# Jet Lag and the Biological Clock


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### Abstract

Jet lag is a resulting disorder of flight travel across several time zones. Circadian rhythms, the approximately 24 hour system that our bodies follow, become distorted following such a trip, as the body's internal biological clock has not yet caught up to the current local time zone. Time cues and other external factors are necessary to adjust the clocks and reverse the negative effects of jet lag.


### Introduction

Long flights across several time zones can result in jet lag, similar to what is known as travel fatigue. The effects of this jet lag are caused by the tight space of the aircraft, limit of food options, dehydration from the dry air, as well as climate and lighting changes. The consequences of such jet lag increases with every additional time zone crossed, as the internal body clock is unable to adjust properly. This can result in the inability to sleep at night and improperly timed daily functions. Circadian rhythms, the internal bodily processes that follow an approximately 24 hour biological clock, require an adjustment period to correct the negative effects of jet lag. Natural clocks follow a morning-night schedule which allows a person to function during daytime and reboot at night. Jet lag can cause a disorder in this natural system. Prolonged and repeated travel over time zones have been linked to health problems such as depression, irregular menstrual cycles, diabetes, fluctuating melatonin secretion, as well as other issues. Upon arrival to the new destination, the traveler should attempt to regulate his biological clock to the local time zone. Planning ahead will assist the traveler to maintain a healthy balance of the body's internal functions.. The goal of this paper is to understand what jet lag is, how it occurs, and how the internal biological clock can be adjusted to relieve or avoid the symptoms.

### Methods

Research articles were obtained from the Touro Library database (tourolib.org), which lead the student to various sites including ProQuest, PubMed, among others. The articles were compiled from an assortment of science journals and experimental studies that discussed the definition of jet lag and its symptoms, the explanation of a body clock and its makeup, with testing and trials to prove the connection between the two. Each article was reviewed intensely, and the findings were subsequently arranged into a comprehensive paper in order to fully describe the term jet lag.

### Discussion

Jet lag, also known as circadian dyschronism, is a temporary syndrome characterized by various physiological and psychological effects that occur following flights across several time zones, most likely resulting from circadian misalignment in the body. An assortment of symptoms have been linked to jet lag, including fatigue, coexisting with insomnia, irritability, disorientation, headaches, loss of concentration, gastrointestinal problems, such as: indigestion, loss of appetite, among others. Comparing the studies can be challenging due to the lack of jet lag symptoms. Yet, fatigue, difficulty concentrating, decreased alertness during the day, weakness, and lethargy have been found as consistent effects (Waterhouse et al, 1997).

The word 'circadian' originates in the Latin 'circa dia,' which means 'about a day,' because circadian rhythms do not equal exactly 24 hours, but vary in that range by each organism. These unalterable rhythms are caused by the constant ticking of the body's biological clock in the brain and other organs, and therefore keep many aspects of our body in sync - specifically behavior, metabolism, and physiology (Rosbash, 2003). Jet lag results from these circadian rhythms breaking out of their natural harmony when the body clock is unadjusted from traveling a great distance. Our sleep/wake cycles seem to be the most disturbed by the journey.

Crossing three or more time zones is what generally causes the desynchronization associated with jet lag. The more time zones crossed, the more severe the jet lag will be. Jet lag will not occur from traveling north or south. Interestingly, it will be worse from eastward travel than westward since traveling west extends the day, thereby allowing for easier correction. After a flight east, travelers are not tired during the local nighttime, which is daytime for their unadjusted body clock, but they get tired as the new day dawns, as it is nighttime for their body. After a flight to the west, people are more tired in the new evening at their destination and yet they awaken early. Although this also a challenging transition, the traveler will be able to go about his day and settle in (Waterhouse et al, 2007). In one study, subjects flew between Europe and the United States, over a 6 hour time difference, and those who traveled on a westward flight adjusted back to peak performance in about 2-4 days. Meanwhile, those who traveled eastward required 9 days to recover, because instead of shortening the day by 6 hours, most of the travelers' internal clocks were delayed by 18 hours (Coleman and Kim, 1998).

The body clock is located on the suprachiasmatic nucleus (SCN), which is connected directly to the retina and receives information about light from the eyes, as well as having receptors for melatonin type 2. Without external inputs and rhythmic time prompts, the body clock and its daily rhythms can continue, but with a period not exactly 24 hours, as circadian means about 24 hours. Regardless of the exact amount of time, for the body clock to function properly it must be adjusted to the solar day via recurring signals in the environment, known as zeitgebers - time-givers.

A zeitgeber's effect on the body clock depends on the time at which it presents; a zeitgeber can produce a phase advance, phase delay, or no phase shift. A phase-curve response is the relationship between the time the zeitgeber is presented and the phase shift. The chief zeitgeber is the light-dark cycle and the secretion of melatonin when a person is asleep at night. The product of one's environment and lifestyle, the exogenous component, together with the body clock, the endogenous component, form a healthy rhythm when they are in sync. However, the span of days after a time zone transition causes the rhythm to falter, because while the exogenous component has changed, the endogenous component has not yet caught up to it. Theoretical statistics evaluate rhythms before and after a time zone transition, showing the loss of synchronization. The external light is being sent through the retina and is telling the body that it is daytime, but the internal body clock still feels as if it is meant to be nighttime, and therefore jet lag reigns. Table 1 advises when exposure or avoidance of bright light will assist in correcting the body clock upon arrival at the new time zone. It is based on the observation that light in the morning of body time will advance the clock, and in the evening of body time will delay it. These times may not coincide with actual day or night, and so wearing sunglasses or seeking a light box that mimics the sun may be necessary to keep the biological clock in its sync (Waterhouse et al, 1997).

*Table 1. Use of bright light to adjust body clock on first day after time zone transition:*

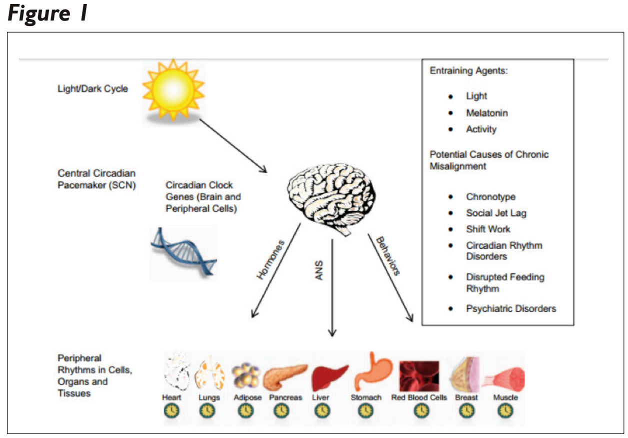
| | Bad local times for exposure to bright light | Good local times for exposure to bright light |
|---|---|---|
| Time zones to the west | | |
| 4 h | 0100-0700* (1:00 - 7:00 am) | 1800-2400+ (6:00 pm - 12:00 am) |
| 8 h | 2100-0300* (9:00 pm - 3:00 am) | 1400-2000+ (2:00 - 8:00 pm) |
| 12 h | 1700-2300* (5:00 - 11:00 pm) | 1000-1600+ (10:00 am - 4:00 pm) |
| Time zones to the east | | |
| 4 h | 0200-0800+ (2:00 - 8:00 am) | 0900-1500* (9:00 am - 3:00 pm) |
| 8 h | 0600-1200+(6:00 am - 12:00 pm) | 1300-1900* (1:00 - 7:00 pm) |
| 12 h | @ | @ |

**Will advance to body clock. +Will delay the body clock.*
*@Treat as 12-14 h to the west, since the body clock adjusts to delays more easily than to advances. Source: Waterhouse et al, 1997*

This concept of an endogenous clock following circadian rhythms has been around for centuries. A French astronomer named Jean Jacques d'Ortous de Mairan conducted a simple experiment on a mimosa plant, which he knew to be a heliotrope. He saw that it was also responsive to the sun by raising its leaves during the day and drooping upon the fall of darkness. De Mairan put a mimosa plant into a cupboard to observe its reactions when kept in the dark. He noticed that the leaves still continued to open and close rhythmically, seemingly by its own internal interpretation of night and day. His clear-cut finding from this was that the plant had an endogenous component with an internal biological clock (Foster and Kreitzman, 2014).

Baron and Reid describe circadian misalignment very clearly: "The term 'circadian misalignment' can describe a variety of circumstances both in the laboratory and natural environment. In the Oxford Dictionary (2010), 'misalignment' refers to 'the incorrect arrangement or position of something in relation to something else.' One of the most common types of misalignment studied is misalignment of the sleep/wake cycle in relation to the biological night. Other types of misalignment include misalignment of feeding rhythms to the sleep/wake or light/dark cycle, or internal misalignment of central and peripheral rhythms. Figure 1 presents a schematic depiction of the organization of the central and peripheral circadian rhythms. This diagram includes zeitgebers (light, melatonin and activity) as well as the potential causes of chronic circadian misalignment.

***Figure 1***




The timing of melatonin onset under dim light conditions (dim light melatonin onset or DLMO) and the core body temperature minimum are often used as markers of circadian timing. The timing of these circadian markers in relation to sleep/wake behaviors is commonly referred to as phase angle, and has also been used as a measure of circadian alignment. For example, the duration between circadian markers (DLMO or core body temperature minimum) and sleep timing (onset, midpoint or wake time) has been evaluated. Individuals with evening chronotype (preference for later timing of sleep and activity) have been shown in some studies to have a shorter phase angle between circadian markers and sleep, indicating that they sleep and wake earlier in their circadian phase. One of the most significant and immediate consequences of misalignment of the sleep/wake cycle to the biological night is sleep disturbance and/or daytime sleepiness. Insomnia, difficulty waking in the morning and sleepiness caused by circadian misalignment are typical symptoms that lead patients to seek care in sleep clinics for circadian disorders. However, the physiological and psychological consequences are much broader than sleep/wake disturbance. These include changes in feeding patterns, metabolic function and risk for mood disorders. Other types of disruption include internal misalignment of rhythms, such as timing of central versus peripheral clocks. For example, research in animal models has demonstrated that altering availability of food timing shifts peripheral (e.g. hepatic) but not central rhythms." (Baron and Reid, 2014).

There are many bodily processes controlled by day-night rhythms, such as blood pressure control, feeding behaviors, and lipid and carbohydrate metabolism, among others. The circadian clock, a continuous internal system of transcriptional loops, is what controls this regulatory biological movement, and these looping pathways balance each other out. In example, transcription factors such as Clock and Bmal1 control the assembly of proteins like Per and Cry, which then regulate the assembly of Bmal1, resulting in the levels of Bmal1, Clock, Per and Cry fluctuating regularly. Various input signals, zeitgebers like light and hormones, can change these loops and 'reset the clock' so to speak (Staels, 2006). In another study of two groups of travelers, after a flight with a 6 hour difference one group remained inside a lab for a week while the other group spent time outside. The group that went out adapted to the new time zone in half the time that the indoor group needed. Local time cues, like light-dark cycles and meal times, among others, are what allowed the second group to synchronize quicker (Coleman and Kim, 1998).

The concept of "social jet lag" has been mentioned in current research as well. This is a form of persistent circadian disruption that corresponds to the time difference between routine sleep cycles during the work/school week and free time on weekends. It is a weekly discrepancy in the internal body clock, which can be comparable to journeying across three to four time zones twice a week for someone who wakes up at 6:00 AM during the week and sleeps until 9:00 or 10:00 AM on the weekend. There has been discovered an association in the affirmative between the extent of this "social jet lag" and body mass index, suggesting yet again that the interference of circadian cycles contributes to weight gain, among other possible issues (Summa and Turek, 2015).

It all seems to come down to the body clock and its adjustment. But what does that truly mean? What is this clock? It was first believed that there was a single master clock in the suprachiasmatic nucleus in the brain which regulated numerous biological processes within the body. It was later discovered that there are additional peripheral clock genes in the liver, kidneys, pancreas, heart, and other tissues. We now know that these clocks manage the activity of three to ten percent of genes in various tissues, and in some cases maybe even as much as 50%. If any of these clocks fall out of sync with the master clock, which is possible from sleeping at the wrong times, the frenzy within the body can lead to obesity, diabetes, depression, and many other complicated disorders. The clock gene in the heart sends signals in the early morning to prepare the heart for the harshness of awakening, an explanation as to why so many heart attacks occur at dawn hours. The peripheral clock in the liver functions strongly with the metabolism, contributing to the regulation of normal blood glucose levels over the course of the day to make certain there is a steady flow of energy for brain function and body processes. There is still a system required to combat excess blood glucose due to eating, with insulin the primary hormone in charge of that regulation by starting the removal of glucose from the bloodstream. Insulin is produced in the pancreas, where there is another biological clock that is vital to sustaining normal blood sugar levels. Any disruption of that clock can damage pancreatic function and result in diabetes, a metabolic disorder in which the body produces too little insulin and causes irregularities in blood glucose levels. An experiment was done by Marcheva and Bass in which pancreatic tissue from mice with mutations in circadian clock genes were isolated and examined. They observed that the amount of insulin secreted in response to a glucose stimulation decreased dramatically. They then bred mice with their pancreatic clocks deleted, and these offspring mice developed diabetes early in life and showed a drastic reduction in insulin secretion. Another experiment with mice allowed the scientists to observe a connection with Night-eating Syndrome, a disorder in which people would consume an excessive amount of food at night and develop obesity and/or metabolic syndrome. It was thought that this condition may be resultant of a deficiency in managing the circadian timing of hunger, causing patients a predisposition to weight gain and metabolic misalignment. These examples just provide further evidence for the fact that the multiple clocks throughout the body are required to maintain equilibrium by synchronizing their timing, all based on the leading master clock (Foster and Kreitzman(2014),. any disruption causes a multitude of health issues, including heart and stomach issues, neurological diseases and psychiatric illnesses among others (Summa and Turek, 2015). Due to the fact that circadian rhythms don't follow an exact 24 hour schedule, they have the ability to 'reset,' or shift, the phase in response to environmental time cues. The central clock in the SCN is mainly reset by light, owing to its direct pathway to the retina. The peripheral clocks, as mentioned above, are controlled by various signals from the SCN clock. For example, melatonin synthesis in the pineal gland, mentioned in depth below, is mainly affected by the light-reliant SCN clock, with nocturnal secretion (Wu et al, 2011).

The core body temperature (CBT) and melatonin secretion, as mentioned above, both play key roles in the body's natural ability to follow a healthy sleep/wake cycle. Professor Jim Waterhouse wrote in the British medical journal The Lancet that "the ease of getting to sleep and staying asleep depends not only on the previous wake time, but also on associations with the circadian rhythm of core temperature. Sleep is easiest to initiate when core temperature is falling rapidly or is at its lowest and most difficult when body temperature is rising rapidly or is high. Waking is the opposite of sleep initiation, because it happens when core temperature is rising or is high." (Waterhouse et al, 2007). In healthy people, core temperature will reach a low point between 3:00 and 5:00 AM, during which time most people are asleep, and steadily begins to increase at about 6:00 AM, reaching a climax at midday when most people are awake (Brody, 2007). CBT measurement is a standard physiological method for studying circadian rhythms, because its rhythm has been determined to be the most reliable endogenous circadian oscillator. Hamilos et al performed an experiment of CBT in patients with Chronic Fatigue Syndrome and documented that "the rhythm of CBT should be a valid benchmark for which to compare other circadian rhythms for desynchronizations" (Hamilos et al, 2001). There has also been a parallel seen between core body temperature and mental performance - performance rises with rising temperature throughout the early hours of the day, allowing for peak performance, and as it gets later, tasks that require central processing and short term memory decline due to the falling evening temperatures. There have also been changes in mood and performance observed under different groupings of the time of day and the amount of time awake, with more deterioration in mental performance with sleep loss (Waterhouse et al, 2007). Melatonin, produced mainly by the pineal gland and then secreted into the bloodstream, is a hormone that is secreted mostly at nighttime, when it is dark, seeming to stimulate the body to sleep. When there is trouble sleeping, oral ingestion of the chronobiotic drug melatonin can assist in inducing sleep. A phase response curve, which describes the relationship between a stimulus and a response, is the resulting reaction to melatonin ingestion, shows that taking it in the morning will cause a delay in circadian rhythms, and taking it at night will cause an advance in them. This phase response curve is about 12 hours out of phase, with the phase response curve of light, which would cause a phase advance in the morning and a phase delay at night (Brown et al, 2009). It seems that the circadian clock regulates the timing of melatonin secretion, although darkness is necessary as well because light will inhibit the secretion. After a long flight, the SCN-generated night-time cue will be set to the home nighttime before the clock adjusts, and thus if a traveler will enter a dimly lit room when it is nighttime at their home, melatonin secretion can occur and cause sleepiness (Sack, 2009). But taking melatonin in the evening and remaining in somewhat darkness can aid in falling asleep, which can additionally help acclimate the body to the local sleep/wake schedule. A word of warning for female travelers: interaction of melatonin and menstrual hormones can lead to a stop of the menstrual cycle. Female athletes can even be at a health risk from this, since many of them already have stalled cycles due to "overtraining" (Reilly et al, 1996).

In reference to athletes, there was a study done on elite athletes that recorded sleep loss and mood changes after long distance flights. Athletes that traveled more than five time zones to the west showed shifts in performance, including grip strength and back and leg endurance, which were in phase with their unadjusted body clocks. A similar result was seen in a group of Olympic athletes who journeyed over ten time zones to the east. It was even observed that for several days after an east or west flight over six to eight time zones, the athletes had distorted grip strength and weak performances in training sessions (Waterhouse et al, 2007).

Now that is it understood what jet lag is and the extent of its affects, counting the misalignment of the internal body clock, what can be done to alleviate the dyschronism symptoms? There are a number of ways to attempt to prevent jet lag, as well as suggestions for adjusting the body clock to combat the desynchronization once it emerges.

Trip planning can play a major part in prevention of jet lag. If possible and extra stress would not be caused, stopovers should be included in the flight plan. Breaking up the number of time zones being crossed by having a stopover can greatly diminish the likelihood of jet lag. Keeping hydrated is also necessary to counteract the dry air of the flight cabin (Waterhouse et al, 1997). Also, unless it is nighttime at the destination, sleep should be avoided during the flight, as it can anchor the rhythms to the home time zone. Staying on home time by remaining concurrent with one's circadian rhythms won't allow the internal clock to be disrupted; however it seems to make sense only for short trips. Supposedly, this approach was employed by President Lyndon B. Johnson when he met with Vietnamese leaders. This may be difficult, but if possible it can help avoid majority of jet lag symptoms. Conversely, coordinating with the local time of the planned travel location, from the get go can adjust the clock quicker and avert negative effects of the journey. This can be done by eating meals by the local schedule, going out in the daytime, going to bed at a reasonable time for the local environment, etc. A sleeping pill may be required the first night to assist in an easy transition, but hopefully after that the adjustment will continue smoothly (Coleman and Kim, 1998). Melatonin, which we have seen to be a somewhat 'darkness signal,' can be helpful in aiding clock acclimation, since it has the ability to induce sleep when necessary. However, the dosage is unclear, and it would seem that the timing of administration is more relevant than the actual amount. In addition, a boost in caffeine consumption may combat daytime tiredness; however caution is required so as not to aggravate insomnia. Exercise has been proposed to alleviate jet lag symptoms, but it has not been studied in clinical trials (Sack, 2010).

## Conclusion

From the research obtained, it is evident that jet lag has no exact, scientific definition, but that it is a lack of synchronization of the body's internal clocks and the external environment. It can take a few days following flight travel over several time zones for the body's circadian rhythms to realign. Repeated travel over an extended period of time can have the same long term consequences as those of shift workers - extended desynchrony with persisting symptoms that exacerbate with age. Resetting the clock requires zeitgebers, the most integral of which by far is the fluctuation of light and darkness. Adjusting is the primary goal to adequately offset jet lag. To do this, travelers should set up a specific itinerary of predetermined sleep and activity times, meal schedules and exposure to light versus remaining in dim lighting. The quicker the circadian system acclimates to the new time zone, the shorter the symptomatic period of jet lag will be. Assistance from the hormone melatonin may be necessary, a chronobiotic which adjusts the timing of the central body clock. Recently the drug called modafinil, meant to resist the tendency to fall asleep, has been registered for use in shift work sleep disorder, and although no records deal with its use in jet lag, the two have similarities and so perhaps this drug would aid in preserving daytime alertness (Arendt, 2009). Each individual must know his body and research the best methods for him to avoid or resolve jet lag.

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