

Jet Lag Modification

Emily Simmons, MD; Owen McGrane, MD; and Ian Wedmore, MD

Abstract

Athletes often are required to travel for sports participation, both for practice and competition. A number of those crossing multiple time zones will develop jet lag disorder with possible negative consequences on their performance. This review will discuss the etiology of jet lag disorder and the techniques that are available to shorten or minimize its effects. This includes both pharmacological and nonpharmacological approaches.

Introduction

In 2013, approximately 45 million people flew to the United States from outside of North or South America and approximately 20 million Americans flew to destinations outside of the Americas (38). These 45 million travelers represent only a fraction of the people worldwide at risk of experiencing symptoms of jet lag. In our modern society, athletes make up many of these travelers and will travel great distances often by air to compete in athletic events. This is true of competitive sports and the increasingly popular “extreme” and adventure sports. Participation in many of these sports often requires travel across multiple time zones, resulting in the development of jet lag disorder (JLD). JLD is a constellation of symptoms, focused around poor nighttime sleep and daytime sleepiness, resulting from circadian dyssynchrony after rapid travel across multiple time zones. Although there is no standardized definition of JLD, there are commonly recognized symptoms associated with it, as follows: insomnia and poor-quality sleep, daytime sleepiness, impaired alertness and concentration, headache, and gastrointestinal complaints.

The overall effect of JLD on athletic performance remains unknown and difficult to quantify because of multiple variables involved in competition. Several studies show it to have a detrimental effect on specific aspects of physical and mental performance (7,24,26,44), although the methodology of many jet lag studies has been noted to be weak and poorly generalizable (6). Studies looking at specific athletic

tasks tested against variables of time of the day, sleep deprivation, vigilance, and forced circadian dyssynchrony demonstrate diurnal variations in strength and performance and larger effects of fatigue and decreased vigilance on complex tasks rather than simple physical performance (17–19,27,32). These studies often do not measure the effects of jet lag directly, but many of the variables tested are seen

also in jet lag; therefore it makes sense that most athletes and trainers believe that JLD does have an overall negative effect on sports performance (17,23), and there is great interest in attempting to minimize the effect of Jet Lag. There is no specific treatment for JLD, but there are multiple mitigation strategies including pretravel schedule shifting, timed light exposure, exogenous melatonin administration, napping, and other pharmacological interventions.

Etiology

Jet lag is caused by dissociation between the body’s overall circadian rhythm and the “clock time” of the external world as well as dyssynchrony among various circadian rhythms.

The body’s overall circadian rhythm is maintained by a complex network of inputs and outputs. The seat of the body clock is in the hypothalamus, specifically the paired suprachiasmatic nuclei (SCN). The SCN receive direct input through the retinohypothalamic tract (42), from a type of nonrod, noncone light-sensitive receptors in the retina known as ganglion cells (3,29). The SCN also receive input through the intergeniculate leaflet, which seems to relay information about physical activity and general excitement (41,42). The output of the circadian rhythm, at its most basic level, is a cycle of sleepiness and alertness, based on factors including core body temperature and secretion of hormones such as melatonin and cortisol (31).

The propensity for sleep is related closely to core body temperature (10,41), and core body temperature traditionally has been used to track circadian rhythm. As body temperature falls, it becomes easier to fall asleep, marking the onset of biologic night. Minimum body temperature tends to occur between 0300 and 0700 h, generally 1 or 2 h before natural waking time. As body temperature rises toward a peak in the evening, it becomes more difficult to fall asleep. During this time, there is a compensatory improvement in mental and possibly physical performance (41), until other factors like cumulative awake time start

Austere and Wilderness Fellowship Program, Madigan Army Medical Center, Joint Base Lewis McChord, Tacoma, WA

Address for correspondence: Ian Wedmore, MD, Austere and Wilderness Fellowship Program, Madigan Army Medical Center, Joint Base Lewis McChord, Tacoma, WA; E-mail: ian.s.wedmore.mil@mail.mil.

1537-890X/1402/123–128

Current Sports Medicine Reports

Copyright © 2015 by the American College of Sports Medicine

to counteract these improvements. Because of external influences, there is no single test yet identified to track the overall circadian rhythm and other measures such as levels of endogenous melatonin or its metabolites also have been used (31).

Using “forced desynchrony” protocols designed to isolate study subjects from external time cues, the average intrinsic circadian rhythm was found to have a periodicity of 24.2 h, with a range of 23.9 to 24.4 h (31). Other studies, particularly in totally blind individuals, have measured the intrinsic rhythm at 24.5 h (31). Extreme morning types (“larks”) tend to have shorter circadian periodicity, whereas evening types (“night owls”) have longer intrinsic rhythm (3). Regardless of the exact periodicity, very few individuals have a circadian rhythm that naturally runs at precisely 24 h, and therefore most people require daily adjustments to entrain to a 24-h clock. To synchronize the circadian rhythm with the 24-h day, the body receives input from various stimuli known as “zeitgebers” (time givers). These zeitgebers serve to slow down (delay) or speed up (advance) the body’s circadian rhythm. The most well-known and best-studied zeitgebers are melatonin and the light-dark cycle (41). Others include socioenvironmental cues such as habitual sleeping time or meal times and hard exercise. Zeitgebers can act agonistically or antagonistically with each other depending on the timing of exposure in relation to the circadian rhythm. When the circadian rhythm is synchronized with the external world, periods of sleepiness (“biologic night”) tend to fall during periods of darkness whereas periods of alertness (“biologic day”) occur during light. This cycle is maintained by the input of bright light in the morning and endogenous melatonin secretion in the evening. A traveler is considered “recovered” from JLD when all of the components of the circadian rhythm are synchronized with each other and with the new time zone (31). In reality, many symptoms of jet lag are mitigated effectively when the sleep-wake rhythm is synchronized, and travelers do not require full resynchronization of all circadian processes (10).

Diagnosis

The American Academy of Sleep Medicine has classified JLD under circadian rhythm sleep disorders and defines it clinically as follows (1):

- A) There is a complaint of insomnia or excessive daytime sleepiness associated with transmeridian jet travel across at least two time zones.
- B) There is an associated impairment of daytime function, general malaise, or somatic symptoms such as gastrointestinal disturbance within 1 or 2 d after travel.
- C) The sleep disturbance is not explained better by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

There are no universal tools for making the diagnosis of JLD, but several questionnaires have been developed. The Columbia jet lag scale (40,41) uses a once-daily questionnaire to assess fatigue, daytime sleepiness, impaired concentration, decreased alertness, memory difficulties, clumsiness, weakness, lethargy, and light-headedness. Weaknesses of this

questionnaire are that it only assesses symptoms once daily, in the evening, and excludes questions regarding nighttime sleep. Studies have shown that self-reported symptoms of jet lag vary throughout the day (41), aside from a common theme of “increased fatigue”; when questioned in the morning, travelers complain about poor sleep the night before. During the day, they focus on lack of motivation and decreased concentration, and when assessed in the evening, they report a lack of readiness for sleep (42). An alternate questionnaire, the Liverpool jet lag questionnaire (40), was developed to remove these concerns. This scale assigns a jet lag symptom severity using 15 questions from six symptom categories (jet lag, last night’s sleep, fatigue, meals, mental performance and mood, and bowel activity today) scored on a scale from -5 to $+5$ and is administered several times daily. Estimates of the prevalence of JLD vary from 30% (10) to 75% of transatlantic travelers (14); many travelers will experience at least some components of jet lag and travel fatigue, but few seek medical intervention.

Travel Fatigue

Travel fatigue is a condition frequently experienced by travelers on any long-distance journey and is not associated specifically with air travel across time zones. It is a separate entity from JLD, although there is overlap of symptoms and travel fatigue can exacerbate JLD (31). Travel fatigue consists of fatigue, increased likelihood of headache, and general travel weariness. Factors that can contribute to travel fatigue include accumulated sleep debt (often related to hectic pretravel preparation and inconvenient travel schedules), poor sleep (due to cramped seating and frequent interruptions), dehydration (due to voluntary decreased intake, limited availability of fluids, and dry environment), decreased exercise, restricted food availability, and choices. Travel by jet adds the stress of mild hypobaric hypoxia and dry cabin air (13,41). Travel fatigue can be mitigated by preparing in advance for travel, starting a trip well-rested, maximizing comfort during travel, staying hydrated with nonalcoholic and noncaffeinated beverages, and resting upon arrival at the destination (42). Travel fatigue generally will resolve by the day after travel, once a traveler has settled in at their destination and slept adequately overnight (42).

Phase Delay and Phase Advance

Symptoms of jet lag typically do not become significant until at least three to five time zones have been crossed (11), although there is significant individual variability. Symptoms of jet lag seem to worsen with age and also vary depending on direction of travel, number of time zones crossed, and individual response to travel (14,41,42). Phase delay refers to delaying the onset of the next phase — essentially creating a longer time spent in the current phase. Phase advance, therefore, is shortening of the current stage and earlier onset of following phases. Generally westward travel is associated with phase delay and eastward travel is associated with phase advance. Most travelers will have a smoother transition during westward travel (phase delay). Phase delay in response to westward travel up to 12 time zones is almost universal. When traveling eastward, most travelers will accommodate by phase advance if fewer than eight time zones are crossed. Beyond that, an increasing percentage of travelers will adjust by phase

delay (3,41,43) and intentionally phase delaying rather than advancing should be considered by those making such a trip. Some travelers will have difficulty adjusting to travel across about 12 time zones because rather than phase advancing or phase delaying, their circadian rhythm becomes disorganized (3,10). This is thought to be due to certain components of the circadian rhythm delaying, whereas others advance, so the net effect is disorganization and difficulty synchronizing to the new time zone. There is significant variability among individuals, and external time cues and constraints (meal times, meetings, etc.) also influence entrainment to a new time zone. Morning types generally have an easier time adjusting to eastward travel but are more sensitive to the effects of sleep loss, whereas evening types entrain better to westward travel (43) — this is thought to be due to the direction of their daily circadian adjustment based on the different average lengths of their intrinsic circadian rhythms.

Effects of Light

The light-dark cycle is considered the most powerful zeitgeber (16). Under normal circumstances, when an individual is entrained to a given time zone and they are sleeping during periods of darkness, a strong light stimulus is experienced in the morning (43). This serves to phase-advance the individual and stimulate alertness. Light exposure decreases endogenous melatonin secretion, thus decreasing signals for sleepiness. Light exposure in the evening also stimulates alertness, in this case by causing a phase delay and extending biologic day (42). Continuous light has essentially the same effect as that of intermittent or pulsed light exposure (21). Bright light produces more effect than dim light, but studies have shown that light exposure down to 100 lux produces measurable effects on circadian processes (43). Light in the blue-green wavelengths produces more effect than other wavelengths of light (40,43).

Bright light, continuous or pulsed, administered just after the core temperature minimum will produce a phase advance. This happens naturally on a daily basis to help maintain entrainment to the 24-h clock and promotes alertness during the day by suppressing melatonin secretion. When administered shortly before the core temperature minimum, bright light produces a phase delay (42). The relative timing of light exposure is therefore critical to produce the desired phase shift. After westward travel across up to eight time zones, natural light tends to facilitate the proper phase shift because exposure in the evening leads to phase delay whereas morning exposure occurs too far after the temperature minimum to cause a phase advance. When traveling eight time zones to the east, however, morning light should be avoided initially because it tends to cause a phase delay and inhibit entrainment (42). If isolation indoors is not possible, dark sunglasses can help minimize light exposure (31). Light boxes have demonstrated mixed results; large units or those mounted directly onto goggles have been shown to produce phase shifts (31), but smaller units were ineffective, and carrying a light box during travel may be impractical (31,42). Unfortunately even if attempted, the practicality and efficacy of light therapy among athletes has been shown to be variable at best (38) Tables 1 and 2 provide the recommended times for light exposure depending on travel to best entrain to the new location.

Melatonin

Melatonin is a hormone produced primarily by the pineal gland (41). It is called the “darkness hormone” sometimes (16) because in normally entrained individuals, it is secreted at the onset of darkness and is suppressed by light (10,41). It is thought to have both central and peripheral effects — it causes peripheral vasodilation, lowering the core body temperature, and also acts via receptors in the SCN, pituitary, and elsewhere in the brain to facilitate nighttime physiology (10,41). When secreted or exogenously administered in the evening, melatonin creates a phase advance and promotes sleep. If administered at the end of normal melatonin secretion, in the early morning, melatonin produces a phase delay, extending biologic night (41).

The literature on melatonin use is mixed with a few studies showing a significant benefit in jet lag symptom reduction (2,8,9,25,36) and several other studies showing only a trend toward benefit (lacking statistical significance) or no benefit (11,13,22,35). Overall it is felt to be beneficial in improving sleep quality and facilitating entrainment to a new time zone when administered properly (41). The exact mechanism of effect of exogenous melatonin is unclear — it may act directly as a soporific, or it may promote phase shifting via the SCN (41). Timing of melatonin administration seems to be more important than the dose as long as the dose results in levels at or above physiological levels (0.3 mg achieves physiological levels in most cases) (43). Low doses (around 0.5 mg) seem to facilitate entrainment, whereas higher doses (3 to 10 mg) produce more direct effects on sleep (43). Especially with relatively low doses, there seems to be little, if any, “hangover” effect the next day, likely because of rapid metabolism (16,41).

During eastward travel, or when a phase advance is desired, melatonin should be administered during the several hours before the desired sleep time up to actual bedtime. This timing allows blood levels to rise before the onset of endogenous melatonin secretion. Specific recommendations vary between 1 and 4 h before bed, depending on whether the intent is to promote sleep directly (shorter latency, 1 h) or facilitate a phase shift (longer latency, 3 to 4 h) (16). When a phase delay is desired, a low dose (0.5 mg) of melatonin should be taken at the offset of natural secretion during early morning (16) to achieve faster phase shift but with minimal direct soporific effect. Caution should be taken when using melatonin for soporific effects, so that there is not an inadvertent disadvantageous phase shift (16). Thus, taking melatonin at bedtime when traveling west when a phase delay is desired actually could result in a phase advance instead (42). The combination of proper melatonin supplementation and light exposure seems to give the most rapid phase shifting (16). For travel across more than 7 to 8 time zones, it is suggested also that melatonin supplementation be initiated 2 to 3 d in advance of travel (6). An area of future development involves the use of ramelteon and agomelatine, which are melatonin receptor agonists with both greater affinity and half-life than melatonin itself (34). Table 1 provides consolidated recommended timing and dosing of melatonin for travel.

In the United States, melatonin is considered a supplement, not a medication, and is therefore not regulated by the Food and Drug Administration (FDA). It is available without a prescription. Although it is considered safe and has few side effects (29), there are no long-term studies on

Table 1.
Consolidated recommended timing and dosing of melatonin for travel

Traveling east up to 9 h requires a phase advance.
Melatonin: take 3 to 5 mg at bedtime or up to 2 h before bedtime at destination.
Start up to 1 to 3 days PTA taking at planned bedtime in the destination time zone if taking before travel.
Light: see Table 2.
Traveling west up to 9 h requires a phase delay.
Melatonin: morning melatonin may be helpful. Take 0.5 mg upon waking.
Light: see Table 2.
Traveling east or west 10 h or more: treat both directions as westward travel requiring a phase delay because this is usually easier for individuals to adjust to.
Melatonin: morning melatonin may be helpful; use a nonsoporific dose of 0.5 mg. Start 2 to 3 d before departure, taking it at "instead of" at the destination.
Light: see Table 2.

its use and individuals need to be aware that as a supplement, its manufacture is not standardized and there may be variability between preparations and a possibility of contaminants (10,16,41). Melatonin is not banned for athlete consumption by the National Collegiate Athletic Association (NCAA), although the NCAA does ban its provision to athletes by the institution. Also as mentioned, because it is a supplement, it is possible that unlisted substances could be found as contaminants in the tablet (21).

Melatonin is found naturally in many foods, including oats, sweet corn, barley, rice, ginger, tomatoes, and bananas (16). It is derived from tryptophan and requires adequate levels of vitamins B3 and B6 as well as calcium and magnesium to be synthesized. Endogenous melatonin secretion is inhibited by alcohol, caffeine, aspirin, ibuprofen, and various prescription drugs (16) including beta blockers (43). Knowledge of these interactions can help a traveler maximize his or her endogenous melatonin levels when unable to take exogenous melatonin (flight crews may be restricted) or in conjunction with supplementation (16).

Other Interventions

In addition to properly timed light and melatonin, there are other strategies and interventions that can help minimize the effects of jet lag and facilitate entrainment to a new time zone. As previously mentioned, the main target in addressing jet lag is the sleep-wake cycle (10). First, a traveler must consider whether it is even viable to attempt to adjust to the new time zone. Because it takes up to 1 d per time zone to adapt fully, visits to a given time zone less than that duration or less than 2 to 3 d for any time zone change may not warrant an attempt to entrain to the new time zone (3,42); this decision depends largely on the purpose of travel and the flexibility of the traveler's schedule to maintain the timing of the home time zone. When possible, events may be scheduled to coincide with daytime in the home time zone,

decreasing the necessity for adjusting to the new time zone. If this is not possible, short trips may be amenable to pharmacological intervention to maintain alertness and allow sleep. For trips of intermediate duration, generally 3 to 5 d depending on the number of time zones crossed, a partial entrainment may be beneficial. Maintaining a block of sleep that falls during the habitual sleep period in the home time zone, ideally keeping the core temperature minimum (and endogenous melatonin peak) within this sleep period, can help maximize alertness and minimize circadian disruption. Strategic napping can help add to the total amount of sleep and thus reduce sleep debt and can be helpful when full entrainment is

Table 2.
Recommendations for the use of bright light to adjust body clock after time zone transitions.

	Bad Local Times (h) for Exposure to Light	Good Local Times (h) for Exposure to Light
<i>Time zones to the west (h)</i>		
3	0200 to 0800 ^a	1800 to 0000 ^b
4	0100 to 0700 ^a	1700 to 2300 ^b
5	0000 to 0600 ^a	1600 to 2200 ^b
6	2300 to 0500 ^a	1500 to 2100 ^b
7	2200 to 0400 ^a	1400 to 2000 ^b
8	2100 to 0300 ^a	1300 to 1900 ^b
9	2000 to 0200 ^a	1200 to 1800 ^b
10	1900 to 0100 ^a	1100 to 1700 ^b
11	1800 to 0000 ^a	1000 to 1600 ^b
12	1700 to 2300 ^a	0900 to 1500 ^b
13	1600 to 2200 ^a	0800 to 1400 ^b
14	1500 to 2100 ^a	0700 to 1300 ^b
<i>Time zones to the east (h)</i>		
3	0000 to 0600 ^b	0800 to 1400 ^a
4	0100 to 0700 ^b	0900 to 1500 ^a
5	0200 to 0800 ^b	1000 to 1600 ^a
6	0300 to 0900 ^b	1100 to 1700 ^a
7	0400 to 1000 ^b	1200 to 1800 ^a
8	0500 to 1100 ^b	1300 to 1900 ^a
9	0600 to 1200 ^b	1400 to 2000 ^a
10	Can be treated as 14 h to the west ^c	
11	Can be treated as 13 h to the west ^c	
12	Can be treated as 12 h to the west ^c	

Reprinted from Waterhouse J, Reilly T, Atkinson G. Jet-lag. *Lancet*. 1997;350:1609–1614. Used with permission.

^a Promotion of a phase advance of the body clock.

^b Promotion of a phase delay of the body clock.

^c Body clock adjusts to large delays more easily than to large advances. This table is based on a T_{min} (temperate minimum) of 0400 h; other values for T_{min} would need the times to be adjusted accordingly. For example, an individual with a T_{min} at 0600 h should, after a journey across three time zones to the west (see row 1), avoid light at 0400 to 1000 h and seek it at 2000 to 0200 h.

not possible, but long naps during the day serve as an “anchor” to the departure time zone and can interfere with attempts at entrainment to the new time zone (42).

One strategy to facilitate entrainment to a new time zone consists of artificially phase-shifting the schedule before initiating travel (3). Depending on the number of time zones to be crossed, this can take significant time and commitment. One strategy for westward travel across 9 time zones (3) is to ensure bright light exposure for 9 h daily, shifting the exposure 3 h later each day for 3 d, then holding that schedule for the 2 d before travel. An example of a strategy for crossing 6 time zones in an eastward direction (29) is to administer melatonin 5 h before habitual bedtime and moving it 1 h earlier each day and exposing the individual to bright light upon awakening in the morning, again advancing it each day. As long as the light exposure falls after the temperature minimum, it will facilitate the phase advancement. The shifts in schedule require strict adherence to light exposure and avoidance, significant planning to conduct business during off hours, and exclusion from participation in normally timed social events in the days leading up to travel (3,43). When possible, it may be advantageous to break up travel into several shorter segments, although this benefit needs to be balanced against the increased logistical challenges that a segmented travel schedule creates (42). After arrival in a new time zone when full entrainment is desired, it may be helpful to adopt the local schedule as soon as possible. Attempting to eat, sleep, and socialize at “normal” local times provides both physiological and socioenvironmental time cues to facilitate entrainment.

Sedatives and Stimulants

A more practical approach in many cases is to supplement appropriately timed light exposure and melatonin with other pharmacological interventions. There are several medications or other substances that can mitigate symptoms of jet lag without actually facilitating entrainment to a new time zone. These agents fall generally into two categories — those that promote sleep and those that promote alertness. Although not recommended for long-term use, for short trips or during the first few days after travel, they can help bridge a traveler until return to the home time zone or until entrainment to the new time zone. Sedative-hypnotic medications such as benzodiazepines and zolpidem are effective at improving sleep duration and quality after travel (10,14,42), although some studies do not demonstrate a corresponding improvement in daytime alertness (43).

Multiple stimulants have been evaluated to address fatigue and decreased alertness associated with jet lag. Studies have shown significant spontaneous increase in caffeine (coffee) consumption after travel (3). Caffeine, in both fast-acting and slow-release preparations, can improve alertness transiently, but adverse effects such as palpitations, arrhythmias, hypertension, tremors, and anxiety may result from excessive dosing (10,42) and study subjects taking caffeine demonstrated increased sleep difficulty compared with those taking placebo (44). Modafinil is a psychostimulant that serves to promote alertness without some of the adverse effects of other stimulants; currently it is approved for use in narcolepsy, but studies have shown efficacy in improving alertness associated with jet lag (23,31,40). Of note, in 2010, the

manufacturer of modafinil petitioned the FDA to include treatment of JLD as an indication for a related medication, armodafinil, but that request was denied. Modafinil is banned by the World Anti-Doping Agency and NCAA except for use under a medical exception policy (37). Other stimulant medications such as amphetamines also have been studied and shown to demonstrate improvement in alertness, but adverse effects, addiction potential, and issues related to their status as controlled substances limit their use (41,42). For competitive athletes, many of these medications are banned from use or have undesirable adverse effects, and this must be considered in choosing pharmacological intervention.

Diet

Dietary changes have been advocated to help reduce jet lag, but there are no specific diets that can be considered scientifically proven to do so. However, the concept remains popular. General recommendations that may decrease the gastrointestinal upset associated with travel include eating familiar and healthy foods, including plenty of fruits and vegetables to promote bowel regularity (41). Additionally higher protein intake may be consumed when alertness is desired, whereas carbohydrates may be favored to promote sleepiness. Two specific diets that have been promoted are the Argonne Anti-Jet Lag diet and the Harvard Anti-Jet Lag fast. Both diets suppose that the circadian rhythm can be reset via gastrointestinal-associated zeitgebers, essentially erasing previous time cues by depletion of glycogen stores and setting the new time by ingestion of a large meal upon arrival at the destination. The Argonne Anti-Jet Lag diet consists of four pretravel alternating “feast” and “fast” days with carefully timed protein and carbohydrate intake, scheduled so that the day of travel is a fasting day, and a large protein-rich meal is eaten at destination breakfast time on the day of arrival. There is limited evidence that this diet may reduce symptoms of jet lag (28), but it is difficult to follow and well-controlled studies are lacking. The Harvard fast is simpler — abstain from food and drink (except water) for approximately 12 to 18 h starting several hours before flight through arrival at destination and eat at the soonest meal time after landing (33). No clinical trials of this diet could be found at this time, but there are anecdotal stories of reduced jet lag symptoms.

Jet Lag Calculators

It is worth mentioning that there are presently many calculators available online, which promote their ability to help mitigate jet lag. These allow you to input your starting time zone or airport along with destination time zone or airport, and they then provide recommendations on when to avoid and when to seek light exposure. There is no available literature evaluating their efficacy. However, two reportedly were developed in conjunction with sleep centers: British Airways Jet Lag Advisor (www.britishairways.com/travel/drsleep/public/en_gb) in conjunction with the Edinburgh Sleep Center and the Jet Lag Rooster (www.jetlagrooster.com) in conjunction with the Mayo Clinic Center for Sleep Medicine and Rush University Medical Center (4). These calculators are available at no cost. There also are numerous iPhone applications available to reduce jet lag, although again, none have been evaluated critically.

Conclusions

Although JLD is generally a self-limited condition, there are advantages to minimizing the severity and duration of symptoms for both leisure travelers (improved enjoyment of a trip) and business or professional travelers (improved decision making and performance). For short trips, partial synchronization supplemented with naps, caffeine, and short-term use of pharmacological agents such as sedative-hypnotics or stimulants may be appropriate. A strategy targeting rapid synchronization of the sleep-wake cycle seems to be the most effective approach for trips lasting longer than a few days. Careful pretravel planning and preparation can minimize sleep debt before travel, and partial entrainment to the destination time zone is possible in travelers who have the commitment and schedule flexibility to do so. Exogenous melatonin and light exposure and avoidance at the proper times can have agonistic effects on entrainment to a new time zone. Medications such as sedative-hypnotics and psychostimulants can facilitate sleep or alertness, respectively, in the first few days after travel but are not without adverse effects, may be banned for use by athletic governing bodies, and are not recommended for long-term use.

The authors declare no conflicts of interest and do not have any financial disclosures.

References

1. American Academy of Sleep Medicine. *The International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 2nd ed. Westchester (IL): American Academy of Sleep Medicine, 2005.
2. Arendt J. Managing jet lag: some of the problems and possible new solutions. *Sleep Med. Rev.* 2009; 13:249–56.
3. Arendt J, Aldhous M, English J, et al. Some effects of jet-lag and their alleviation by melatonin. *Ergonomics*. 1987; 30:1379–93.
4. BBC Travel [Internet]. Jet lag calculators. Available from: <http://www.bbc.com/travel/blog/20130430-online-calculators-combat-jet-lag>. Accessed 2015 January 10.
5. Brown GM, Pandi-Perumal SR, Trakht I, Cardinali DP. Melatonin and its relevance to jet lag. *Travel Med. Infect. Dis.* 2009; 7:69–81.
6. Caldwell JA, Caldwell JL. Fatigue in military aviation: an overview of U.S. military-approved pharmacological countermeasures. *Aviat. Space Environ. Med.* 2005; 76:C39–51.
7. Chapman DW, Bullock N, Ross A, et al. Detrimental effects of west to east transmeridian flight on jump performance. *Eur. J. Appl. Physiol.* 2012; 112:1663–9.
8. Claustrat B, Brun J, David M, et al. Melatonin and jet lag: confirmatory result using a simplified protocol. *Biol. Psychiatry*. 1992; 32:705–11.
9. Comparatore AC, Krueger PG. Circadian rhythm desynchronization, jet lag, shift lag and coping strategies. *Occup. Med.* 1990; 5:323–41.
10. Coste O, Lagarde D. Clinical management of jet lag: what can be proposed when performance is critical? *Travel Med. Infect. Dis.* 2009; 7:82–7.
11. Edwards BJ, Atkinson G, Waterhouse J, et al. Use of melatonin in recovery from jet-lag following an eastward flight across 10 time-zones. *Ergonomics*. 2000; 43:1501–13.
12. Fowler PM, Duffield R, Morrow I, et al. Effects of sleep hygiene and artificial bright light interventions on recovery from simulated international air travel. *Eur. J. Appl. Physiol.* 2014; [Epub ahead of print].
13. Hughes RJ, Sack RL, Lewy AJ. The role of melatonin and circadian phase in age-related sleep-maintenance insomnia: assessment in a clinical trial of melatonin replacement. *Sleep*. 1998; 21:52–68.
14. Jamieson A, Zammit G, Rosenberg R, et al. Zolpidem reduces the sleep disturbance of jet lag. *Sleep Med.* 2001; 2:423–30.
15. Jet Lag Rooster [Internet]. Available from: <http://www.jetlagrooster.com/>. Accessed 10 January 2015.
16. Lathrop N, Lentz M. Melatonin, light therapy, and jet lag. *Air Med. J.* 2001; 20:30–4.
17. Leatherwood WE, Dragoo JL. Effect of airline travel on performance: a review of the literature. *Br. J. Sports Med.* 2013; 47:561–7.
18. Lericollais R, Gauthier A, Bessot N, et al. Time-of-day effects on fatigue during a sustained anaerobic test in well-trained cyclists. *Chronobiology Int.* 2009; 26:1622–35.
19. Lericollais R, Gauthier A, Bessot N, et al. Morning anaerobic performance is not altered by vigilance impairment. *PLoS One.* 2013; 8:e58638.
20. McCarty D. Ready for takeoff? A critical review of armodafinil and modafinil for the treatment of sleepiness associated with jet lag. *Nat. Sci. Sleep.* 2010; 2:85–94.
21. Naylor S, Johnson KL, Williamson BL, et al. Structural characterization of contaminants in commercial preparations of melatonin by on-line HPLC-electrospray ionization-tandem mass spectrometry. *Adv. Exp. Med. Biol.* 1999; 467:769–77.
22. Nickelsen T, Lang A, Bergau L. The effect of 6-, 9-, and 11-hour time shifts on circadian rhythms: adaptation of sleep parameters and hormonal patterns following the intake of melatonin or placebo. In: Arendt J, Pevet P, editors. *Advances in Pineal Research*, London (United Kingdom): John Libbey & Co.Ltd.; 1991. p. 303–6.
23. O'Conner PJ, Youngstedt SD, Buxton OM, Breus MD. FIMS Position Statement: air travel and performance in sports. International Federation of Sports Medicine. 2004. Available from: <http://www.fims.org>. Accessed 2014 September 27.
24. Petit E, Mougin F, Bourdin H, et al. Impact of 5-h phase advance on sleep architecture and physical performance in athletes. *Appl. Physiol. Nutr. Metab.* 2014; 39:1230–6.
25. Petrie K, Dawson AG, Thompson L, Brook R. A double-blind trial of melatonin as a treatment for jet lag in international cabin crew. *Biol. Psychiatry*. 1993; 33:526–30.
26. Reilly T, Atkinson G, Waterhouse J. *Biological Rhythms and Exercise*. Oxford (United Kingdom): Oxford University Press, 1997.
27. Reilly T, Edwards B. Altered sleep-wake cycles and physical performance in athletes. *Physiol. Behav.* 2007; 90:274–84.
28. Reynolds N, Montgomery R. Using the Argonne diet in jet lag prevention: deployment of troops across nine time zones. *Mil. Med.* 2002; 167:451–3.
29. Revell VL, Burgess HJ, Gazda CJ, et al. Advancing human circadian rhythms with afternoon melatonin and morning intermittent bright light. *J. Clin. Endocrinol. Metab.* 2006; 91:54–9.
30. Revell VL, Eastman CI. How to trick mother nature into letting you fly around or stay up all night. *J. Biol. Rhythms*. 2005; 20:353–65.
31. Sack R. The pathophysiology of jet lag. *Travel Med. Infect. Dis.* 2009; 7:102–10.
32. Sedlak M, Finni T, Cheng S, et al. Effect of time-of-day-specific strength training on serum hormone concentrations and isometric strength in men. *Chronobiol. Int.* 2007; 24:1159–77.
33. Skerret P. A “fast” solution to jet lag. *Harvard Business Review*. 2009.
34. Srinivasan A, Spence DW, Pandi-Perumal SR, et al. Jet lag: therapeutic use of melatonin and possible application of melatonin analogs. *Travel Med. Infect. Dis.* 2008; 6:17–28.
35. Spitzer RL, Terman M, Williams JB, et al. Jet lag: clinical features, validation of a new syndrome-specific scale, and lack of response to melatonin in a randomized, double-blind trial. *Am. J. Psychiatry*. 1999; 156:1392–6.
36. Suhner A, Schlagenhauf P, Johnson R, et al. Comparative study to determine the optimal melatonin dosage form for the alleviation of jet lag. *Chronobiol. Int.* 1998; 15:655–66.
37. The World Anti-Doping Agency [Internet]. The world anti-doping code, the 2014 prohibited list international standard. Available from: <http://www.usada.org>. Accessed 2014 September 27.
38. Thompson A, Batterham AM, Jones H, et al. The practicality and effectiveness of supplementary bright light for reducing jet-lag in elite female athletes. *Inj. J. Sports Med.* 2013; 34:582–9.
39. U.S. Department of Commerce, International Trade Administration, Office of Travel and Tourism Industries [Internet]. Available from: <http://www.travel.trade.gov>. Accessed 2014 August 31.
40. Waterhouse J, Edwards B, Nevill A, et al. Do subjective symptoms predict our perception of jet-lag? *Ergonomics*. 2000; 43:1514–27.
41. Waterhouse J, Reilly T. Managing jet lag (guest editorial). *Sleep Med. Rev.* 2009; 13:247–8.
42. Waterhouse J, Reilly T, Atkinson G. Jet-lag. *Lancet*. 1997; 350:1609–14.
43. Waterhouse J, Reilly T, Atkinson G, Edwards B. Jet lag: trends and coping strategies. *Lancet*. 2007; 369:1117–29.
44. Wright JE, Vogel JA, Sampson JB, et al. Effects of travel across time zones (jet lag) on exercise capacity and performance. *Aviat. Spac. Environ. Med.* 1983; 54:132–7.