬНИЙ ДЖЕТЛАГ

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Пандемія Covid-19 змусила уряди багатьох країн вибрати політику щодо закриття місць колективного перебування людей, зокрема університетів і шкіл, для запобігання поширення хвороби. Це змусило мільйони людей залишатися вдома протягом декількох тижнів і навіть більше. Перебування вдома протягом тривалих періодів часто призводить до збою циклів сну та неспання (свого роду соціальний джетлаг) і пов'язаного з цим зсуву у часі приймання їжі та зміни типу їжі. Крім того, підвищена тривожність і депресія, спричинені зниженням фізичної активності та поганими новинами, також можуть посилити соціальний джетлаг. У цьому дослідженні розглянуто можливі небезпечні наслідки таких змін, а також запропоновані деякі пропозиції щодо ефективнішого управління такою ситуацією. Пошук в базах даних Pubmed, SCOPUS, WOS і Google Scholar проводили за такими ключовими словами: джетлаг, соціальний джетлаг, хронобіологія, фотоперіод, метаболічні та серцево-судинні захворювання, цикл сну/активності. Показано, що тривале закриття місць колективного перебування змінює життєві цикли людей, і це може впливати на когнітивні функції мозку, спричинювати психічні захворювання, метаболічний синдром, резистентність до інсуліну, старіння мітохондрій та серцево-

судинні захворювання. З огляду на ці факти важливо розробити реабілітаційні програми для всіх членів суспільства на постпандемічний період.

Ключові слова: COVID-19, вимушена ізоляція, соціальний джетлаг, депресія, метаболічні порушення, тривога, ожиріння.

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