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Circadian Rhythms, Jet Lag, and Shift Work, With Particular Reference to Athletes

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Changes in individuals' sleep-wake cycles lead to negative side effects. This review considers how side effects can be reduced, the recommendations being based largely on work performed at our institute. Subjects journeying to Australia had symptoms of jet lag that did not adjust synchronously, and the best predictors of jet lag were their travel arrangements. The value of melatonin in reducing jet lag was not confirmed but, in a laboratory-based study, evening administration of melatonin did not result in worse performance the next morning. The effects of exercise upon the phase of the body clock were insubstantial. Gut temperature, unlike insulated axilla temperature, was an acceptable substitute for rectal temperature. Ascertaining by questionnaire why people ate or did not eat at a particular time indicated that night work exerted a considerable disruptive influence, one of the main factors being time pressure. Compared with day workers, night workers had less appetite, ate cold rather than hot meals, and felt more bloated after a meal. Actimetry provided objective measures of the adjustment of the sleep-wake cycle to time-zone transitions and to night work. These measures could be applied to data from long-haul pilots, in whom there are both time-zone transitions and night work.

Key Words: time-zone transition, melatonin, core temperature, feeding habits, activity

Key Points:

1. Different symptoms of jet lag do not adjust to time-zone transitions at the same rate.
2. Melatonin does not reduce jet lag in athletes, and exercise does not promote phase shifts of the body clock.
3. Altered food intake (smaller meals) in night workers is determined by time pressure and habits rather than by inadequate facilities.
4. Actimetry is a simple alternative for assessing the negative effects of shift work and time-zone transitions.

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A. General Background

Humans, like other animals, possess a body clock, situated in the suprachiasmatic nuclei (SCN) in the hypothalamus. In the absence of external time cues, this clock tends to run with a period of about 24.3 hours. By means of rhythmic changes in the external environment (zeitgebers), coupled with rhythmic signals from melatonin (released by the pineal gland, an "internal zeitgeber"), the clock becomes synchronized to the environment and solar day. The body clock influences the whole body, acting via the rhythmic changes it produces in core temperature, the autonomic nervous system, blood-borne hormones, and the sleep-wake cycle (4).

Normally, the body clock is responsible for: increasing alertness, and mental and physical activity, in the daytime; preparing the body in the evening for sleep; enabling consolidated sleep to take place at night; and preparing the body towards the end of sleep for wakening to face the new day. The timing of the body clock is stable, and transient changes to a normal routine—for instance, waking in the middle of the night to empty one's bladder or taking a nap in the daytime—producing no change in the phase of the body clock (20).

However, humans are abnormal insofar as they sometimes change their habits, thereby acting against the effects that this timing system exerts upon the body. First, a substantial proportion of the working population works at night (and sleeps in the day) and, second, it is becoming increasingly common for humans to undertake long-haul flights across time zones, for business or pleasure. In both of these circumstances, the normal synchrony between the body clock and the environment is transiently lost, and the individual feels "below par".

After a time-zone transition, these negative feelings are called "jet lag"; during night work, they are called "shift workers' malaise" (8, 9, 20, 23). In both cases, individuals feel tired and perform less well during their wake time, because the body clock is indicating that they should be asleep; and yet they have difficulty sleeping well, since the body clock is now indicating that they should be awake.

The purpose of the present report is to review and synthesize the findings from a series of studies that have been conducted to understand better these problems and to alleviate them.

B. Time-Zone Transitions

Much effort (reviewed in 9, 23) has gone into assessing: the factors that are responsible for jet lag; the time course of recovery from it while staying in the new time zone; how its severity depends upon the direction of flight and upon the individual; and various means of reducing its severity (melatonin ingestion being one of the main ones). Many of these studies have assessed jet lag once per day. For this assessment, a tick is placed somewhere along a 10-cm visual analogue scale (VAS), the ends of which are labeled 0 (*no jet lag*) and 10 (*very bad jet lag*). Alternatively, a number in the range 0–10 is recorded. The advantages of these methods are their simplicity and convenience.

Our recent work has concentrated on various aspects of jet lag and its possible treatment with melatonin. The subjects we have used generally flew from the United Kingdom (UK) to Australia, in preparation for the 2000 Olympic Games, or other events in this area of the world (transitions across 8–10 time zones). The flight was in two legs, with a short stopover (1–2 hours) in Singapore or Bangkok. All journeys took about 24 hours. The subjects were highly motivated—elite athletes, their coaches or other administrators, or academics attending a scientific conference.

B.1. The Symptoms of Jet Lag and the Time Course of Their Recovery After a Time-Zone Transition.

Background. Jet lag produces a group of symptoms (9, 20, 23), included amongst which are the following:

- loss of motivation, commitment, and the ability to concentrate;
- increased irritability and frequency of headaches;
- knowing that one is hungry, and yet loss of appetite;
- indigestion and bowel irregularities;
- fatigue in the daytime, and yet inability to sleep uninterruptedly at night.

In general, it would be predicted that, if the above symptoms were equally valid assessments of jet lag, then they would all be raised most on the first day after arrival, and then decline on subsequent days with similar time courses. However, it would appear that the amount of jet lag might depend upon the time in the new time zone that the assessment was made. Thus, on waking, it might reflect the inadequacy of the previous night's sleep; during much of the daytime, jet lag would reflect increased fatigue and decreased motivation and, when retiring at night, it would be more likely to reflect an inappropriate feeling of wakefulness at this time. Also, jet lag is likely to be influenced more by changes to appetite and enjoyment of food if it were measured just after a mealtime.

Therefore, the first question addressed was whether all subjective symptoms of jet lag showed the same time course of adjustment, and if all predicted an assessment of jet lag equally reliably (25).

Methods. Thirty-nine subjects were studied for the first 6 days in Australia after their flight from the UK. Each subject was asked to assess jet lag five times each day: soon after rising in the morning (08:00 h); at about noon; in the late afternoon (16:00 h); in the early evening (20:00 h); on retiring at about midnight. At the same time, they were asked to answer the Jet Lag Questionnaire, which we had designed for this study. In the morning, this questionnaire asked about aspects of sleep (ease of getting to sleep, number of waking episodes, early waking, and so on); at noon and 16:00 h, about mood and mental performance; at noon, 16:00 h, and 20:00 h, about meals: on retiring, about bowel activity; and at all five times, about fatigue. Subjects were not advised as to the exact meaning they should assign to jet lag or to any of the other symptoms used in the questionnaire.

Results. The daily means of the ratings of jet lag were compared with the mean daily assessments of the other variables. There were parallel time courses (that is, the symptoms were most marked on the day of arrival and decreased on successive days) for mean daily jet lag and mean daily fatigue, some aspects of sleep assessment (number of waking episodes, waking too early and decreased alertness 30 min after waking), and the mean daily fall of concentration. By contrast, the other variables did not change reliably, or not in parallel, with the amount of jet lag (Figure 1).

Multiple linear regression analyses indicated that 29% of the total variance in jet lag assessments was accounted for by fatigue, 22% by the significant sleep

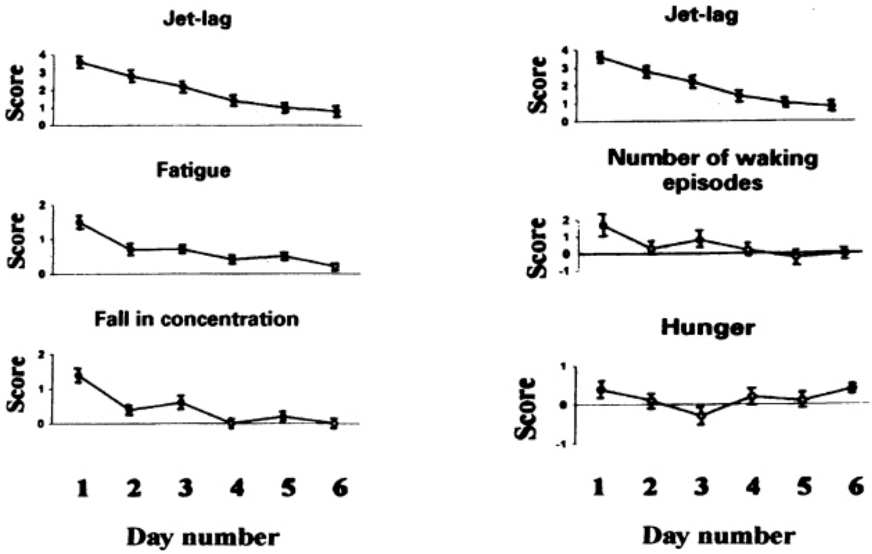

Figure 1 — The time courses of adjustment of jet lag and some of its symptoms in the 6 days after a flight from the UK to Australia (10 time zones to the east). Daily means (±*SE*) for 39 subjects shown. (Based on 25.)

predictors, and 28% by the fall in concentration. These relationships, though highly significant statistically, indicate that the parallelism is by no means exact. The percentage of total variance accounted for by the other variables was less than 3%.

Discussion and Conclusions. Ratings of jet lag show a general parallelism with some of its symptoms—alterations to sleep, daytime fatigue, and loss of concentration—but not with others—appetite or bowel habits, for example. An association with a specific symptom might depend upon the time of day of assessment. Thus, there were moderately strong links between assessments of jet lag and:

- some aspects of sleep in the morning;
- a fall in the power to concentrate in the middle of the day;
- an increase in fatigue throughout the daytime.

These findings argue for the time of assessment of jet lag to be the same on successive days in a study. They also suggest that assessments in the morning are likely to be more influenced by sleep problems than would assessments during the waking period, when effects of daytime fatigue and loss of concentration also might contribute to the overall rating of jet lag.

B.2. Can Those Who Will Be Most Adversely Affected By Jet Lag Be Predicted?

Background. It is suggested (see, e.g., 11) that the following characteristics of individuals might alter their rate of adjustment to a time-zone transition:

- Age: younger subjects will have less difficulty and adjust more rapidly;
- Chronotype: Those who are "larks" (morning types) will adjust to an eastward shift more readily than "owls" (evening types), since their body clock is phased earlier and might have a slightly shorter inherent period. The opposite should hold for time-zone transitions to the west.
- Flexibility of sleeping habits: Those who are better able to adjust their times of sleeping, and the conditions in which they sleep—the hardness of the mattress, for example—should be at an advantage.
- Languor: Those who score highly on this measure have an inability to disregard feelings of fatigue, and experience difficulties with continuing their activities effectively if they feel fatigued. These should be disadvantaged.
- Fitness: Those who are physically fitter should experience less difficulties with adjustment.

However, the experimental support of these predictions is weak; therefore, the objective (28) was to establish whether any of the above act as predictors for the amount of jet lag and its symptoms experienced after a long-haul flight. To these possible predictors were added possible effects of gender, experience of long-haul travel (defined as *yes* or *no*), time of arrival in Australia (the morning or late afternoon by Australia time), and direction of phase adjustment (advance or delay, see below).

Methods and Measurements. Eighty-five subjects participated in this study. Their exposure to light in Australia was not controlled, but subjects were not allowed to sleep in the daytime in Australia, except for a short nap, if desired, immediately after arrival. Before leaving the UK, their scores on the questionnaires referred to above and the other relevant information were obtained. They were required to give details of their two flights (before and after the stop-over in Singapore or Bangkok), in particular, the amount of sleep taken on each flight.

For the first 6 days after arrival in Australia, they were required to answer the jet lag questionnaire on 4 or 5 occasions per day. On the first full day, and the 3rd and 5th days after arrival, subjects also measured intra-aural temperature (Genius 1000, Sherwood, Nottingham, UK) and right hand grip strength (Takei Kiki, Kogyo, Tokyo, Japan) just before answering the jet lag questionnaire. (Precautions were taken that subjects had been seated indoors for about 30 min before these measurements.) The profiles of the temperature and grip strength rhythms were used to estimate if adjustment of the body clock had been by phase advance or delay.

Stepwise multiple regression analyses were used to assess significant predictors for jet lag and its symptoms; results from all days and times of day were pooled. (Details of these times are given in the previous study.)

Results. The scores for chronotype, flexibility of sleeping habits, languor, gender, and fitness were rarely significant predictors. The only predictors that were found at all frequently were previous experience of long-haul travel, age, and time of arrival in Australia.

The main findings were:

- previous experience of long-haul travel was associated with retiring to bed earlier;
- both age and arriving in the afternoon (rather than the morning) in Australia were associated with less jet lag and less fatigue;

- adjustment of circadian rhythms by a phase advance was associated with increased jet lag in the middle of the day during the last days (days 5 and 6) of the study.

Discussion and Conclusions. The main conclusion was that, in subjects who are highly motivated, the choices of itinerary and lifestyle are more important for reducing jet lag than are personality characteristics such as chronotype or flexibility of habits.

Those for whom such a long-haul flight was a new experience wanted to stay up rather than retire; by contrast, those who had done the flight before tended to go to bed earlier. This is hardly surprising, there being an element of "adventure" for those who had not traveled this far before. The finding that age was associated with less jet lag was the opposite of prediction, but accords with the view from laboratory simulations that older subjects are better able to "pace themselves" when dealing with the effects of sleep loss (18).

Those subjects who arrived in Australia in the afternoon appeared to have several initial disadvantages in comparison with those who arrived early in the morning. They had left the UK in the morning, so having had to get up earlier than those who had left in the evening. Also, for those who departed in the morning, their first flight had been in the daytime, and they had slept significantly less on this flight compared with those who had left in the evening and flown through the night (about 1.5 vs. about 5.5 hours). Both groups had spent about the same amount of time sleeping during the second flight (about 2.5 hours). Why might the afternoon arrivals suffer less jet lag, therefore? We suggest that their advantage was that they could attempt their first full sleep in a bed during the Australian night about 30 hours after having risen from their last sleep at night in a bed in the UK. By contrast, those who had arrived in the morning, even though they had taken a nap on arrival and had slept more on the plane, did not have the opportunity for a full sleep in a bed at night until about 50 hours after rising from their last sleep at night in a bed in the UK.

For all subjects, immediately after arrival in Australia, their temperature minimum, and time of worst performance, was at about 15:00 h by local time. For those who adjusted by phase delay, this time would become later, soon coinciding with the evening and time for relaxation. By contrast, for those who adjusted by phase advance, the time of worst performance would advance through the early afternoon and then the morning. This would account for their greater feelings of jet lag on the 5th and 6th days after arrival.

In summary, these results stress the importance of planning travel schedules and lifestyle in the new time zone, if the aim is to minimize the inconveniences of jet lag. If disruptions during the working day are to be minimized, then there would also seem to be an argument for attempting to use light to promote adjustment to the new time zone by a delay rather than an advance of the body clock.

B.3. Can Melatonin Aid Recovery From Jet Lag?

Background. There is a large amount of scientific literature indicating that the timed ingestion of melatonin can alleviate jet lag (9, 23). In most of these studies, jet lag was measured by a simple VAS (see above), and only once per day, this time not always being reported. Moreover, even though melatonin is believed to act as a "natural hypnotic", and its evening ingestion would accord with this role, there is other evidence to indicate that it might act as a chronobiotic, that is, as an agent to promote a phase shift of the body clock (14). In this case, the chronobiotic effect will depend upon the time of ingestion. After a flight to the east through 10 time zones, evening ingestion (by the new local time) would be predicted to cause a phase delay, for example.

The objectives were to determine whether melatonin ingestion in the evening on local time alleviated the symptoms of jet lag at all times of the day, and whether it influenced the direction of phase adjustment of the body clock (5).

Methods. Seventeen control subjects (placebo pill) and 14 experimental subjects (5-mg melatonin) participated in a double-blind design. The pill was taken at 18:00 h by departure time when on the plane, and then 20:00 h by local time after arrival. Subjects answered the jet lag questionnaire four times per day (08:00, 12:00, 16:00, and 20:00 h) for the first 7 days in Australia. For the purposes of analysis, Day 1 was defined as starting at 16:00 h on the day of arrival, Day 2 as starting at 16:00 h on the day after arrival, and so on. This gave 6 complete days. Grip strength (Takei Kiki Kogyo, Tokyo, Japan) and intra-aural temperature (Genius, Ballymoney, N. Ireland) were measured immediately before answering the questionnaire. (Whenever possible—subjects all had a very busy schedule—precautions were taken that subjects had been seated indoors for about 30 min before these measurements were taken). The profiles of the temperature and grip strength rhythms were used to estimate if adjustment of the body clock had been by phase advance or delay.

Three-way ANOVA with repeated measures was used to compare the Groups (2 levels), Days (6 levels), and Times of Day (4 levels).

Results. The mean ratings of jet lag are shown in Figure 2. Whilst they suggest that melatonin was associated with a fall in jet lag of about 0.5 unit, the ANOVA did not lend statistical support to this, due to the large amount of variation in the results;

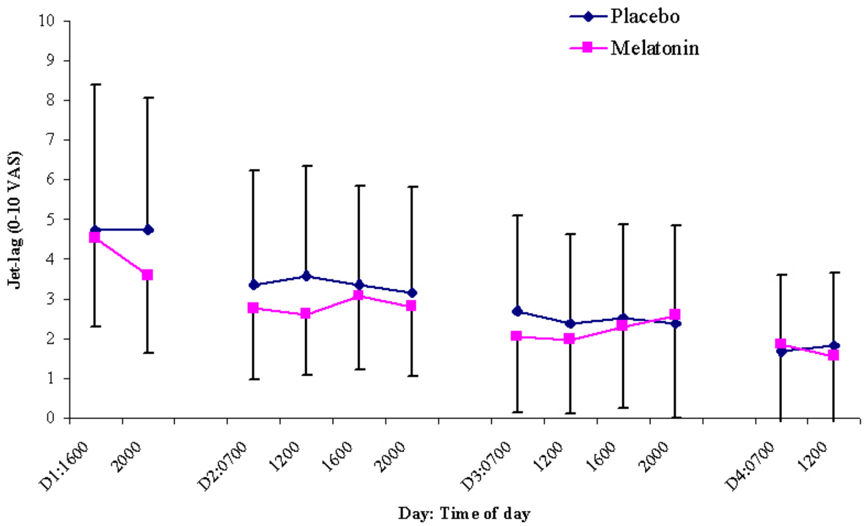

Figure 2 — Mean (±*SD*) jet-lag in control group (placebo, *N* = 17) and experimental group (melatonin, *N* = 14), during the first days after a flight from UK to Australia. (Based on 5.)

even though there were significant effects of Day number and Time of Day, there was no significant group effect or interaction between Group and the other ANOVA factors. A lack of significant difference between the groups was also found if the results from only the first 3 days were analyzed, during which time the lack of adjustment to the new time zone would be greatest. Ratings of fatigue and the other symptoms of jet lag gave very similar results—namely, significant effects of Day number and Time of Day, but no significant group effect or interactions between Group and the other ANOVA factors.

There was no significant difference between the groups in the distribution of phase advances and phase delays.

Discussion and Conclusions. In these subjects, melatonin appeared to exert no significant effects upon jet lag or its symptoms, or upon the process of phase adjustment. These negative conclusions are similar to those from another group that used a questionnaire similar to ours to assess the components of jet lag (22). Nevertheless, most studies have shown a positive effect of melatonin, and this raises the question why such a difference might exist.

It is important to realize that some of our subjects were highly trained, and all were very highly motivated—they saw their visit to Australia as an opportunity, and were not prepared to let "jet lag" detract from that aim. Possibly, such a degree of motivation overrides some of the symptoms of jet lag, and obviates the need for, or value of, melatonin. In addition, the present study involved more than recording jet lag once per day; subjects were required to consider jet lag itself, as well as its separate symptoms, on four occasions throughout the day. If, for example, melatonin exerted a hypnotic effect and if jet lag were assessed in the morning soon after waking, then it seems likely that the improvement to sleep brought about by melatonin would be perceived as combating jet lag. By contrast, if jet lag were assessed at some other time of day, then it seems equally possible that changes in some other symptom (fatigue, irritability, loss of power of concentration, or appetite) might be perceived as being a more relevant marker of jet lag at that time—and melatonin might be less effective in changing this symptom. More work is required to assess if the different symptoms of jet lag vary in their perceived importance at different times of day.

B.4. Are There Residual Effects the Morning After Evening Ingestion of Melatonin?

Background. Even if the benefits of melatonin ingestion are not invariably found, the fact remains that most studies do show such a benefit, and many people, including athletes, take it for improving sleep in the new time zone. Accepting this, we have investigated (2) if any effects from melatonin ingestion had worn off by the next morning. Clearly, for athletes and businesspeople, for example, it would be disadvantageous if residual effects were present.

Methods. In a laboratory-based study, 12 healthy males who trained regularly were given 5-mg melatonin or placebo in the evening (double-blind crossover design). None of these subjects had recently traveled on long-haul flights or done night work. It is reasonable to assume that they were fully adjusted to local time.

The following morning, subjects gave estimates of sleep latency and maintenance. Intra-aural temperature (Genius, Ballymoney, N. Ireland) and grip strength (Takei Kiki Kogyo, Tokyo, Japan) were also measured, and then subjects underwent a 4-km time trial on a cycle ergometer (Cybex Met 100, Ronkonkoma, New York, USA) in the laboratory.

Results. There were no significant differences between placebo and melatonin groups in their assessments of sleep, or in the other measured variables. In particular, there was no improvement in performance at the time trial. The power of this test was such that, had any difference in performance been present (that is, a Type II error had been made), it would have been less than 2% of the overall performance.

Discussion and Conclusions. As with the field study, the findings indicate that melatonin was without effect in promoting sleep, but there was also no evidence that the use of melatonin was associated with any residual effects the next morning. This last finding is of obvious benefit to those who take melatonin, but it should be borne in mind that the margin between winning and losing in competitive sports is often well under 2%.

Again, the subjects were highly motivated and determined to perform at their best, and this raises the possibility that such groups might not be representative of travelers and their difficulties in general.

C. Other Areas Related to Altered Sleep–Wake Cycles

C.1. Exercise and Adjusting the Body Clock

Background. For athletes in particular, the question arises whether exercise can promote adjustment of the body clock to a new time zone. In hamsters, it has been shown that the excitement produced by giving the animal access to a new running-wheel (which induces large amounts of running activity) can promote clock adjustment. In humans, by contrast, the evidence is less clear, phase advances in particular having proved to be difficult to demonstrate convincingly (19).

Methods. We investigated in the laboratory (6) the effect of 30-min exercise on a cycle ergometer (Cybex Met 100, Ronkonkoma, New York, USA) at 70% of peak rate of VO_2. Subjects ($N = 17$) were healthy males who exercised on between 1 and 4 occasions at times that were spread throughout the 24 h of the "exercise day". On all occasions, the laboratory was lit normally (about 350 lux), and its temperature (20 ± 2 °C) and humidity (50 ± 5%) were maintained at normal values.

The effect of the exercise upon the phase of the body clock was assessed by comparing the phases of the circadian rhythm of rectal temperature (Grant Instruments, Cambridge, UK) on the day before and day after this exercise day. These temperature measurements were made while the subjects slept and lived normally. Therefore, to correct for the direct effects of sleep and activity (Actiwatch, Cambridge Neurotechnology Instruments, Cambridge, UK), the measurements were "purified", using methods already developed by us (26).

Results. Exercise performed in the period from 4 h before the temperature minimum to 1 h after it produced a phase delay of 1.03 ± 0.78 h (mean ± *SD*); exercise performed in the period from 3–8 hours after the minimum produced a mean phase advance of 1.07 ± 1.23 hours; and exercise performed around the time of the temperature plateau had no significant phase-shifting effect. The direction and size of these shifts were similar to those found in a previous study (24), in which the subjects had been mainly sedentary and exposed to similar lighting intensities.

Discussion and Conclusions. The similarity between the phase shifts produced in exercising and sedentary subjects suggests that exercise per se has only a very weak effect in humans. Even so, such results suggest that a combination of light and exercise at the appropriate times, coupled with relaxation in dim light at others, would be one way for athletes to combine training and adjustment of the body clock to a new time zone. In subjects living normally and adjusted to their environment, the times of light and exercise that produce phase shifts (during the night, either side of the temperature minimum) are inconvenient, but it must be remembered that, after a time-zone transition, the temperature minimum of the unadjusted clock appears during the waking period.

C.2. Alternatives to Rectal Temperature for Assessing Core Body Temperature—Insulated Axilla and Gut Temperatures

Background. The rectal probe has never been a popular tool with volunteers and is not possible to use with athletes on the sports field. There is a considerable amount of literature comparing the readings from different measurement sites, but comparatively few studies have compared the temperature rhythms throughout the 24 hours (reviewed in 7). Intra-aural, oral, and mid-stream urine temperatures are all limited in their applicability to circadian studies, since they can only be used intermittently and when the subject is awake. Moreover, there are further constraints when accurate measurement of core temperature in field circumstances is considered; the device must not only be portable and unobtrusive but also must reliably reflect the fall produced by sleep and the increases produced by physical activity.

In this study, we investigated two alternatives to rectal temperature as a measure of core temperature, both of which are fairly convenient for the user: gut temperature (from a thermistor pill that was swallowed) and insulated axilla temperature. In both cases, the signal can be recorded continuously, so circadian studies are practicable.

Methods. For gut temperature, a thermistor pill (CorTemp 100, HTI Technologies Inc., Palmetto, FL, USA) was swallowed at about 8 hours before recordings began. Another pill was swallowed if the signal had been lost due to evacuation. For insulated axilla temperature, a flat temperature probe (Grant Instruments, Cambridge, UK) was secured by tape to the surface of the skin under the axilla, and then a layer of thermal insulation was taped over it. At the end of the recording period, it was established by observation that the insulation of the axilla was still securely in place; in those few cases where this was not the case, the data were discarded.

Recordings from these two sites, together with those from a rectal probe (Grant Instruments, Cambridge, UK), were obtained over the course of at least 24 hours from a group of subjects who lived normally, sleeping in the night and performing normal activities—sitting, standing, and walking (but not exercising)—during the daytime. Both raw (measured) temperature data and "purified" temperature data (that is, data corrected for the effects due to sleep and to activity, using Actiwatch, Cambridge Neurotechnology Instruments, Cambridge, UK) and methods previously developed by us, see 26) were subjected to cosinor analysis. From this analysis were obtained the daily mean (mesor) of the rhythm, its amplitude, and the time of peak of the fitted curve (acrophase).

Results. Readings from the thermistor pill were about 0.2 °C higher than those from the rectal probe, but this difference was consistent. The temperature profiles from rectal and gut temperatures were therefore very similar and showed high correlations. Moreover, the time courses and sizes of the changes that could be attributed to standing and walking (transient increases) and to nocturnal sleep (a more sustained fall) were very close. Such similarities between rectal and gut temperatures extended to activities outdoors as well as indoors. Cosinor analysis of the raw results showed narrow limits of agreement between the acrophases, the times the rhythms peaked (Table 1).

Table 1 The Limits of Agreement (h) Between the Times of Peak (Acrophases) of Rectal, Gut, and Insulated Axilla Temperatures (From 7)

Data type	Rectal vs. Gut	Rectal vs. Insulated Axilla
Raw data	–0.31 ± 0.89	0.75 ± 6.03
Purified data	–0.30 ± 1.12	0.58 ± 6.69

By contrast, results from the insulated axilla probe were generally about 1 °C lower than those from the rectal probe and, more importantly, this difference was variable. Consequently, the temperature profiles from rectal and insulated axilla temperatures were rather different, showing low correlations that were even not statistically significant for some portions of the 24 hours. The changes in temperature due to standing and walking were dissimilar between the two recording methods, activity sometimes producing a transient fall in insulated axilla temperature before the expected rise, this anomaly being particularly marked when the subjects was outdoors. Also, sleep produced an unreliable change in insulated axilla temperature, there sometimes being a sustained rise. Cosinor analysis of the raw results indicated a mean phase difference of about 0.7 hours, with the insulated axilla temperature being later, but with limits of agreement being so wide as to be valueless (Table 1).

After purification of the temperature data, the narrow limits of agreement between rectal and gut temperatures and the much wider limits between rectal and insulated axilla temperatures were still found for the acrophases of the rhythms (Table 1).

Discussion and Conclusions. These results indicate that gut temperature can be regarded as a reliable substitute for rectal temperature in circadian rhythm studies. Its disadvantages, however, are its cost and the need to have a spare thermistor pill ready for ingestion, should a pill be evacuated by bowel activity.

By contrast, as in a previous study (3), insulated axilla temperature was found to be a poor substitute for rectal temperature. There are two reasons why this could be the case. First, on theoretical grounds (1), it would be predicted that skin temperature in this region of the body might, unlike rectal temperature, not reflect core temperature but rather the rate of heat loss from the body. This loss of heat would be highest when core temperature was falling most quickly (in the evening), and lowest when it was rising most rapidly (in the early morning at about the time of waking).

However, a reliable phase difference between the two measurement sites would not pose a problem. The second reason, and one that does pose a problem and undermines the value of insulated axilla temperature for circadian rhythm studies, is the unreliable effect of activity and sleep upon this site. This unreliability does not seem to arise from inadequate insulation of the probe from the external environment but rather because the temperature of the blood passing through the skin at this site will have been cooled or warmed, according to the skin temperature of adjacent parts of the body. Thus, it will generally fall if the subject goes outdoors, when the chestwall or arms have become cooler, and generally rise if these parts of the body are warmed by the insulating effects of bedclothes.

C.3. Night Workers and Eating Habits—Why Do They Eat, or Not Eat, At a Particular Time?

Background. It has been known for some time that the eating habits of those working at night differ from those working in the daytime (13, 21). This is not due to differences between groups of individuals, since it is still found in workers on rotating shifts. Whereas the total 24-hour intake of food is found not to change significantly, night workers are less likely to eat a large, cooked meal during the night shift but rather more likely to eat a small meal or cold food, or even to "nibble" their way through the shift. This alteration of feeding habits has been linked to the increased frequency of indigestion and of ulcers, and even to the increased incidence of cardiovascular morbidity.

The exact reasons for these changed habits is unknown, though several possibilities have been suggested. These can be considered as due to external or internal factors. External factors might include inadequate facilities for buying or preparing palatable meals, or an inappropriate place for eating a meal. Internal factors might include a loss of appetite and decreased ability to digest food (due to an unadjusted body clock), or the sense that it is the "wrong time" to eat.

Clearly, it would be advantageous to have a better understanding of the reasons for the changed food intake patterns, since this would provide a rationale for giving advice to the night worker. We have devised and tested a questionnaire that is aimed to provide information about this issue.

Methods. The questionnaire requires the subjects to answer, at 3-hour intervals, whether they had eaten. If they had not, but were awake, the questionnaire then proceeds to establish why they had not eaten (e.g., habit, lack of appetite, lack of time, lack of facilities). By contrast, if a subject had eaten a meal, then the reasons for having done so (e.g., habits, appetite, schedule), the type of meal eaten (e.g., snack, cold meal, small hot meal, large hot meal), and the factors that determined the type of meal eaten (e.g., appetite, availability, time, cost), were asked. Also, the subjects' appetite before the meal, their enjoyment of it, and degree of feeling satisfied by it were requested.

The questionnaire was tested upon a group of 43 night workers (recruited from local hospitals) during the course of a "typical" week that contained both work and rest days. All subjects reverted to a conventional lifestyle (sleep at night) during their rest days. Since they did not perform day shifts, it was not possible to assess whether differences in eating habits between work and rest days were due to the work itself and/or to the fact that the subjects' sleep-wake pattern had changed. Therefore, a separate group of day workers—staff and post-graduate students from the Research Institute—was studied also, again for a "typical" week, with work days during the weekdays, and rest days at the weekend. A comparison of work and rest days in this group would reflect the effects of work without the added complication of a change in the sleep-wake schedule.

Results. When the food intake of night workers during their night shifts was compared with that during the daytime on rest days, there were several significant differences. The main ones were a decreased frequency of eating meals when at work, and for those meals that were eaten to be a snack or a cold meal rather than a hot one. The reasons for not eating that were given more frequently on work than rest days were habit and lack of time. Time available during work was important also in determining the reason for eating a meal and the nature of it. The evening meal (18:00–21:00 h) was smaller before the night shift than on rest days.

These results point to the roles of time pressure and habit rather than food availability, but the relative importance of the work schedule itself, rather than the changed sleep-wake schedule, cannot be deduced.

With day workers, some of the main findings—that the work schedule determined when the subjects could not eat as well when they had to, and that there was a significantly greater intake of cold food rather than hot food—were the same as those already described for night workers. Again, food availability was not cited frequently when decisions about food intake were taken. The evening meal was not significantly different between work and rest days.

If there was evidence for time pressure during work, whether this was at night or during the daytime, there were differences between the two groups of workers also. Habit played a smaller role for day workers. Also, even though night workers had less appetite before a meal at work than did day workers, they indicated that they felt more “over-full/bloated” after it.

Discussion and Conclusions. Several similarities between day and night workers point to there having been a sense of time pressure associated with work, at whatever time it was performed. However, it is the differences between day and night workers that formed the main focus of our study.

For night workers, there was an increased role of habit rather than appetite in determining whether a meal was eaten. This suggests that advice needs to be given to indicate that eating a full meal in the middle of the work shift, even though it is at night, is not wrong. Also, the choice of meal type (something more substantial than a snack) and the value of its social accompaniments might be stressed. Achieving these aims is likely to require action by management—to provide suitable rotations for a meal break and a site for eating the meal in comfort—as well as by the workers themselves. Such action might also contribute to an improvement in the diet itself.

When the food eaten at work was considered, the workforce felt less hungry before the meal, and yet more over-full after it. This has been reported before, and seems to be one of the reasons that workers then start to “nibble” rather than eat a full meal (13, 21). We found no clear evidence that a changed pattern of food intake on the night shift was due to the limited choice of food that was available; instead, it was found that the role of appetite in determining the food eaten was less, and that substantial meals caused individuals to feel over-full. This might indicate that the mechanisms promoting food intake and its digestion are less active in the night, due to a lack of adjustment of the body clock.

Finally, there was evidence that the evening meal at home was altered on days when there was night work, with a smaller meal on rest days. Whilst it seems reasonable not to eat a large meal just before starting work, the negative aspects of skimping on food and possibly reducing the amount of time spent with one's partner and family could be advised against.

C.4. Alternatives to Rectal Temperature for Assessing the Phase of the Body Clock—Wrist Actimetry

Background. Another alternative marker of the body clock might be the use of an activity meter, worn on the non-dominant wrist. Wearing such a device is acceptable to subjects, and it can give readings every minute for several days.

Most studies so far have used the actimetry record for estimating the times when a subject goes to sleep or wakes up. Such a record is an objective alternative to subjective recordings of these events, but any circadian effects upon the sleep-wake cycle are far more difficult to assess. However, two "dichotomy indices", which compare the subject's median activity levels when in bed with those when out of bed, have been developed previously (15); the greater the dichotomy in activity, the higher the indices. It was shown that such indices could give an objective estimate of healthy individuals' sleep-wake cycles, and could also quantify altered sleep-wake cycles in patients who had difficulty in maintaining a regular sleep-wake cycle. Moreover, some information about circadian effects upon the sleep-wake cycle could be inferred from the dichotomy indices. Thus, they were altered in healthy subjects who were performing night work (17) and in subjects who were living on non-24-hour "days" and so had a sleep-wake cycle that was at variance with the phase of their circadian oscillator (16).

In the current studies, we first confirmed that there were changes in the dichotomy indices in night workers similar to those found previously (17). We have then investigated further indices derived from the activity record that focus on those parts of it that would be predicted to change during night work and after time-zone transitions (Table 2). For example, during night work, it would be predicted that there would be a fall in activity in the waking phase, and a rise during the sleeping phase. Also, after a flight to the east across 8 time zones, it would be predicted that getting to sleep would be difficult (because of decreased time awake and a high core temperature—equivalent to 16:00 h on home time), and that waking up in the morning would be difficult (because core temperature would be low and falling—equivalent to 24:00 h on home time). The opposite would apply after a flight to the west across 8 time zones; now it would be easy to get to sleep (extended time awake and a low core temperature, equivalent to 08:00 h on home time), but staying asleep would be difficult (due to a rising core temperature).

We first confirmed many of these predictions from the activity records of night workers and of passengers who had undergone time-zone transitions, and then used the validated indices to assess changes to the activity record, during long-haul flights, of airline pilots, in whom there are shift-work and time-zone transition elements. In this report, we describe only the results from travelers and pilots.

Methods. For assessment of the value of those indices, which were postulated to indicate a lack of adjustment of the body clock to the new time, 8 staff from the Research Institute, who were taking part in conferences abroad, were studied as passengers on the flights. Their journeys entailed crossing 5–9 time zones to the west or east, and staying in the new time zone for 5 or more days before returning home. All subjects wore an actimeter (Actiwatch, Cambridge Neurotechnology Instruments, Cambridge, UK) on the non-dominant wrist for at least 1 day before

Table 2 The Activity Indices, Derived From Actimetry Records

Index	Description
%OB > IB	Percentage of out-of-bed counts greater than in-bed median
%IB < OB	Percentage of in-bed counts less than out-of-bed median
Predictive value	The original dichotomy indices (15–17). Would fall if time in bed were restless and/or if there were lethargy when out of bed.
WA50%	50th percentile of out-of-bed counts
WA90%	90th percentile of out-of-bed counts
WA95%	95th percentile of out-of-bed counts
Predictive value	Would fall if there were lethargy when out of bed.
SP90%	90th percentile of in-bed activity counts
SP95%	95th percentile of in-bed activity counts
Predictive value	Would rise if there were restlessness when in bed.
FHOB-50%	50th percentile of activity counts in the first hour out of bed
FHOB-90%	90th percentile of activity counts in the first hour out of bed
FHOB-95%	95th percentile of activity counts in the first hour out of bed
Predictive value	Would fall if there were lethargy at the start of the out-of-bed period.
LHIB-0	The number of counts of zero activity in the last hour in bed
LHIB-90%	90th percentile of activity counts in the last hour in bed
LHIB-95%	95th percentile of activity counts in the last hour in bed
Predictive value	Would rise if there were restlessness at the end of the in-bed period.

their journey and for at least 5 days after it. In some cases, the monitor was worn also for the return flight.

For the purpose of analysis, whether away from home or back to home, flights were divided into those in a westward or eastward direction. The first day after the flight was defined as beginning 2 hours after arrival in the new time zone. The actimetry record was used to calculate the dichotomy indices each day, as well as estimates of activity in the hour before retiring, the first hour in bed, the last hour in bed, and the first hour after rising the next morning.

The sleep-wake schedules of the pilots were complex. Essentially, they began and ended with a long-haul flight that was to the south (1 time zone crossed), the east (7 time zones), or the west (6 time zones). These flights entailed working at night by home time. In the new time zone, pilots had three “layover” days before the return flights. Whereas the 1st and 3rd layover days were rest days, when the pilots had no duties, in some cases there were duties on the 2nd layover day; these were local flights without night work. The pilots did not use the activity meter either immediately before the flights or after returning home, because they found this too intrusive. Even so, by comparing the appropriate days during these schedules, and by comparing the different groups of pilots, it was possible to measure differences in the activity record that could be associated with night work, day work, or rest days, and with no time-zone transition, a transition eastwards or one westwards.

Results. For the group of passengers, in the day immediately after the flight, the dichotomy indices were decreased, indicating a decrease in out-of-bed activity and/or a rise in in-bed activity. This decrease below baseline rapidly rose towards normal on subsequent days. After flights to the west, there were, on the first night in the new time zone, significant increases in activity in the last hour in bed, when compared with baseline values. After flights to the east, activity in the last hour in bed was decreased, again in comparison with baseline values. These changes were more marked after eastward than westward flights, but rarely persisted for more than 2 days.

For the pilots, only the briefest outline of the results can be given here.

As predicted, the dichotomy between activity during the daytime and inactivity during the night time was severely compromised during the outward and inward long-haul flights, both of which took place, at least in part, during the night. Dichotomy indices were normal on the layover days after the north-south flights, slightly lower after flights to the west, and lowest after flights to the east. These differences indicate an effect from an unadjusted body clock, particularly after the eastward flight. Daytime activity and the dichotomy indices were highest on the layover day when flight duties were performed; again, this is to be predicted on the assumption that a day involving flight duties is more active than a rest day.

When activity in the hours adjacent to retiring and rising were considered, there was no effect after the north-south flights, in accord with the view that such flights would not lead to a desynchronization between a body clock that was still on home time and the destination. After a flight to the west, on the other hand, activity at the end of the sleep period was higher, indicative of an unadjusted body clock. However, as found in other studies (8), all pilots adjusted their hours of sleep to coincide with night in the new time zone. After the eastward flights, whereas most of the pilots attempted to sleep during the new local night, a significant proportion of them opted to remain on home time. For both groups of pilots, however, the activity records indicated that their sleep-wake cycle was compromised, with decreased dichotomy indices. Those pilots attempting to adjust their sleep rhythm to coincide with the new night, showed more disturbed sleep-activity cycles than did those who had flown to the west.

Discussion and Conclusions. The results from the passengers indicate that information about lack of adjustment of the body clock can be gained from suitable analysis of the activity record. Both sets of indices indicate that eastward transitions were more disruptive than those to the west. Such indications of inappropriate phasing of the body clock are by no means new, of course (see, e.g., 10, 12), but the use of an activity record is so much simpler and cheaper than more conventional measures of sleep or of markers of the body clock.

The results from the pilots also confirm findings from previous studies, particularly with the difficulties experienced with sleep (8). Moreover, from a chronobiological viewpoint, the problems for pilots are extremely complex, their duty schedules having elements of time-zone transitions as well as of night work. The activity indices could be used to quantify the negative effects of both these elements, as well as the fact that the difficulties were particularly marked after eastward flights.

While the present indices have extended considerably the information that can be obtained from actimetry, their limitations should also be borne in mind. Thus, even though we have succeeded in quantifying some of the effects of an unadjusted body clock, the present indices are still too insensitive when the time course of adjustment of the clock is considered. Thus, we found that the indices appeared to return to normal values—implying that the body clock had adjusted to the local time zone—in under 4 days, but evidence from more established markers of it (12) indicates that the process of adjustment is slower. It remains to be seen if the present indices can be refined to become more sensitive markers.

D. Concluding Comments

The recent and continuing research program, summarized above, has contributed significantly to the scientific rationale that forms the basis of advice to travelers in general, and to athletes in particular. From our findings, this advice is focused in particular on travel arrangements and the question of whether adjustment of the body clock, by means of exposure to and avoidance of light outdoors, should be by an advance or a delay. Current work is exploring further results from the jet lag questionnaire, investigating if the time of day when jet lag is assessed affects the symptom with which jet lag is associated most closely.

The value of the demonstration that gut temperature can act as a substitute for rectal temperature is that gut temperature is much preferred by subjects, and this reduces any difficulties that might exist with recruiting volunteers. The recent opening of a custom-built isolation unit means that simulation studies can be performed conveniently and with a greater control of potentially confounding variables. The environment of the isolation unit can be controlled so that it is equally conducive to sleep or to wakefulness throughout the 24 hours. Planned studies will establish how closely the phase shifts of the body clock that follow a simulated time-zone transition, and estimated using the several purification methods that we and our collaborators have developed (26, 27), agree with those assessed by the "gold standard", the constant routine method.

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