Sleep and circadian influences on cardiac autonomic nervous system activity

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Burgess, Helen J., J. John Trinder, Young Kim, and David Luke. Sleep and circadian influences on cardiac autonomic nervous system activity. Am. J. Physiol. 273 (Heart Circ. Physiol. 42): H1761–H1768, 1997.—To assess the separate contributions of the sleep and circadian systems to changes in cardiac autonomic nervous system (ANS) activity, 12 supine subjects participated in two 26-h constant routines, which were counterbalanced and separated by 1 wk. One routine did not permit sleep, whereas the second allowed the subjects to sleep during their normal sleep phase. Parasympathetic nervous system activity was assessed with respiratory sinus arrhythmia as measured from the spectral analysis of cardiac beat-to-beat intervals. Sympathetic nervous system activity was primarily assessed with the prejection period as estimated from impedance cardiography, although the 0.1-Hz peak from the spectral analysis of cardiac beat-to-beat intervals, the amplitude of the T wave in the electrocardiogram, and heart rate were also measured. Respiratory sinus arrhythmia showed a 24-h rhythm independent of sleep, whereas prejection period only showed a 24-h rhythm if sleep occurred. Thus the findings indicate that parasympathetic nervous system activity is mostly influenced by the circadian system, whereas sympathetic nervous system activity is mostly influenced by the sleep system.

Determination of the nature of the influence of sleep on cardiac activity is of considerable interest because of its potential clinical relevance. For example, there are cardiovascular consequences of the nighttime arousals that occur in disorders such as sleep apnea (29). It is generally accepted that compared with wakefulness (usually assessed just before sleep), non-rapid eye movement (NREM) sleep in humans is associated with an increase in cardiac parasympathetic nervous system (PNS) activity [as measured by noninvasive methods such as respiratory sinus arrhythmia (RSA)] (2, 23, 32–35, 37). More specifically, most agree that PNS activity progressively increases across the four stages of NREM sleep (21, 32, 34, 36), although not all have found this (35, 37). In rapid eye movement (REM) sleep, PNS activity appears to decrease compared with NREM sleep (2, 21, 23, 32–34, 36, 37).

In addition to the influence of sleep on autonomic nervous system (ANS) activity, there has been interest recently in a possible circadian influence on ANS activity. This interest stems from reports of an increased incidence of cardiovascular events in the morning (e.g., Ref. 20). However, the existence of an endogenous circadian influence on ANS activity has not yet been established because the majority of past studies have either failed to control for the confounding effects of sleep (13) or because of changes in posture and physical activity (e.g., Ref. 12). With these factors controlled for, PNS activity has shown no change (9, 32) or a decrease during the daytime (5, 14), with SNS activity remaining relatively stable (5, 14, 18, 32). In this study, ANS activity was assessed over two 26-h periods while subjects were supine and their activity was kept to a minimum. During one period, the subjects were allowed to sleep during their normal sleep period (circadian and sleep influence present), whereas in the other, they were not (circadian influence present). It was hypothesized that both the PNS and SNS would be affected by sleep but that only the PNS would be influenced by the circadian system.

METHODS
Subjects
Twelve male subjects [19.0 ± 2.3 (SD) yr] of average body mass index (20.97 ± 1.74 kg/m²) participated. Women did not participate because of their toileting requirements. The subjects were free of physical illness, nonsmokers, and not taking any medication (currently or in the past week), regular heavy caffeine (<350 mg/day), or alcohol doses (≤5 standard drinks/wk). The subjects participated in a moderate amount of exercise (≤10 h/wk) and had no known personal or family history of hypertension, cardiovascular disorders, and respiratory problems. All subjects were screened for major psychopathology (8). The subjects had not undertaken any shift work or transmeridian travel in the past 3 mo and had no history of sleep problems. They were not experiencing any major life stress and had no examinations scheduled for a few days before, during, or after the study.

The laboratory procedures were approved by the Human Ethics Committee of the University of Melbourne (Australia),
and all subjects gave written informed consent before their participation. The subjects received financial reimbursement for their time.

Design

To assess the relative contributions of the sleep and circadian systems to changes in ANS activity, a repeated-measures design based on the “constant-routine” procedure was used. This procedure aims to control for the “masking” effect by requiring subjects to remain supine for a period > 24 h. The effect of food intake is also minimized because the subjects are fed small meals every 2 h (19). In this study, there were two constant-routine sessions separated by 1 wk: a routine in which all subjects were deprived of sleep (nonsleep routine) and a routine in which all subjects were allowed their normal sleep (sleep routine). The order of the two routines was counterbalanced across subjects. For one-half of the subjects, data collection in both routines began at 1200, whereas for the other half, it began at 2100. This was done so as not to confound the circadian phase and sleep with time in the experiment, possibly associated with accumulating stress and/or sleepiness over the course of the experiment.

Procedures

General laboratory procedures. The study was conducted in the Psychophysiology Laboratory at the School of Behavioural Science, University of Melbourne. The subjects refrained from consuming alcohol and caffeine 24 h before each session and maintained a constant sleep-wake cycle (based on their self-reported sleep-wake cycle) for the week before their first session and between the two sessions.

In each session, each subject was confined to a supine position for 26 h. In both routines, the subjects were permitted to assume an upright position for 5 min, 2 h after their normal waking time. During the sleep routine, this allowed each subject to move out of his separate bedroom into the general laboratory space and during both routines to empty his bowels if he wished. Room temperature and ambient light were kept constant, and the laboratory was well ventilated. The effects of food intake on ANS activity were minimized because the subjects received 250-calorie snacks (noncaffeinated) every 2 h and free access to water but only during those time periods when the subjects were awake. On one occasion, a subject expressed hunger after a meal and was supplied with an additional 100-calorie snack. Bottles for urination were available.

The subjects were asked to arrive at the laboratory 4 h before the start of data collection for each session. The rectal probe was inserted, the appropriate electrodes were attached, and the subjects assumed a supine position at least 2 h before the onset of data collection. Fifteen-minute data-collection periods occurred hourly (30 min during the sleep phase of the sleep routine). In the sleep routine condition, electrodes to monitor sleep-wake state were attached 2–3 h before the start of data collection for each session. The rectal thermistor was taped to the skin until it reached the waist where it was attached to the recorder. A 4-mA AC current at 100 kHz was passed through the two outer (current) electrodes and basal impedance and rate of change in the impedance waveform on a given beat (dZ/dt) were recorded. The thermistor was inserted by each subject 10 cm into his anus, and the lead from the thermistor was taped to the skin until it reached the waist of the subject. Data from the thermistor were transmitted to a computer and analyzed off-line by computer software developed within the laboratory.

Data Analysis

ANS activity. Five-minute epochs of stable respiration were selected from the 15-min wakefulness recordings. Thus data containing abrupt respiratory changes or body movements were discarded. Each 5-min epoch consisted of a number of shorter intervals of stable data. From the 30-min sleep recordings, continuous 5-min epochs were selected using the same criteria. As a consequence of these procedures, a value for each variable was obtained for each hour of the experiment.

Data from the rectal thermistor were transmitted to a computer and analyzed off-line by computer software developed within the laboratory to calculate HR, RSA, 0.1-Hz peak, TWA, and PEP for every cardiac cycle (see Data Analysis).
density estimate for each frequency bin, and these were combined to form frequency bands 0.02 EqHz wide. The power spectrum ranged from 0 to 0.50 EqHz. A program searched the frequency spectrum for two major components: a high-frequency component in the region of the respiratory rate (RSA), defined as the largest peak > 0.16 EqHz, and a low-frequency component at ~0.10 EqHz, defined as the largest peak < 0.16 EqHz but > 0.03 EqHz (< 0.03 EqHz was designated as the DC component). The subject’s respiration rate was calculated for each epoch to confirm that it corresponded to the peak that the program identified as the RSA component. Each frequency bin of each power spectrum was recalculated as a proportion of the adjusted total power of the spectrum (total power minus DC noise; Refs. 12, 24). Thus, from each power spectrum, the normalized areas of the RSA and 0.1-Hz peaks were determined. HR was also determined from the R-R intervals and averaged across each 5-min epoch.

TWA and PEP. The positions in time of the B point in the dZ/dt signal and the Q and T waves in the ECG were detected. The epochs were visually scanned and edited when the algorithm failed to correctly detect these points. PEP was then calculated for each cardiac cycle as the time interval between the Q wave on the ECG signal and the B point on the dZ/dt signal. The amplitude of the T wave for each cardiac cycle was calculated as the difference between the baseline (0 V) and the peak of the T wave. The PEP and TWA for each cardiac cycle were then averaged across each 5-min epoch.

Statistical analysis. Three forms of analyses were conducted. First, analysis of variance (ANOVA) methods assessed the effect of sleep on each dependent variable. The subjects’ data were separated into “wake time” and “sleep time” in both routines according to their regular sleep-wake schedule. Thus, in the nonsleep routine, sleep time was the period in which the subjects were awake but would normally be asleep. A 2 × 2 ANOVA with repeated measures on each variable was used to compare state (wake time vs. sleep time) with type of routine (nonsleep vs. sleep). Second, the presence of a circadian component was tested by fitting functions to the time series ordered according to time from normal sleep onset. The data in each routine were fitted with 24-h (simple) and 24-h + fundamental with 12-h harmonic (complex) curves, with the significance of an F-test indicating goodness of fit. The complex curves were viewed to be a better fit than the simple curves if they significantly increased the variance accounted for as determined with a stepwise regression. The third analysis compared the time series derived from the cardiac variables with the body temperature time series with cross-correlational methods.

RESULTS
Preliminary Analyses

All variables were found to be normally distributed. A number of preliminary analyses were conducted to evaluate potential methodological artifacts. Analyses were conducted to determine the effects of 1) combining blocks of stable data to make up 5-min epochs, 2) variations in respiratory rate, 3) harmonic influences, 4) the 5-min period of upright posture, and 5) time in the experiment (reflecting the role of stress or fatigue). With the exception of time in the experiment, these analyses did not identify any methodological artifacts affecting the integrity of the data. As a function of time in the experiment, HR decreased during the nonsleep routine (P < 0.05) but did not change during the sleep routine (P > 0.05). RSA significantly decreased (decrease in PNS activity) in both the nonsleep (P < 0.001) and sleep (P < 0.05) routines. The 0.1-EqHz peak did not change during the nonsleep (P > 0.05) or sleep (P > 0.05) routine, and TWA increased during the nonsleep routine (P < 0.001) but did not change during the sleep routine (P > 0.05). Finally, PEP significantly increased (decrease in SNS activity; P < 0.001) and P < 0.01 for nonsleep and sleep routines, respectively). Although these analyses suggest that time in the experiment influenced ACS activity, the effects did not consistently indicate an overall increase or decrease in arousal because PNS activity (decrease in RSA) and SNS activity (increase in PEP) both decreased over time. These trends were not removed in subsequent analyses, having been controlled for by counterbalancing starting time over subjects. Within subjects, all autonomic variables were recalculated as the distance from each subject’s individual mean. The variables were then averaged over subjects and represented according to 24-h clock time (Fig. 1) and normal sleep onset time (Fig. 2).

Ideally, for each subject in each routine, there were 25 hourly measurements of each dependent variable (RSA, PEP, HR, 0.1-EqHz peak, and TWA). Because of a range of technical difficulties, 5% of the hourly measurements was lost. If the missing data consisted of one sample between two available samples, then it was replaced with the mean of the before and after samples. If there were more than one missing consecutive sample (this occurred on only three occasions), then the values of the missing samples were estimated from the group trend adjusted by the particular subject’s average level for the variable.

Of the 12 subjects, 9 in the nonsleep and 8 in the sleep routine yielded reliable temperature data with no probe slippage. The recordings taken every 2 min were averaged to yield hourly estimates of rectal temperature, recalculated to reflect the average change from the mean, and plotted according to clock time and sleep onset time (Fig. 3).

RSA

RSA was predominantly influenced by the circadian system, with little effect of sleep. ANOVA of the RSA data did not show any significant effects for routine, state, and interaction between routine and state (P > 0.05; Table 1), indicating that there was no effect of sleep on RSA and that if there was an effect of the circadian system, it was out of phase with the usual sleep period. Consistent with this possibility, RSA in both the nonsleep (P < 0.01) and sleep (P < 0.01) routines was best fit by a complex curve, with no differences in phase (P > 0.05) or amplitude (P > 0.05) between the two routines. Furthermore, the cross-correlation of the nonsleep routine RSA with body temperature showed a maximal and significant negative correlation when body temperature had a lag of 5 h. Thus RSA began to rise ~2 h before sleep onset and...
Importantly, with the effect of sleep added (sleep routine), the correlation became nonsignificant as body temperature changed, but RSA remained essentially the same.
PEP

PEP was influenced predominantly by the sleep system, with little circadian influence. This was evident in the significant effects of routine (P < 0.05), state (P < 0.01), and routine by state (P < 0.05) obtained in the ANOVA (Table 1). Thus PEP was highest when the subjects slept during their normal sleep time (sleep routine), with this difference disappearing when the subjects were awake during their normal sleep time (nonsleep routine). Furthermore, PEP was not fit by a simple (P > 0.05) or a complex curve (P > 0.05) during the nonsleep routine, whereas in the sleep routine, it was best estimated by a complex curve (P < 0.01). Thus PEP was essentially constant during the nonsleep routine but varied as a function of state in the sleep routine (Fig. 2). Finally, in the nonsleep routine, PEP did not have a significant relationship with body temperature, but with the effect of sleep added, there was a dramatic increase in the correlation, with little lag between the two signals (Table 2).

HR

HR was influenced by both the circadian and sleep systems. The circadian influence decreased HR during sleep time regardless of the routine (Table 1), with the data showing a significant effect of state (P < 0.001) but not of routine (P > 0.05) or an interaction between state and routine (P > 0.05). Furthermore, in both the nonsleep (P < 0.01) and sleep (P < 0.01) routines, HR showed a significant fit to a simple curve. The phase (P > 0.05) and amplitude (P > 0.05) of the curves were the same in both routines. The influence of sleep was also evident in the cross-correlational analysis. In the nonsleep routine, with only a circadian influence present, HR and body temperature were significantly positively correlated (Table 2). The peak in HR occurred 1 h before the peak in body temperature (Fig. 2). With the influence of sleep added (sleep routine), body temperature and HR remained highly correlated.

0.1-EqHz Peak

The 0.1-EqHz peak was influenced primarily by the circadian system, although with some suggestion of a sleep influence (Fig. 2). The results from ANOVA of the 0.1-EqHz peak data did not show significant effects for routine, state, and interaction between routine and state (P > 0.05; Table 1), suggesting little or no sleep effect. In both the nonsleep (P < 0.01) and sleep (P < 0.05) routines, the peak was best fit by a simple curve, with no difference in phase (P > 0.05) or amplitude (P > 0.05) between the routines, indicating a circadian influence. The cross-correlational analysis showed that a substantial positive correlation existed between body temperature and the 0.1-EqHz peak during the nonsleep routine and remained with the sleep routine (Table 2). The general pattern of cross-correlations was similar in both routines, with positive correlations for lags between −12 and −4 h and negative correlations for lags between 1 and 12 h. However, the maximum correlation was positive for the nonsleep routine and negative for the sleep routine. The essential similar

Table 1. Change in ANS variables during normal wake and sleep periods in the 2 routines

<table>
<thead>
<tr>
<th></th>
<th>Nonsleep Routine (Circadian)</th>
<th>Sleep Routine (Circadian and Sleep)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wake time</td>
<td>Sleep time</td>
</tr>
<tr>
<td>∆RSA</td>
<td>−0.0039 ± 0.0036</td>
<td>0.0083 ± 0.0072</td>
</tr>
<tr>
<td>∆PEP *†§</td>
<td>0.0418 ± 0.5620</td>
<td>0.0905 ± 1.1489</td>
</tr>
<tr>
<td>∆HR‡</td>
<td>1.0599 ± 0.2298</td>
<td>−2.1147 ± 0.4737</td>
</tr>
<tr>
<td>∆0.1-EqHz peak</td>
<td>0.0016 ± 0.0015</td>
<td>−0.0033 ± 0.0103</td>
</tr>
</tbody>
</table>

Values are means ± SE of changes (Δ) in respiratory sinus arrhythmia (RSA; in proportion of power spectrum), preejection period (PEP; in ms), heart rate (HR; in beats/min), spectrum frequency expressed in units equivalent to cycles (0.1-EqHz peak; in proportion of power spectrum), and T wave amplitude (TWA; in µV); n = 12 subjects, ANS, autonomic nervous system. Wake time and sleep time, subjects’ regular sleep-wake schedule except sleep time in nonsleep routine was period in which subjects were awake but would normally be asleep. *Main effect of routine, P < 0.05; †main effect of state, P < 0.01; ‡main effect of state, P < 0.001; §interaction between routine and state, P < 0.05. See RESULTS for details.
ties of the cross-correlation profile in the two routines suggest that sleep was affecting the 0.1-EqHz peak.

**TWA**

TWA was also influenced primarily by the circadian system, with some sleep effect. TWA was higher during the sleep period than during wakefulness; however, the main effect of state, routine, and state by routine interaction was not significant (P > 0.05; Table 1). Additionally, in both the nonsleep (P < 0.01) and sleep (P < 0.01) routines, TWA was best fit by simple curves, with no difference between the routines in phase (P > 0.05) or amplitude (P > 0.05). Thus the circadian influence predominated. Peak activity tended to be in the second half of the sleep period, and the low point was in the afternoon/evening (Fig. 2). However, TWA did remain negatively correlated with body temperature in both routines (Table 2), with TWA showing a 2- to 5-h lag, indicating some sleep effect.

**Group Differences**

The subjects who had their first data collection at 2100 (group 21) were compared with the subjects who started at 1200 (group 12) by redoing the main analyses for each group. In the 2 x 2 ANOVA, there were only two differences between the groups. These differences resulted from group 21 not showing a main effect of routine for PEP, whereas in group 12, this did reach significance. In contrast, HR had a significant main effect of routine in group 12 but not in group 21.

In terms of group differences in the phase and amplitude of the autonomic variables across routines, there were two differences. Group 21 showed a higher amplitude in their RSA measurement during the nonsleep routine (P < 0.05). Because the two groups showed similar trends across time, this difference appeared to be due to group 21 being further in time from their last sleep period than group 12. Thus group 21 had a larger presleep increase and postsleep decrease in RSA. A more critical group difference occurred with TWA in the nonsleep routine where the position of the phase of group 21 was more advanced in time compared with that of group 12 (P < 0.05). This finding is reflective of a general difference in the TWA pattern between the two groups (Fig. 4). Considering that PEP and 0.1 EqHz did not show such dramatic group differences, this suggests that TWA was more sensitive to the experimental situation than the 0.1-EqHz peak and PEP.

**DISCUSSION**

The results from this study indicate that the PNS is primarily influenced by the circadian system and not by sleep, whereas the SNS is primarily influenced by sleep and not by the circadian system. RSA and PEP are believed to be relatively pure measures of PNS and SNS activity, respectively. Physiologically, RSA is the shortening and lengthening of the beat-to-beat intervals during inspiration and expiration, respectively. RSA is viewed by most as a “pure” measure of PNS activity because SNS efferents cannot operate at the respiratory frequency (1, 3, 6). This interpretation has been supported by many experimental manipulations (e.g., Refs. 6, 26). PEP is the time interval from the onset of ventricular depolarization to the opening of the semilunar valves. Because of the predominance of SNS innervation of the ventricular myocardium, PEP is regarded as being inversely proportional to cardiac SNS activity (6).

HR, the 0.1-EqHz peak, and TWA were influenced by both the circadian and sleep systems. This was anticipated because all three measures are influenced by the PNS and SNS. Although some regard the 0.1-EqHz peak as a primary measure of SNS activity (e.g., Refs. 12, 32, 34), it most likely represents both PNS and SNS afferents and efferents in the baroreflex control of blood pressure (e.g., Refs. 1, 17, 26). TWA is also a disputed measure of SNS activity. It represents myocardial...
ventricular repolarization, and because the PNS influence on the ventricular myocardium is believed to be slight, TWA has been regarded as an index inversely proportional to cardiac SNS activity (e.g., Refs. 10, 11). Others (7, 28), however, have criticized its use. Indeed, in this study, it appeared to be more reflective of mental stress rather than of tonic SNS activity and so highlighted the group differences in time from the last sleep period (Fig. 4).

Thus, as hypothesized, cardiac PNS, but not SNS, activity was found to be influenced by the circadian system. Previous suggestions of a circadian influence on PNS activity, but not on SNS activity, have come from previous studies that controlled for posture and changes in physical activity. They found PNS activity (RSA) decreased (5, 14), whereas SNS activity (0.1-EqHz peak or microneurography) remained relatively stable during the daytime (5, 14, 18, 32). The one study showing little circadian influence on PNS activity (5) collected only three assessments of ANS activity in a 24-h period, in contrast to the hourly measurements taken in this study. Contrary to expectations, PNS activity was not influenced by the sleep system. There have been previous findings of changes in cardiac PNS activity between sleep stages (21, 32, 34, 36), but in these studies, changes in the influence of the circadian system were not controlled for. Furthermore, in dogs, increases in HR with arousal from NREM sleep have been mainly attributed to an increase in SNS activity rather than to a decrease in PNS activity (15).

Given the circadian influence on PNS activity, it was interesting to compare the variations in RSA and core body temperature across the 24-h period. Although RSA was found to correlate with body temperature and was fit significantly with complex curves in both routines, it is important to note that there were marked phase differences between the two variables (Figs. 2 and 3). Although it is possible that PNS activity is influenced by an oscillator separate from the circadian oscillator that influences body temperature, it is important to note that other “markers” of the endogenous circadian oscillator believed to control body temperature, such as cortisol, do not show a similar pattern to body temperature. Thus it is not possible to determine from these results the nature of the circadian control of PNS activity. The finding of a circadian influence on PNS activity and the fact that PNS activity began to increase in anticipation of sleep onset suggest that there is some circadian control of ANS functioning in preparation for sleep onset. Thus the circadian system appears to downregulate ANS activity as sleep onset approaches by increasing PNS activity rather than by decreasing SNS activity. Indeed, it may be that a failure of PNS activity to increase in anticipation of sleep onset might be as important as SNS arousal in causing sleep onset insomnia.

The decrease in SNS activity with sleep, as measured here for the first time with PEP, has implications for the earlier findings based on the 0.1-EqHz peak. Previously, invasive and thus necessarily peripheral measurements of SNS activity such as microneurography in humans have found marked decreases in SNS activity with sleep (16, 22, 30, 31), whereas the more central and noninvasive measure, the 0.1-EqHz peak, has not consistently shown this effect (2, 23, 32–36). With the present results, it now seems likely that this discrepancy is due more to the dubious nature of the 0.1-EqHz peak as a pure measure of SNS activity rather than to either the invasiveness or peripheral nature of the microneurographic technique. Because of the design of this experiment, the focus of the study was not on sleep stage differences in ANS activity. However, the decrease in SNS activity with sleep onset rather than in anticipation of sleep onset is consistent with previous findings (5, 9, 14, 32). Thus the sleep influence on SNS activity may have implications for the cardiovascular sequelae of sleep disorders such as obstructive sleep apnea, which is associated with repetitive arousals from sleep (29).

In terms of the methodological limitations of this study, it is important to note that although the constant routine procedure was originally designed to control for the masking effects of food intake, sleep, and changes in posture and physical activity, the increase in fatigue and stress due to the desire to be more active than the procedure permitted and/or the effect of a maintained supine posture may have produced additional masking effects (19). However, as mentioned in Design, this was controlled for by having two groups of subjects who started the experiment at different times during the day. It is also possible that in the week between the two routines, the subjects may have phase shifted slightly from the sleep-wake schedule they had just before their first routine. Nevertheless, this would have been controlled for by the counterbalancing of routines across subjects.

The results from this experiment also indicate that evidence for a circadian influence on SNS activity most likely reflects postural, physical activity, and sleep confounds in the design of previous studies. Indeed, of the three previous studies that did control for these factors (5, 14, 32), SNS activity was not found to vary markedly during the daytime, consistent with the findings of this experiment. Therefore, the recent interest in identifying the cause of the increased incidence of cardiovascular events in the morning may be better aimed at examining the influence of increased physical activity and/or postural change during morning awakening. Another important factor may be the phasic bursts of SNS activity or general autonomic disruption in REM sleep (2, 16, 25).

In conclusion, the activity of the PNS was found to be predominantly influenced by the circadian system and SNS activity by the sleep system. Future research should focus on examining more closely these separate influences, for example, changes in PEP in different sleep stages, the importance of decreased SNS activity for the initiation of sleep (e.g., Ref. 4), and the mechanisms of the circadian influence on PNS activity.
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We thank Prof. Alexander A. Borbély for comments on the manuscript.

This work was supported by an Australian Research Council grant to J. Trinder.

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Received 9 December 1996; accepted in final form 26 June 1997.

REFERENCES


