CIRCADIAN RHYTHMS

Jim Waterhouse

We do not feel tired only because we have been awake and active for several hours. If that were so our feelings of fatigue would increase inexorably and progressively during the time that had elapsed since our last sleep. Instead, when we stay up all night fatigue increases until it reaches a peak at about 0500, but then it decreases at least until the next evening. Superimposed on the general increase in fatigue are three daily cycles, each of which show a "fatigue maximum" in the middle of the normal time for sleep and a "fatigue minimum" in the late afternoon. Fatigue has a rhythmic component, therefore, and this is associated with rhythmic changes in our ability to fall asleep and to stay asleep.

Such rhythms are only a few of the many that permeate the physiology, psychology, and biochemistry of the individual. When several rhythms are considered those that are linked causally show characteristic and reliable phase relationships between each other. For example, in the case shown in the first figure, the rhythms of urinary adrenaline excretion and the speed of shooting at a target are in phase with each other and the rhythm of fatigue is always the inverse.

Body temperature

The length of sleep is also associated with body temperature and this is most usefully examined in free running experiments—that is, ones in which subjects are studied individually in an environment from which all external indicators of the passage of time have been excluded. In such conditions most subjects have synchronised rhythms and go to sleep just before their body temperature falls to its minimum. By contrast, in some, there is no synchronisation between the rhythms of body temperature and the sleep/wake cycle. As a result sleep is initiated at all phases of the temperature rhythm and this influences the length of sleep that is achieved. Because the temperature minimum occurs at about 0500 in people with a normal life style and sleeping about eight hours, there is considerable agreement between the results of free running experiments, laboratory studies, and common experience.

Sleep/wake rhythms

There is also an inverse relationship between the length of time spent awake and the duration of the subsequent period of sleep. This is more easily understood if sleep is seen as part of a sleep/wake rhythm in addition to a time of recuperation; going to bed late means that you will get less sleep, and vice versa.

The constant association that normally exists between rhythms is biologically adaptive, so in the evening body temperature and plasma adrenaline concentration fall, we feel tired, and it is easy to have unbroken sleep. By contrast, even if we have been awake all night, it is difficult to have unbroken sleep starting at about 0800 because our rhythms of body temperature, adrenaline, and general alertness will all be on their rising phases.
Loss of sleep and naps

Loss of sleep is associated with a decline in performance of many tasks, particularly those that are repetitive or require vigilance. Such decrements become more pronounced as the total time that has elapsed since the last sleep increases, and if the task is being performed at a time coincident with the trough in the temperature rhythm. The graph shows the levels of performance that were associated with two prolonged spells of vigilance, one starting at noon and the other at midnight. In both cases there was a general decline in performance as the experiment progressed, but when it ended at night and body temperature was low the deterioration was much more pronounced than when it ended during the day. Short sleeps or naps seem to reduce this deterioration, but the most effective length of a nap or the time to take it are important issues that remain to be resolved.

Controlling the body clock

Free running experiments have also shown that without external time cues the body clock runs slow. Because it lasts about 25 hours it is called a circadian clock (from the Latin: circa = about, diem = a day). Such an inaccurate and potentially useless clock is adjusted to the solar day by environmental rhythms called synchronisers of Zeitgebers (from the German: Zeit = time, Geber = to give). The rhythmic pattern of dark and light (particularly of an intensity similar to that found outdoors and much brighter than that normally used domestically) is one means by which this can be achieved. In addition, humans in modern societies gain much information about time from their daily routine, affecting as it does social factors, activity, and meal times. For example, the observation that imposing a regular light/dark cycle adjusted a person’s sleep/wake cycle, with sleep times coinciding with the imposed darkness, does not mean that the light/dark cycle alone was acting as a Zeitgeber. Rather, the light/dark cycle acted in combination with rhythms of activity and meal times, and of other things that are natural behavioural consequences of the light/dark cycle.

The complex interactions between the environment, the body clock, and the rhythms that it produces, enable rhythmic humans to integrate into a rhythmic environment. Not only are they “primed” during the day and partially “shut down” at night, but also their bodies can predict—and so prepare for—environmental changes. They can therefore prepare for sleep during the falling phase of adrenaline, alertness, and body temperature rhythms, and prepare for the next day as these rhythms continue beyond their minimum values.
Jet lag and sleep problems

The effects of possessing such a body clock can turn to our disadvantage if we change our pattern of sleep and activity, as when we cross several time zones. Under such circumstances a person experiences a general malaise, which includes headache, loss of appetite, irregularities of bowel movement, difficulty in concentrating, fatigue during the new day time, and yet an inability to sleep properly at night. These symptoms are known collectively as circadian dysrhythmia or "jet lag." The symptoms are worse after a flight to the east than after one to the west, and their severity is directly related to the number of time zones that have been crossed. The difficulties cannot be attributed either to the stress of the flight itself or to any "culture shock" because they do not arise after north/south flights and yet do arise in simulated time zone transitions in the laboratory (in which culture shock and the stress of flying are omitted).

The symptoms arise because of mismatching between the body clock (which initially continues to run on the time of the departure time zone) and the new environment with all its new time cues. As a result, after a flight to the east (for example, one that crosses six time zones) we will feel most tired and our ability to carry out many mental tasks will be lowest from 0600 to 1400 on the new time scale, and our new bed time will be at 1800 "body time"—a time associated with high alertness and mental performance. The loss of sleep will result in a decreased ability to function well. The quality of sleep will also change. Normally we have most slow wave sleep towards the beginning of a night’s sleep. We also have most rapid eye movement (REM) sleep towards the end of sleep because it shows a circadian rhythm with a peak at about 1000 and a minimum at about 2200.

After a westward flight across six time zones, therefore, the amount of REM sleep will decline during the latter half of sleep, because the sleep period of 2400 to 0800 corresponds to 0600 to 1400 on body time. As a result, slow wave sleep is sometimes "squeezed out" of its normal position and distributed sporadically throughout more of the period of sleep than normal. This may contribute to the sense that sleep has been of poor quality. On subsequent nights the normal distribution of sleep stages begins to be restored.

Combating jet lag

The symptoms of jet lag decline after a few days as the body clock and the rhythms that it drives synchronise with the new time zone under the influence of the new Zeitgebers. Attempts to deal with jet lag have concentrated on the sleep disturbance and associated fatigue. There are two main approaches: to minimise loss of sleep and to maximise the rate of adjustment of the body clock to the new time zone.

Adjustment of the body clock

Adjustment of the body clock is generally accelerated by strengthening the Zeitgebers in the new time zone ("When in Rome... "). Adopting the new local hours for sleeping, for being awake and active, and for taking part in social functions, are the most important. Travellers should be encouraged to rest in a quiet, darkened room when it is bed time even if they do not feel tired, and to start the new day with gentle exercise even if they still feel sleepy. Naps are not recommended as they will tend to mislead the body about when it is night time. Exposure to natural daylight is beneficial but, particularly during the days immediately after the journey, its correct timing is important.

Distribution of sleep stages before and after a flight from east to west through six time zones. The dashed line indicates the shift in the time of maximum portions of REM sleep.

Good and bad local times for exposure to natural light in the first 2-3 days after a time zone transition

<table>
<thead>
<tr>
<th>Time zones to the east</th>
<th>Bad local times</th>
<th>Good local times</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 hours</td>
<td>0100-0700**</td>
<td>1700-2300**</td>
</tr>
<tr>
<td>8 hours</td>
<td>2100-0300*</td>
<td>1300-1900**</td>
</tr>
<tr>
<td>12 hours</td>
<td>1700-2300*</td>
<td>0900-1500**</td>
</tr>
</tbody>
</table>

*Will tend to advance the body clock.
**Will tend to delay the body clock.
**Shift work**

The fatigue and loss of sleep that accompany night work are obviously similar to those that follow time zone transitions, both in cause and effect. The problem is worse, however, in that they affect a larger section of the population and for extended periods. Chronic fatigue and sleep disturbances are often cited as reasons why some shift workers leave night work. The problem is exacerbated because of the continual use of any drug to combat the effects is undesirable and rigid adherence to a routine that might promote adjustment of the body clock (or retain stable phasing of it in the case of those who work rapidly rotating shift systems) will make it much more inconvenient to shoulder or share domestic, family, and social responsibilities and pursue hobbies.

At present there is no clear solution to these conflicting interests but many patterns of shift work can be improved by careful consultation with the workforce and consideration of circadian influences. Recent studies have suggested that a short period of sleep in the middle of a night shift may mean that performance later on in the shift will be better maintained, as well as permitting the circadian rhythms to stabilise. This would make it easier for them to remain adapted to normal daily routines and would be advantageous to the worker, for example, during rest days.


Dr Jim Waterhouse is reader, Department of Physiological Sciences, University of Manchester.

The ABC of Sleep Disorders has been edited by Professor C M Shapiro, Department of Psychiatry, University of Toronto, Canada.