Light Treatment for Sleep Disorders: Consensus Report.

VII. Jet Lag

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Abstract Sleep disturbances are an all-too-familiar symptom of jet lag and a prime source of complaints for transmeridian travelers and flight crews alike. They are the result of a temporary loss of synchrony between an abruptly shifted sleep period, timed in accordance with the new local day-night cycle, and a gradually reentraining circadian system. Scheduled exposure to bright light can, in principle, alleviate the symptoms of jet lag by accelerating circadian reentrainment to new time zones. Laboratory simulations, in which sleep time is advanced by 6 to 8 h and the subjects exposed to bright light for 3 to 4 h during late subjective night on 2 to 4 successive days, have not all been successful. The few field studies conducted to date have had encouraging results, but their applicability to the population at large remains uncertain due to very limited sample sizes. Unresolved issues include optimal times for light exposure on the first as well as on subsequent treatment days, whether a given, fixed, light exposure time is likely to benefit a majority of travelers or whether light treatment should be scheduled instead according to some individual circadian phase marker, and if so, can such a phase marker be found that is both practical and reliable.

Key words sleep, jet lag, circadian rhythms, light, phototherapy, entrainment, phase shift

INTRODUCTION

Rapid transmeridian travel across multiple time zones elicits a range of symptoms that include difficulty in initiating or maintaining sleep, daytime sleepiness and decrements in subjective alertness and performance, gastrointestinal distress, and other psychosomatic manifestations (Comperatore and Krueger,

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1990; Winget et al., 1984). Collectively known as jet lag, these symptoms are attributable to three major concomitants of long-distance air travel: flight-related stress and fatigue, sleep loss, and altered temporal relations between the circadian timing system and the new local day-night cycle, as well as between different rhythmic functions within the individual traveler. Of these, the disruptions in circadian phase relations are unique to east-west flights (Hauty and Adams, 1966c; Gerritzen et al., 1969; Sasaki et al., 1985; Buck et al., 1989), and, due to the gradual nature of circadian reentrainment, their effects can last considerably longer than the 1 or 2 days required to recover from flight-induced fatigue and sleep loss.

The following sections will examine the course and duration of reentrainment of circadian rhythms following time zone changes, the nature of the sleep disturbances resulting from such changes as determined by polysomnography, and, finally, recent attempts to accelerate the reentrainment process and alleviate the symptoms of jet lag using timed exposure to bright light.

CIRCADIAN REENTRAINMENT FOLLOWING TIME ZONE CHANGES

The time required for circadian rhythms to resynchronize to a shifted day-night cycle depends not only on the size of the shift (the number of time zones crossed) but also on its direction, the rate of readjustment being generally faster after westward than after eastward travel. For flights across 5 to 11 time zones, mean reentrainment rates of 92 min/day (westward) and 57 min/day (eastward) were derived from one set of studies (Aschoff et al., 1975), and rates of 88 min/day (westward) and 56 min/day (eastward) from another (Klein and Wegmann, 1980).

This directional asymmetry is not dependent on whether the flights are outbound or homebound or on whether they are day or night flights (Klein et al., 1970, 1972a, 1972b; Wegmann et al., 1970). Rather, it is generally attributed to the fact that, following westward travel, circadian rhythms reentrain to the delayed day-night cycle by gradual phase delays, that is, by temporarily assuming periods longer than 24 h, while after eastward travel, circadian rhythms usually reentrain by gradual phase advances, that is, by temporarily assuming periods shorter than 24 h. Since the natural periods of human circadian rhythms, measured in the absence of daily time cues, tend to be longer than 24 h, it follows that reentrainment will be faster after westward than after eastward flights (Aschoff et al., 1975).

This explanation also accounts for the occasional occurrence of reentrainment by phase delay following phase advances of the day-night cycle. Such an antidromic phase response (Klein and Wegmann, 1980) has been observed in laboratory studies after 6-h and 9-h phase advances (Wever, 1980; Moline et al., 1992; Samel et al., 1991b) as well as in field studies after eastward flights across 8 to 11 time zones (Colquhoun, 1979; Klein and Wegmann, 1980; Gander et al., 1989; Nickelsen et al., 1991; Spencer et al., 1994). In some of these cases, one rhythmic function reentrained antidromically while another did so in the usual direction, by phase advance, a phenomenon termed reentrainment by partition (Aschoff, 1978; Samel et al., 1991b).

The reentrainment rates listed above are average figures across the entire reentrainment period, and across different rhythmic functions, different subjects, and different conditions. As such, they hide a number of complexities. First, the rate of reentrainment is rarely constant over time. Rather, the size of the daily phase adjustment tends to be proportional to the phase angle difference between the circadian timing system and the shifted zeitgeber (Klein and Wegmann, 1980). Thus reentrainment rate is generally highest immediately after the shift, decreasing progressively thereafter (Aschoff et al., 1975).

Different rhythmic functions often reentrain at different rates (Klein and Wegmann, 1980; Fèvre-Montange et al., 1981; Halberg et al., 1977; Elliott et al., 1972; Hauty and Adams, 1966a, 1966b), leading to a transient internal dissociation within the individual (Aschoff, 1978). Klein and Wegmann (1979, 1980) have pointed out that the more slowly adapting functions tend to show more robust circadian oscillations under normal entrainment conditions than rapidly adapting functions, suggesting that the rate of adaptation of a given function may reflect the relative contributions of endogenous circadian timing and exogenous masking effects in determining its daily pattern. For some functions, assessment of reentrainment rate is further complicated by distortions of the daily waveform, with different phase references—daily maxima and minima, for example—resynchronizing at different rates (Désir et al., 1981; Wegmann et al., 1970; Sasaki, 1964; Härmä et al., 1993). Reductions in the range of oscillation and changes in mean daily level have also been reported (Klein and Wegmann, 1979, 1980). Recent computer simulations (Daan and Beersma, 1992) indicate that masking effects, waveform distortions, and the specific curve-fitting procedures used for phase assessment can all lead to unequal reentrainment rates for different overt rhythms, even when these rhythms are generated by the same circadian pacemaker.

The conditions travelers are exposed to and the activities they engage in after transmeridian flights can markedly affect the duration of readaptation. Klein and Wegmann (1974) found that reentrainment of psychomotor performance rhythms following 6-h time zone shifts was 50% faster in subjects allowed outdoor activities every other day than in subjects confined to their hotel rooms. The authors attributed this result to differences in the strength of social time cues experienced by the two groups. However, recent demonstrations that human circadian rhythms can be reset by bright light suggest that the faster adaptation seen in the outdoor group may have been due, at least in part, to their being exposed to daylight (Lewy et al., 1981). Exposure to strong social and light cues may also account for the unusually rapid initial adjustment reported in military units following eastward airlifts (Adam et al., 1972; Colquhoun, 1979; Graeber, 1980; Graeber et al., 1981), as military populations frequently engage in both group and outdoor activity. Finally, there is some evidence that reentrainment following transmeridian flights may be faster in summer than in winter, possibly because the longer daylengths afford greater opportunity for exposure to natural daylight (Suvanto et al., 1993).

There are also marked individual differences in the rate of adjustment after time zone transitions (e.g., Klein et al., 1977). One of the factors underlying these differences is age. Following flights between Oklahoma City and Tokyo, 40- to 48-year-old subjects required longer to reentrain their body temperature rhythms and reported greater fatigue than 19- to 23-year-old subjects (Hauty and Adams, 1965). In a laboratory study simulating a 6-h eastward (advance) transition, middle-aged subjects showed more sleep disruption than young subjects and reported larger decrements in daytime alertness and a greater increase in sleepiness (Moline et al., 1992). Although the mean rate of reentrainment of body temperature rhythms did not differ between the two groups, two of the eight older subjects showed an antidromic (delaying) response, whereas all six young subjects reentrained by phase advance. Greater sleep disturbances in older travelers were also observed after flights between London and San Francisco (Evans, 1970; Evans et al., 1972). Flight crews operating long-haul routes showed no age-related differences in sleep alterations during the first layover after a transmeridian flight (Nicholson et al., 1986a), but older crew members showed greater cumulative sleep loss during commercial and military long-haul flight operations with multiple layovers (Preston, 1973; Gander et al., 1993). The higher susceptibility of older persons to jet lag has been attributed to greater difficulty in sleeping at abnormal circadian phases (Klein and Wegmann, 1980; Graeber, 1982; Moline et al., 1992).

Other factors contributing to interindividual variations include such rhythm characteristics as phase angle of entrainment (Colquhoun, 1979), and, possibly, rhythm amplitude and stability (Comperatore and Krueger, 1990; Klein and Wegmann, 1980; Graeber, 1982; Winget et al., 1984). Personality variables, among them introversion/extraversion and neuroticism, may also play a role (Colquhoun and Folkard, 1978; Suvanto et al., 1993).

Overt daily rhythms are the product of endogenous circadian timing as well as exogenous masking influences from the environment and from one's own behavior, particularly activity, sleep, and meal patterns. Most transmeridian travelers immediately shift their daily habits to conform with the new local time, thereby influencing the apparent rate of reentrainment of their rhythmic functions. When masking influences are minimized through the use of constant routines (Mills et al., 1978), or when their estimated effects are eliminated mathematically (Folkard, 1989; Folkard et al., 1991), reentrainment rate is consistently slower than when it is assessed using standard procedures.

SLEEP DISTURBANCES

Westbound transmeridian flights are typically scheduled as day flights. Passengers boarding an airplane in San Francisco at 1200 h would, after an 11-h flight, reach Tokyo at 1600 h local time. Due to the 7-h time difference, this would correspond to 2300 h San Francisco time, roughly the time at which they would normally retire for the night. By immediately adopting local time schedules, however, they would delay their sleep for several hours, eventually retiring at about 2300 h Tokyo time, or 0600 h San Francisco time.

Eastbound flights, on the other hand, are typically night flights. Passengers departing San Francisco at 1700 h would arrive in London at 1100 h the next morning, local time, having crossed eight time zones in the course of a 10-h flight. By postponing sleep until 2300 h London time, they would be going to bed at 1500 h San Francisco time.

Thus, in both cases, the travelers would be going to sleep at abnormal circadian phases after being awake considerably longer than usual. Sleep characteristics under these conditions have been documented by polysomnography in passengers (Evans, 1970; Evans et al., 1972; Klein et al., 1976; Sasaki and Endo, 1977; Athanassenas and Wolters, 1981; Endo et al., 1981; Sasaki et al., 1985; Désir et al., 1981; Nicholson et al., 1986b, 1988), as well as in aircrew, both during the first layover after transmeridian flights (Dement et al., 1986; Sasaki et al., 1986; Nicholson et al., 1986a; Wegmann et al., 1986) and throughout a 6- or 7-day polar flight schedule between London and tokyo (Spencer et al., 1991; Sasaki et al., 1993). The results are generally consistent with current understanding of circadian and homeostatic regulation of sleep, itself derived largely from laboratory studies of sleep displacement and deprivation.

Sleep latency is usually reduced on the first night after both eastward and westward travel, mainly as a result of prior sleep deprivation. On subsequent nights, sleep latency returns to normal after westward flights, in some cases gradually, while after eastward flights sleep latency may return to or exceed normal values.

Total sleep time is often unchanged following flights in either direction, although decreases after the first night have been reported following westward flights. Early awakening, sleep interruptions in the later part of the night, and, occasionally, a reduction in sleep efficiency are also observed after westward flights.

An increase in slow wave sleep (SWS) is generally reported on the first night after both eastward and westward travel, as well as after north-south flights, and is attributable to prior sleep loss. Two or more days may be required before SWS levels return to baseline.

Rapid eye movement sleep (REMS) is frequently reduced on the first night, particularly after eastward travel. This effect is due to the advance in sleep onset time after eastward flights and, possibly, to competition from SWS, which may have a higher priority after prolonged wakefulness. The decrease in REMS can persist for 2 nights or more after eastward flights, but REMS levels return to or exceed baseline levels following westward flights. Westward travel is also followed by a decrease in REMS latency, with occasional sleep onset REMS episodes and a shift in REMS to an earlier time of the night.

As with other functions, the time required for all sleep parameters to return to baseline levels tends to be longer after eastward than after westward travel (Nicholson et al., 1986b; Sasaki et al., 1985; Gander et al., 1989).

Sleep disturbances are of particular concern in airline personnel on transmeridian routes. Such disturbances are consistently reported by flight crews (Raboutet et al., 1958; Lavernhe et al., 1965; Cameron, 1969; Smolensky et al., 1982; Sasaki et al., 1985; Suvanto et al., 1990; Härmä et al., 1994; Haugli et al., 1994), with night wake and difficulty falling asleep as the prime complaints (Sasaki et al., 1985). In a survey of French aircrew on transatlantic routes, 25% to 35% of the respondents reported needing 3 nights or more before achieving normal sleep (Lavernhe et al., 1965). Sleep deficits may also be incurred on long-haul routes with multiple layovers (Preston and Bateman, 1970; Preston, 1973; Samel and Wegmann, 1988; Samel et al., 1991a; Sasaki et al., 1993), although many crewmembers are able to obtain normal amounts of sleep during such routes, often by supplementing nocturnal sleep with daytime naps (Nicholson, 1970; Preston, 1973; Schreiber et al., 1988; Spencer et al., 1991). However, in a study of military transport aircrew on transmeridian missions lasting several days, crewmembers reported sleeping slightly longer during the mission than before departure (7.3 h versus 6.8 h), yet slept for 9.9 h, 9.2 h, and 8.9 h on the first 3 nights after the mission (Hartman, 1971). These results suggest that changes in sleep quality, resulting from sleep displacement and fragmentation, can contribute to the accrual of a significant sleep debt even when sleep quantity is unchanged.

BRIGHT LIGHT TREATMENT FOR JET LAG

Recent demonstrations of entrainment and resetting of the human circadian system with bright light (see related task force section, Dijk et al., 1995 [this issue]) hold the promise for the development of similar procedures to alleviate the effects of jet lag by accelerating reentrainment to new time zones. That promise, however, remains largely unfulfilled, as only a handful of field studies, all preliminary, have been performed to date, and even laboratory simulations have thus far yielded mixed results.

Laboratory Simulations

The laboratory studies reviewed below are those specifically described by their authors as jet lag simulations, with the exception of one study described as being applicable to both jet lag and shift work (Honma et al., 1991). Other, related studies are reviewed in the task force section on shift work (Eastman et al., 1995 [this issue]). It is clear, however, that the distinction between jet lag and shift work simulations is somewhat arbitrary, and in neither case are subjects exposed to the full complement of time cues normally encountered by transmeridian travelers.

Wever (1985) compared reentrainment rates of two subjects following two phase delays of an artificial light-dark (LD) cycle in a laboratory study simulating westward time shifts. The first shift was performed under normal indoor light intensities (< 1500 lux), the second under bright light (2000 to 5000 lux in most parts of the experimental room). Mean reentrainment rates of body temperature over the first 3 postshift days were 1.0 h/day under normal illumination and 1.4 h/day under bright light.

In a more recent study (Honma et al., 1991), five subjects twice underwent an 8-h advance of their sleep-wake schedule, during which they were exposed to either bright (5000 lux) or dim light for 3 h on 3 successive days. Light treatment began at 0700 h on the day of the shift, and was advanced by 3 h on each of the following 2 days. Faster reentrainment of body temperature and plasma melatonin rhythms during the bright light condition was observed in four subjects, the fifth subject showing antidromic reentrainment in both conditions.

Other simulation studies have been less successful. Moline et al. (1989; 1990) exposed subjects to 2500 lux for 4 h following a 6-h phase advance of a dim, indoor level, LD cycle (300 to 500 lux). The light treatment began at the preshift midsleep time on the first postshift day, and immediately after waking on the next 3 days. Thus a subject whose normal sleep period is 2400 to 0800 h would be exposed to light starting at 0400 h on the first day and at 0200 h on the following days. During the first 5 days after the shift, the temperature rhythms of the bright light subjects advanced at the same rate as those of dim light controls but then appeared to delay again on the following 2 days. Some of the bright light subjects also showed long-lasting reductions in circadian amplitude. Polygraphic sleep recordings revealed no substantial differences between the two groups. More recently, Samel et al. (1992) exposed subjects to bright light for 4 h following a similar 6-h advance shift. The treatment was scheduled on 2 consecutive days, starting either at 0400 h or at 1300 h. Reentrainment rates of body temperature rhythms did not differ between the two light exposure times, except on the first postshift day when the phase shift of the morning light group exceeded that of the afternoon group by 1.16 h.

The failure of bright light treatment to accelerate reentrainment in the latter two studies may be attributable to the timing of light exposure, which was earlier than in the study by Honma et al. (1991). A common feature of single-pulse and triple-pulse human phase response curves (PRCs) for light is the occurrence of the delay-to-advance transition point near (Minors et al., 1991; Czeisler et al., 1989) or 1 hour after (Van Cauter et al., 1994) the time of the minimum of the body temperature rhythm, T_{min}, initially reported to precede habitual wake onset by 2 to 3 h (Minors et al., 1991; Czeisler et al., 1989). When measured in young men during constant routines, T_{min} was found to occur around 0500 h (Dijk et al., 1992; Dawson et al., 1992; Van Cauter et al., 1994), although in one study, T_{min} occurred on average at 0614 h (Shanahan and Czeisler, 1991), and in another at 0648 h, only 1.5 h before habitual wake onset (Czeisler et al., 1992). Some of these authors also report considerable variability in the timing of T_{min}, both within and between subjects (Dawson et al., 1992; Czeisler et al., 1992; Van Cauter et al., 1994). It is possible, therefore, that in the two largely unsuccessful studies, the light pulses did not fall entirely within the advance region of the PRC, as was intended. Other procedural differences, including light intensity levels and number of light exposures, may also have contributed to the differing outcomes.

It should be noted that in the simulation studies described above, phase shifts of the temperature rhythm were assessed in the presence of masking effects, including, on treatment days, possible direct effects of bright light exposure on body temperature (see related task force section, Campbell et al., 1995 [this issue]). In one case, subjects in both dim and bright light conditions showed phase advances of up to 8 h on the first day postshift (Honma et al., 1991, Fig. 1). Such phase shift estimates may be more a reflection of the subjects' altered sleep-wake pattern than of endogenous circadian phase, as recent evidence indicates that in dim light, when measures are taken to minimize masking effects, the circadian temperature rhythm shows little or no adjustment to a shifted sleep-wake schedule and may free-run instead at a period slightly longer than 24 h (Czeisler at al., 1990; Kronauer et al., 1993).

Field Studies

The first field attempt at bright light treatment for jet lag relied on scheduled exposure to natural daylight following eastward flights across nine time zones (Daan and Lewy, 1984). Two subjects were studied, one of whom was asked to expose himself to daylight for 3 h starting at 0700 h local time (2200 h in the original time zone), the other starting at 1000 h (0100 h original time). The schedule was followed for 7 days, starting on the first postflight day. The timing of light exposure was derived from animal PRCs, as human PRCs had not yet been published. Accordingly, the transition between light-induced delays and advances was assumed to lie midway between dusk and dawn. Thus daylight at 0700 h was intended to induce a phase delay, and daylight at 1000 h a phase advance. Based on sleep logs and oral temperature readings during waking hours, the subject exposed to light at 1000 h advanced to the new phase in about 6 days, whereas the subject exposed to light at 0700 h appeared to reentrain antidromically, by phase delay, and was still not fully adapted after 13 days.

These results, however, are difficult to reconcile with the more recent human PRCs, according to which both exposure times would have fallen within the delay region; indeed, light exposure would be expected to cause a larger phase delay at 1000 h than at 0700 h. It is worth noting that, except during scheduled light treatments, the subjects in this and other field studies were free to engage in activities of their choice, and no attempt was made to limit their exposure to bright light at times when such exposure might hinder reentrainment.

The phase-resetting protocol developed by Czeisler et al. (1986) has proven highly effective in a laboratory setting. This protocol was applied to a single subject upon his return from Tokyo to Boston (Czeisler and Allan, 1987). The phase of his body temperature rhythm was first assessed during constant routine, and the subject was then exposed to bright artificial light (7000 to 12000 lux) for several hours on 3 consecutive days starting in early afternoon. Reassessment of temperature phase during a second constant routine 5 days after the flight indicated a large delay of 11.25 h.

Two additional field studies have examined the effects of morning bright light treatment on postflight sleep patterns. In the first (Cole and Kripke, 1989, and unpublished manuscript), 19 travelers returning to California from trips to the Orient or South Pacific (advance shifts of 6.5 to 10 h) were instructed to expose themselves to either bright white light (2000 lux) or dim red light (< 100 lux) for 2 to 3 h upon awakening in the morning. This schedule was followed for 3 days, during which the subjects kept daily sleep logs. No differences were observed between the group means for any sleep measure, but in the bright light group, the time of light exposure on the first postflight day correlated negatively with percentage nighttime sleep averaged across the first 3 postflight days. Thus exposure to bright light early in the morning appeared to facilitate the consolidation of sleep into a single nighttime episode.

In the second study (Sasaki et al., 1989), polysomnographic recordings were obtained from four subjects before and after a flight from Tokyo to San Francisco (8-h advance). In San Francisco, the subjects were required to go to bed at 2300 h and be up by 1000 h and were exposed on 3 consecutive days to either bright (> 3000 lux) or dim (< 500 lux) light for 3 h starting at 1100 h (0300 h Tokyo time). On the first 4 nights, the bright light subjects showed higher sleep efficiency and less wake after sleep onset than dim light subjects, the latter exhibiting prolonged wakefulness during the first half of the night. These observations suggest that the bright light treatment may have been effective in accelerating circadian reentrainment, despite the fact that the timing of light exposure was even earlier than in the two largely unsuccessful simulation studies described above. With only two subjects per condition in the field study, it is of course impossible to rule out individual differences as a factor. However, light treatment in the laboratory studies began on the day of the shift, whereas in the field study it began on the day after the flight, by which time the subjects' rhythms may have advanced somewhat in response to local zeitgebers.

For aircrew scheduled to return to home base after brief layovers, staying on home time may be preferable to trying to adjust to local time, as this eliminates the need for readjustment after the return flight. Indeed, a survey of flight personnel (Lavernhe et al., 1965) showed that, after flights from Paris to North America, 23% of all respondents (and 41% of those over 50 years) reported going to bed before 1900 h local time, or 0100 h Paris time. In such cases, bright light treatment may be used to maintain entrainment to home time rather than to accelerate reentrainment to new local times.

In summary, although decades of animal and human research attest to the efficacy of timed exposure to light as a means of manipulating circadian timing systems, much remains to be learned before procedures can be developed that are at once effective, reliable, and practical. For this to happen, optimal combinations of several light exposure parameters—timing, intensity, spectral composition, duration, and number of repetitions—must first be defined and tailored to specific flight situations.

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