

Jet Lag: Minimizing It's Effects with Critically Timed Bright Light and Melatonin Administration

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*"Truly the light is good and it is beneficial for the eyes to behold the sun."
—Ecclesiastes 11:7*

Abstract

The symptoms of jet lag cause distress to an increasing number of travelers. Potentially they may impair sleep, mood and cognitive performance. Critically timed exposure to bright light and melatonin administration can help to reduce symptoms. Bright light is one of the most powerful synchronizers of human rhythms and melatonin serves as a "dark pulse" helping to induce nighttime behaviors. Thus, enhancing day and night signals to the brain, appropriate to the environmental light/dark cycle of the new time zone, can serve to reestablish adaptive timing relationships between the body's internal biological rhythms and the external environment, and thereby reduce the symptoms of jet lag. Specific recommendations using bright light and melatonin for eastward and westward travel before and after departure are provided for time zone changes of up to 6, 7–9 and 10 or more hours.

Introduction

An increasing segment of the population experiences the symptoms of jet lag. These groups include not only tourists, but also transmeridian business travelers, military personnel, politicians, diplomats, athletes and night shift workers, whose functioning and performance can be impaired by the attendant sleep deprivation that may occur. Leger *et al.* (1993) reported that among 507 business travelers, nearly half suffered from fatigue during international business trips, approximately 78% reported disturbed sleep and approximately 27% complained of intellectual disability. It is interesting to speculate that the Yalta conference may have had a different outcome if its major participants had not been suffering from symptoms of jet lag.

Jet lag is characterized by symptoms of fatigue, lethargy, mood changes, cognitive impairment,

gastrointestinal disturbances and sleep disturbances. It results from a desynchrony between the endogenous circadian clock that regulates important biological rhythms such as melatonin, cortisol and the core body temperature rhythm and the sleep-wake cycle regulated largely by the environmental light/dark cycle. Normally the body's internal biological rhythms are synchronized with an individual's approximately 24-h sleep/wake cycle and the environmental light/dark cycle. With travel to a different time zone, in which the environmental light/dark cycle no longer coincides with the same time intervals as those of the body's underlying biological rhythms, the traveler, for example, often must try to sleep at times of the day conducive to waking, not sleeping.

Light is one of the most powerful synchronizers of human circadian rhythms. Light in the morning advances circadian rhythms; light in the evening delays them. Perhaps because the human species has adapted over the years to fire and indoor lighting, however, it generally requires light in the range of 2,500 lux (five times the intensity of normal room light of about 500 lux) to significantly shift human rhythms. Wavelengths in the blue-green spectrum (400–500 nanometers) appear to be the most effective in shifting human rhythms. Based on these principles, bright light then can be used to help advance underlying biological rhythms when undergoing a phase-advance (in which rhythms shift earlier) associated with eastward travel, and to delay rhythms when undergoing a phase-delay (in which rhythms shift later) associated with westward travel. Alternatively, by wearing dark sunglasses or goggles or avoiding light exposure at critical times during evening hours (based on the body's internal clock time, which may be different from the local time) after eastward flight can help prevent the delay of rhythms antagonistic to the phase-advance needed to adjust to the earlier time zone. Likewise, avoiding morning light on westward travel helps to prevent a phase-advance antagonistic to the phase-delay needed to adjust to the later time zone. Advancing or delaying underlying biological rhythms with light serves to shift these rhythms more rapidly than would normally occur and allow them to be more in accordance with the environmental light/dark cycle of the destination zone. With his/her own biological rhythms readjusted to the new time zone, the traveler then can sleep at a circadian phase more congruous with the environmental light/dark cycle. Without specific interventions, an individual's biological rhythms generally shift 1–2 h/day with changing time zones (although this change generally occurs more slowly for older individuals). For destinations with time zone differences of less than 3 h, jet lag symptoms are minimal. For time zone changes for ≥ 3 h, however, interventions can

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help speed the process of adaptation. The primary mode of action of light in shifting rhythms is thought to be mediated by stimulation of impulses originating in the retina and propagated via the retinohypothalamic tract to the suprachiasmatic nucleus of the anterior ventral hypothalamus, the anatomic location of the biological clock. Via a multisynaptic pathway, fibers subsequently impinge on primarily B-adrenergic receptors in the pineal gland where serotonin is converted to melatonin by a process of acetylation and methylation. From the majority of evidence available to date, the eyes then need to be open to receive the light impulses in order to shift human rhythms, although a recent report by Campbell and Murphy (1998) suggest that light exposure to vascular areas such as the popliteal region (behind the knee) also may shift these rhythms.

The hormone, melatonin, synthesized from serotonin in the pineal gland, also can serve to shift human circadian rhythms. It serves as a chemical "dark pulse" indicating to the body that physiological responses and behaviors appropriate to night are to be instituted. Thus, it serves as a chemical transducer which sends a signal to the brain opposite to that of light: Melatonin administration in the morning delays circadian rhythms; melatonin in the evening advances them. Since melatonin is regarded as a food supplement, it is not approved by the Food and Drug Administration. At present, therefore, it generally must be obtained from health food stores, where dosages may not be regulated accurately. Studies to date indicate that <1 mg is sufficient to shift human rhythms. Slightly larger dosages (5 mg) may have soporific side effects and may be used to help induce sleep, although the use of melatonin as a hypnotic for insomnia has not been established in persons sleeping at normal circadian phases. It seems to be most useful as a chronobiotic, to induce shifts in circadian phase for short term usage. The safety and efficacy of long term use has not been established.

Bright light has its maximum phase-shifting effects when administered in the middle of the night; alternatively, melatonin has its most potent phase-shifting effects during the middle of the day. It is not practical to administer light in the middle of the night, and administration of melatonin in the middle of the day at higher dosages may induce sleepiness. Thus to mitigate jet lag symptoms, often combining (not simultaneously) light and melatonin administration, each approximately at their critical time points, can be beneficial. The timing of the light or melatonin administration should be based on internal body clock time at the point of departure, not the local time of the destination zone, as the internal clock time must gradually shift to that of the new local time zone. Critically timed light administration of sufficient intensity then can be used, in conjunction with melatonin in appropriate dosages, to shift human circadian rhythms so that they are more in phase with the environmental light/dark cycle of the destination time zone. By realigning these rhythms, the traveler can adjust to the new time zone more rapidly and thereby minimize the symptoms of jet lag. Such interventions may reduce symptoms by up to 50%, but they may not be beneficial in all individuals. More specific

recommendations for light and melatonin administration for eastward and westward change in time zones of 3–6, 7–9 or ≥ 10 h, before and after the day of departure are described below. (The effects of 1–2 h time zone changes generally are minimal, but the same recommendations for 3–6 h. time zone changes also would apply in these cases).

Travel from West to East

In going from west to east, the traveler is shifting to an earlier time zone and thereby undergoing a phase-advance. In order to adjust to the new time zone, he/she must shift their internal biological rhythms earlier. Since the sleep/wake cycle can be more readily shifted than other biological rhythms, treatment is aimed at shifting the timing or phase of melatonin, cortisol, core body temperature and other internal rhythms, that once realigned, allows sleep to occur more readily at appropriate circadian phases. Ideally, interventions should be instituted prior to departure, and depending on the time zones crossed, maintained for 3–4 days following departure.

For a 3–6 h (h) eastward time zone change (for example, 3 h. from Los Angeles, California to New York City or 6 h. from New York City to Paris, France):

The day before and the day of departure: Light: Get bright light (outdoor if possible, or from commercially available light sources—see references, Rosenthal, 1998) in the morning shortly after awakening (before 9:00 a.m.) to advance rhythms. For light intensity in the range of 2,500 lux, 2 h. of exposure is required; for 10,000 lux, 30 minutes. Avoid evening light exposure that would delay circadian rhythms. Melatonin: Before departure, take melatonin in the afternoon (about 3:00 p.m.) in small dosages (< 1 mg to avoid sleepiness) to help advance circadian rhythms. For eastward travel of 6 time zones (e.g. New York City to Paris, France at specific times of the year), taking melatonin at 3:00 p.m. in the departure time zone (in New York City) would be 9:00 p.m. in the destination time zone (in Paris). Allowing 1–2 h. for absorption of the drug, taking melatonin in New York City in the mid-afternoon would be prior to bedtime in Paris. By using this intervention at this time, the brain would receive the chemical message that it was "dark" and begin to respond by inducing nighttime behavior, including sleep, in preparation for the new time zone change. For eastward travel of 3 h. (e.g., from Los Angeles, California to New York City), it would not be necessary to take the melatonin until 6:00 p.m. (Los Angeles time), as bedtime in the destination zone (New York City) at that time would be 9:00 p.m., although melatonin in the midafternoon (at 3:00 p.m. Los Angeles time) is likely to induce maximum phase-shifting effects (Lewy *et al.*, 1998).

Upon arrival: Light: Get morning light to advance circadian rhythms and avoid evening light that would delay them. Melatonin: On day 1, take the medication when it is the same time at your destination point that you took it the previous day at your departure point. For example, if you took the melatonin at 3:00 p.m. in New

York City prior to departure, take melatonin at 9:00 p.m. upon arrival in Paris. As circadian rhythms advance 1–2 h. each day with time zone changes, on day 2 and 3 after arrival in the destination zone, take melatonin 1–2 h. earlier each day. For example, upon arrival in Paris from New York City as described above, if you took melatonin at 9:00 p.m. on day 1, take it at 7:00 or 8:00 p.m. on day 2, and 6:00 or 7:00 p.m. on day 3.

For a 7–9 h. eastward time zone change (for example, from Los Angeles, California, to London, England):

The day before and the day of departure: Light: Get morning light to advance circadian rhythms, and avoid evening light that would delay them. Melatonin: Take a small dose (<1 mg) of melatonin about 2:00 p.m. (about 10:00 p.m. destination time).

Upon arrival: Light: Avoid morning light (as it would be evening time at your departure point, reflective of the timing of your own internal rhythms), which would delay circadian rhythms, antagonistic to the desired phase-advance. Get afternoon light (as this time would be morning in your departure zone), to advance circadian rhythms. Melatonin: Take melatonin (a larger dose of 5 mg is appropriate to induce sleepiness, a side-effect of higher dosages) prior to bedtime when it is the same time at your departure point that you took it the previous day. For example, if you took melatonin at 2:00 p.m. Los Angeles time prior to departure (10:00 p.m. London time), upon arrival, take melatonin at 10:00 p.m. London time on day 1 of arrival. On day 2 and 3 after arrival, take melatonin 1–2 h. earlier each day (for example at 9:00 p.m. on day 2 and 8:00 p.m. on day 3).

For 10 or more eastward time zone changes (for example, from Los Angeles to Jerusalem): Note that for a time zone change near 12 h., it is easier to delay rather than advance rhythms, as the human free-running period (the duration of a rhythm without external influences such as the light/dark cycle) is slightly greater than 24 h. Therefore, given the human tendency to delay rhythms on a daily basis when there are not external constraints, jet lag symptoms generally are shorter and less severe for westward travel (when undergoing a phase-delay) than for eastward travel (when undergoing a phase-advance).

The day before and the day of departure: Light: Get light in the evening and avoid light in the morning to delay circadian rhythms. Melatonin: Take melatonin (<1 mg) on awakening.

Upon arrival: Light: Get morning bright light, and avoid light the rest of the day. Melatonin: On day 1, take melatonin when it is the same time at your departure point that you took it the previous day. For example, if you took melatonin at 7:00 a.m. Los Angeles time before departure, take melatonin at 5:00 p.m. Jerusalem time upon arrival. On day 2 and 3, take melatonin 1–2 h. earlier each day, for example at 4:00 p.m. on day 2 and 3:00 p.m. on day 3.

Travel from East to West

For 3–6 h. westward time zone change (for example, 3 h. from New York City to Los Angeles, California and 6 h. from Paris, France to New York City):

The day before and the day of departure: Light: Get light late in the day to help delay circadian rhythms and avoid light early in the day that would advance circadian rhythms. Melatonin: Take melatonin (<1 mg to avoid sleepiness) on awakening.

Upon arrival: Light: Get light late in the day to help delay circadian rhythms and avoid light early in the day that would advance them. Melatonin: Take a small dose (<1 mg) of melatonin on awakening. On days 2 and 3, take melatonin 1–2 h. later than on the previous day.

For 7–9 h. westward time zone change (for example, from London, England to Los Angeles, California):

The day before and the day of departure: Light: Get light in the evening to delay circadian rhythms and avoid light in the morning that would advance them. Melatonin: Take a small dose (<1 mg) of melatonin on awakening.

Upon arrival: Light: Get midday light (that represents evening light body clock time at your point of departure in London) to delay circadian rhythms and avoid late-day light (that represents morning light body clock time in London) which would advance circadian rhythms. Melatonin: Take melatonin on awakening (<1 mg) to delay circadian rhythms. On days 2 to 4 after arrival, take a small dose of melatonin (<1 mg) 1–2 h. later each day than on the previous day (e.g., at 8:00 and 9:00 a.m. on subsequent days Los Angeles time).

For 10 or more westward time zone changes (for example, from Jerusalem to Los Angeles):

The day before and the day of departure: Light: Get bright light in the evening to delay circadian rhythms and avoid light in the morning that would advance them. Melatonin: Take a small dose (<1 mg) of melatonin on awakening.

Upon arrival: Light: Get morning light (which would be evening light Jerusalem time) to help delay circadian rhythms; avoid evening light (which would be morning light in Jerusalem) that would advance circadian rhythms. Melatonin: Take melatonin (5 mg to induce sleepiness if needed) when it is the same time at the point of departure that you took it yesterday. For example, if traveling from Jerusalem to Los Angeles, if you took melatonin at 7:00 a.m. Jerusalem time before departure (9:00 p.m. Los Angeles time), take melatonin at 9:00 p.m. Los Angeles time on day 1 of arrival and take it 1–2 h. later than on the previous day for days 2–4 after arrival (for example, at 10:00 p.m. and 11 p.m. on subsequent days).

Summary

Appropriately timed bright light and melatonin administration, by helping to adjust underlying circadian rhythms to the new time zone, can serve to mitigate the symptoms of jet lag. Bright morning light advances circadian rhythms; bright evening light delays them. Melatonin in the evening advances circadian rhythms; melatonin in the morning delays them. These principles, applied to the timing of the body's internal biological rhythms, can advance rhythms for eastward travel and delay them for westward travel. Reducing

the symptoms of jet lag by these methods can lessen the mood, cognitive and behavioral symptoms resulting from these desynchronized rhythms.

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