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Age-Related Differences in Recovery from Simulated Jet Lag

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Summary: Six healthy young men and eight early middle-aged men were isolated from environmental time cues for 15 days. For the first 6–7 days (one or two nights adaptation, four nights baseline), their sleep and meals were scheduled to approximate their habitual patterns. Their daily routines were then shifted 6 hours earlier by terminating the sixth or seventh sleep episode 6 hours early. The new schedules were followed for the next 8 or 9 days. Important age-related differences in adjustment to this single 6-hour schedule shift were found. For the first 4-day interval after the shift, middle-aged subjects had larger increases of waking time during the sleep period and earlier termination of sleep than young subjects. They also reported larger decreases in alertness and well-being and larger increases in sleepiness, weariness and effort required to perform daily functions. The rate of adjustment of the circadian core temperature rhythm to the new schedule did not differ between groups. These results suggest that the symptoms reported by the middle-aged subjects may be due mainly to difficulty maintaining sleep at early times of the circadian day. The compensatory response to sleep deprivation may also be less robust in middle-aged individuals traveling eastbound. **Key Words:** Jet lag—Sleep—Circadian rhythms—Aging.

A constellation of symptoms known as jet lag frequently afflicts people who travel rapidly across time zones. It includes insomnia, fatigue, weakness, sleepiness, gastrointestinal complaints, irritability and malaise (1,2). Travel across time zones has also been associated with impaired cognitive performance (2), recurrence of depression (3), diabetic ketoacidosis (4), sleep paralysis (5) and decreased athletic ability (1). Similar symptoms have been reported by shift workers.

The symptoms of jet lag and shiftwork have been attributed to the slow and uneven rate of adjustment of internal circadian rhythms to the new time zone or schedule (6). The circadian timing system (biological clock) responds to external time information and synchronizes biological rhythms such as temperature, sleep and alertness to the 24-hour solar day. Light–dark patterns and social cues seem to be the most important external time sources for humans (7,8).

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There is a limit to the amount by which the circadian timing system can adjust on a daily basis (9,10) and there is a directional asymmetry (6,11). It is easier to delay the sleep–wake cycle, i.e. stay up later and sleep later as in westbound travel, than it is to advance it (12). This asymmetry is probably explained by the tendency of the human timing system to run slow relative to solar time. This tendency can be shown by eliminating external sources of temporal information. Under such conditions, rhythms free-run at periods slightly greater than 24 hours (8).

The rates of adjustment to a new schedule are not the same for every biological rhythm (13). As a result, the phase relationships of several rhythms following a schedule change may differ from their usual pattern. This has been hypothesized to be the cause of symptoms. However, sleep deprivation invariably accompanies jet lag (2,11), and it is possible that the symptoms associated with jet lag and shiftwork are mostly caused by the sleep loss (14).

These questions become especially important for older shiftworkers and travelers, who may be more at risk for impaired adjustment to both shiftwork (15)

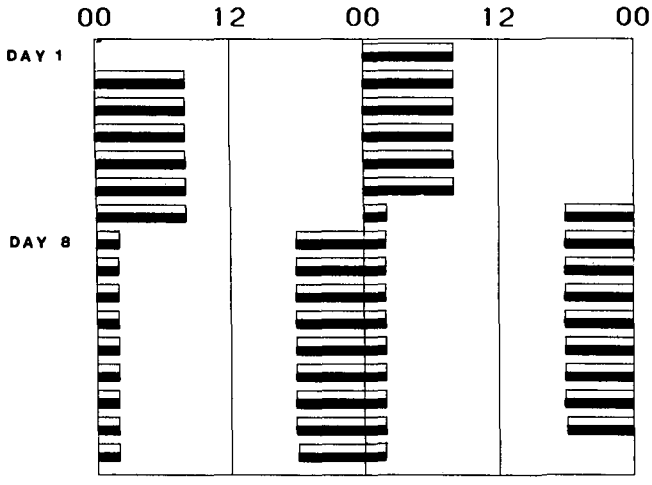

FIG. 1. Schematic diagram of the experimental design. Open rectangles represent scheduled periods of bedrest. Filled rectangles represent periods of sleep. Starting on day 8, bedrest was scheduled 6 hours earlier.

and travel across time zones (16,17). The age-related differences have been attributed to decreased ability of circadian rhythms to adjust (15,16), increased amplitude of rhythms (18,19), more time required to recuperate (15) and more sleep disturbances in older individuals (16). Age may also affect the response to benzodiazepines in simulated shiftwork paradigms (20). However, not all authors agree that age affects the ability to adjust to schedule shifts (21).

We have begun to look for age-related differences in the ability to adapt to acute schedule changes. We chose a single 6-hour phase advance, as 6 hours would cause a substantial perturbation of the circadian timing system. In this paper, we ask whether these differences are due to an age-related ability to recover from sleep deprivation, to circadian adjustment factors related to age or to both.

METHODS

Six young men aged 18–25 years and eight early middle-aged men aged 37–52 years completed the study. All subjects were physically and psychologically healthy and were not taking any medications. Each signed informed consent. The data from one young subject were excluded because he did not complete the study. Some of the data from the middle-aged subjects have been reported previously (2).

Subjects lived individually in apartments from which all sources of time information were excluded. Subjects therefore had no information regarding the time of day and no means of measuring the passage of time. The laboratory has been described in detail previously (22). A single 6-hour phase advance in each subject's schedule was accomplished as follows. Subjects were scheduled to sleep according to their habitual sleep–wake patterns for a baseline period lasting either 6 days (middle-aged subjects) or 7 days (young subjects; Fig. 1). The first 2–3 days (one to two nights) were considered adaptation, and the next 4 days (four nights) comprised the baseline interval for data analysis. Habitual patterns were determined by sleep logs kept by the subjects for 7–14 days before entering the laboratory. During the sixth or seventh night, subjects were awakened 6 hours earlier than usual. For the remainder of the study, all scheduled events—bedtime, waking and meals—occurred 6 hours earlier than during baseline. For example, a subject who was scheduled for bed from 0000 to 0800 hours during baseline would be in bed from 1800 to 0200 hours following the schedule change. Subjects remained on the altered schedule for eight or nine sleep periods following the abbreviated night. Only data from the first eight postshift sleep periods that were completed by all subjects have been analyzed, except where noted.

Room lights were extinguished during the bedrest periods (0 lux). At other times, tungsten lamps provided up to 300 lux. During the entire study, meals, sleep periods and voluntary exercise sessions were scheduled at the same time of the subjective day for all subjects.

Data included core temperature, polysomnographic recordings of every sleep episode, self-ratings of mood and alertness and tests of performance. Core temperature was measured every minute with rectal temperature probes (Yellow Springs series 400). Sleep records were scored manually in 30-second epochs by experienced scorers using standard criteria (23). Sleep onset was defined as the first epoch of stage 1 (from a series of one or more) followed by any other stage of sleep.

Moods and alertness were rated by subjects using visual analogue scales (100–mm lines). Alertness was rated at intervals that averaged 20 minutes. Mood scales (alertness, weariness, sleepiness, happiness, effort required for daily activities and overall well-being) were completed six or seven times per day on average. Daily means were calculated for each subject before a daily group mean was calculated.

Temperature values were smoothed using a method similar to band-pass filtering (24). In all young subjects and all but two of the middle-aged ones, a single minimum and maximum value of the smoothed data were found each circadian day. Using the smoothed data, the daily amplitude of the temperature rhythm was defined as the difference in degrees Fahrenheit between the minimum and the subsequent maximum. The time of each minimum was measured as the number of hours it occurred after the preshift scheduled bedtime.

Data were analyzed by repeated measures MANO-

TABLE 1. *Sleep parameters during the baseline, early postshift and late postshift intervals*

Parameter[a]	Group	Baseline	Early postshift	Late postshift
Time in bed, A	Middle-aged	439.3 ± 11.3	439.3 ± 11.3	438.3 ± 11.6
	Young	474.1 ± 16.3	475.9 ± 15.3	474.4 ± 16.4
Total sleep time, B[b], C	Middle-aged	408.5 ± 8.0	360.0 ± 15.8	372.5 ± 15.2
	Young	442.9 ± 15.0	432.3 ± 24.3	403.4 ± 33.1
Sleep efficiency, B[b], C	Middle-aged	93.2 ± 1.5	82.0 ± 3.0	85.1 ± 3.3
	Young	93.4 ± 0.4	90.6 ± 2.9	84.5 ± 5.0
Sleep latency, A, D	Middle-aged	9.1 ± 1.9	5.0 ± 1.0	11.3 ± 4.7
	Young	15.6 ± 3.9	14.8 ± 2.5	33.4 ± 10.1
Terminal wake latency	Middle-aged	1.8 ± 1.3	13.1 ± 9.2	20.7 ± 11.8
	Young	0.5 ± 0.3	4.0 ± 2.7	0.9 ± 0.7
Wake during sleep, C	Middle-aged	15.3 ± 4.6	57.2 ± 15.4	29.8 ± 14.3
	Young	12.4 ± 1.9	21.3 ± 7.4	31.6 ± 15.1
Stage 1 sleep, A, C	Middle-aged	47.6 ± 5.2	35.3 ± 5.1	37.1 ± 4.5
	Young	27.9 ± 2.7	23.1 ± 2.6	26.5 ± 3.0
Stage 2 sleep	Middle-aged	240.7 ± 8.6	216.1 ± 14.2	220.9 ± 18.0
	Young	202.1 ± 11.2	195.0 ± 15.4	186.9 ± 14.7
Slow-wave sleep, A, B, C	Middle-aged	38.1 ± 8.1	49.1 ± 8.2	46.2 ± 6.6
	Young	119.4 ± 9.8	133.2 ± 7.3	115.1 ± 10.4
REM sleep, B, C	Middle-aged	84.9 ± 7.9	62.6 ± 7.5	70.6 ± 5.7
	Young	96.4 ± 9.2	83.8 ± 9.6	79.3 ± 11.2
REM latency	Middle-aged	64.4 ± 7.9	58.8 ± 12.1	57.4 ± 8.8
	Young	68.9 ± 6.8	59.7 ± 4.4	67.8 ± 9.2

[a] Expressed as percent for sleep efficiency, minutes for other parameters. Capital letters indicate significant results ($p < 0.05$) for the following comparisons: A = between groups, B = condition (baseline, early postshift, late postshift) × group interaction, C = baseline vs. early postshift interval, D = early vs. late postshift interval. See text for significance levels. All values are means ± SEM.
[b] $p = 0.07$.

VA with three conditions: baseline, early postshift and late postshift. These conditions were defined as follows: (1) baseline was the last 4 days before the schedule shift; (2) early postshift was the first 4 days or the first four complete night sleep periods after the shift; and (3) late postshift was the fifth through eighth days (or nights) after the shift. The short night of sleep was not included in the early postshift interval, but the following day was included in that interval for analysis of the daytime measures. Post hoc comparisons between groups were made using Fisher's least significant difference test (25).

RESULTS

Sleep parameters

Scheduled sleep period time (time in bed)

Based on differences in habitual sleep time as recorded in sleep logs, the middle-aged subjects were scheduled to spend 439 minutes in bed, which was approximately 35 minutes less than the young subjects ($p < 0.05$; Table 1). On the shift night, subjects in the middle-aged group spent 79 minutes in bed vs. 116 minutes for subjects in the young group ($p < 0.05$). These represented 18.2% and 24.1% of the habitual sleep period times, respectively.

Total sleep time and sleep efficiency

The young subjects averaged somewhat more sleep throughout the study ($p < 0.08$; Table 1 and Fig. 2A).

Because there were differences in total sleep between groups, and because sleep time was limited by the amount of time spent in bed by each subject, the effects of the shift on sleep may best be described in terms of the amount of time spent sleeping as a percent of time spent in bed (sleep efficiency; Fig. 2B). Sleep efficiency was high in both groups during the baseline period (>93%). It decreased in both groups in the early postshift interval (main effect of condition, $p < 0.05$) but showed a greater decline in the middle-aged group. By the late postshift interval, sleep efficiency was once again equivalent in the two groups, though still lower than during the baseline period. Although the young group showed only a slight decline in the early postshift interval compared to the middle-aged group, their sleep efficiency continued to decrease from the early postshift interval to the late postshift interval, whereas that of the middle-aged group showed a slight increase. Using total sleep time as the measure, there was a significant interaction between condition and group ($p = 0.05$). Post hoc comparison showed that the two groups differed only in the early postshift interval ($p < 0.05$).

A closer look at the day-by-day pattern of sleep efficiency reveals that the young group had an increase

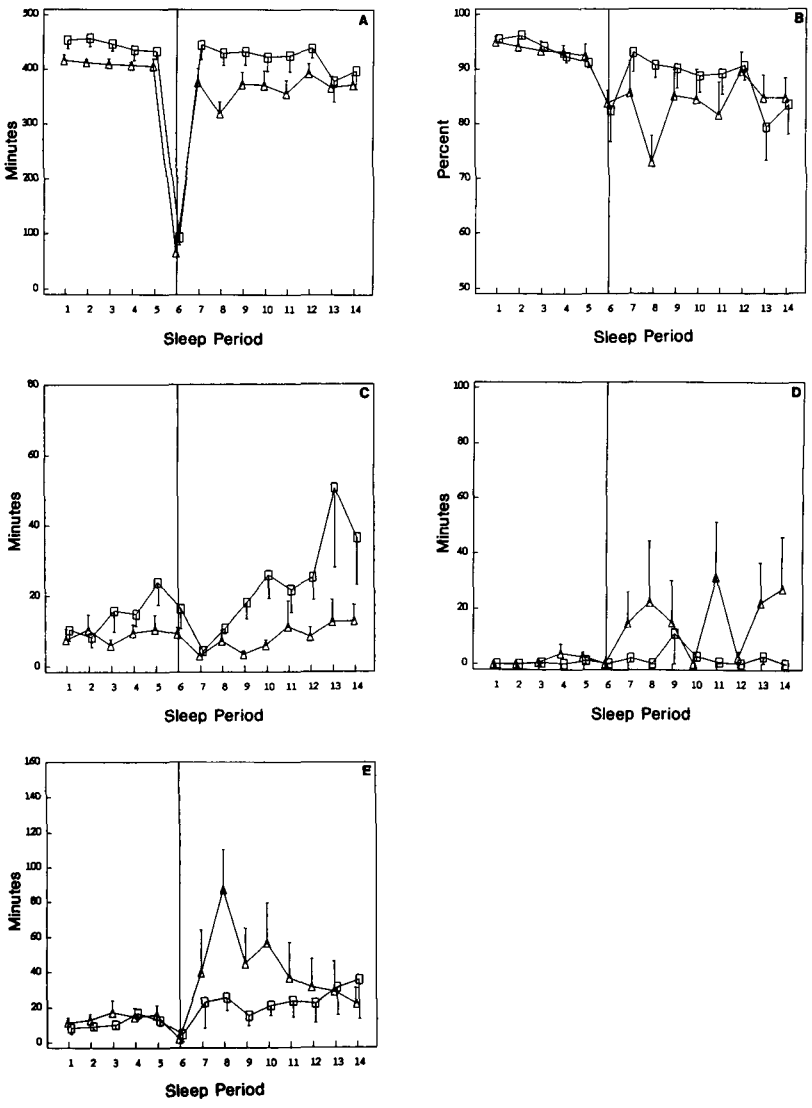

FIG. 2. Sleep parameters in the middle-aged and young groups. Each point represents daily mean ± SEM. Boxes: young subjects; triangles: middle-aged subjects. A: total sleep time; B: sleep efficiency; C: sleep latency; D: terminal wake latency; E: wakefulness during sleep. The y-axis units are in minutes with the exception of sleep efficiency, which is in percent. Sleep periods across the study are plotted on the x-axis. Sleep period 6 is the short night of sleep.

in sleep efficiency on the night following the shift, whereas the middle-aged group showed a decrease in sleep efficiency compared to baseline on this night and an even greater decrease on the following night. On this second night following the shift, the average sleep efficiency of the middle-aged subjects reached 72.9%, compared to 90.3% in the young group. This night was the worst single night for the middle-aged subjects in terms of sleep efficiency.

Sleep latency

Sleep latencies were slightly but significantly longer in the young subjects regardless of condition ($p < 0.01$; Fig. 2C and Table 1). In the early postshift interval, sleep latencies tended to decrease in both groups. Latencies then increased from the early to the late postshift interval (contrast, $p < 0.05$). By the late postshift interval, the sleep latencies of the young subjects approximately doubled from 15 minutes during baseline to 33 minutes. In the middle-aged subjects, mean sleep latency returned to baseline from the early to the late postshift interval.

Terminal wake latency

This parameter is defined as the interval between the final awakening of the sleep period and the scheduled end of the sleep period. Before the shift, it was very short in both groups (Fig. 2D and Table 1). After

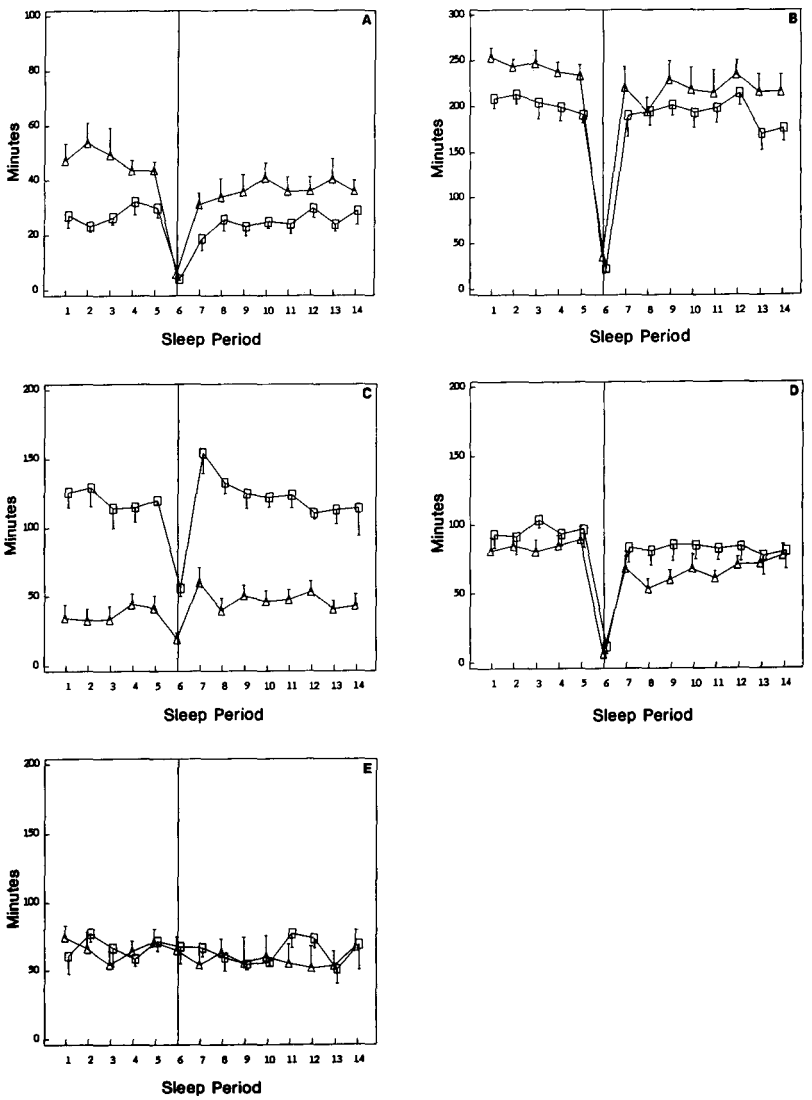

FIG. 3. Sleep parameters in the middle-aged and young groups, continued. Each point represents the daily mean ± SEM of the parameter. Boxes: young subjects; triangles: middle-aged subjects. A: stage 1 sleep; B: stage 2 sleep; C: slow-wave sleep; D: REM sleep; E: REM latency. The y-axis units are in minutes, and sleep periods across the study are plotted on the x-axis. Sleep period 6 is the short night of sleep.

the shift, several subjects in the middle-aged group had large increases that accounted for a part of this group's decrease in sleep efficiency. Due to the large variance in this parameter, statistically significant differences between the groups were not found.

Wakefulness during sleep

This parameter is defined as the amount of waking time in minutes after sleep onset but before the last awakening of the sleep period. It increased during the early postshift interval in both groups (Fig. 2E and Table 1; main effect of condition, $p < 0.05$); the increase tended to be larger in the middle-aged group. The low sleep efficiency in the middle-aged subjects on the second night following the phase advance was primarily accounted for by an increase in wakefulness during sleep. During the early postshift interval, 73% of total wake time during the scheduled sleep period consisted of wakefulness during sleep, with the terminal wake latency accounting only for an additional 19% of the waking time. During the late postshift interval, wakefulness during sleep remained elevated above baseline in both groups.

Stage 1

As expected (12), the middle-aged subjects had significantly more stage 1 sleep throughout the study ($p < 0.05$; Fig. 3A and Table 1). Both groups showed a decrease in minutes of stage 1 in response to the shift.

TABLE 2. *Sleep periods with short (<15 minutes) REM latencies*[a]

Comparison	Group	Preshift			Postshift		
		n	No.[b]	%	n	No.	%
By number of nights	Middle-aged	40	1	2.5	72	16	22.2[c]
	Young	35	2	5.7	48	2	4.2
By number of subjects	Middle-aged	8	1	12.5	8	5	62.5
	Young	6	2	33.3	6	2	33.3

[a] These data reflect values from all nights available for each subject.
[b] Number of sleep periods with REM latency less than 15 minutes.
[c] $p = 0.052$ by likelihood ratio statistic (G square) (26).

Stage 2

There were no significant changes in stage 2 across the study (Fig. 3B and Table 1).

Slow-wave sleep (SWS)

As expected (12), young subjects had significantly more SWS across the study ($p < 0.001$; Fig. 3C and Table 1). In the early postshift interval, both groups showed similar significant increases in the minutes of SWS ($p < 0.05$). SWS then returned to baseline levels in the young group and remained elevated in the middle-aged group (condition by group interaction, $p < 0.05$). On the night following the schedule shift, middle-aged subjects obtained an average of 60 minutes of SWS compared to their baseline average of 38 minutes, whereas the young subjects obtained 154 minutes compared to a baseline average of 119 minutes.

Rapid eye movement (REM) sleep

There were no significant differences between groups in the amount of REM sleep. The schedule shift led to a decrease in the mean number of minutes of REM sleep in both groups (main effect of condition, $p < 0.01$; Fig. 3D and Table 1). The decrease in REM time persisted through the late postshift interval.

REM sleep latency

Mean REM latency, defined as number of minutes from sleep onset to the first 30-second epoch of REM sleep, did not differ between groups and did not change after the shift (Fig. 3E and Table 1). However, the probability of having a REM latency of 15 minutes or less increased in the middle-aged subjects following the shift [baseline vs. all postshift nights, G square (26), $p = 0.052$; Table 2].

Temperature rhythms

Amplitude

The young subjects tended to have higher amplitudes of the core temperature rhythm throughout the study ($p = 0.08$; Fig. 4A and Table 3). In both groups, mean amplitude decreased following the shift (main effect of condition, $p < 0.05$). This effect lessened (i.e. amplitudes increased) from the early postshift interval to the late postshift interval, but mean amplitude had still not returned to baseline levels by the end of the study in either group.

Phase

Temperature minima occurred earlier in the middle-aged subjects over the entire study ($p < 0.05$; Fig. 4B).

TABLE 3. *Temperature amplitude and time of minimum during baseline and early and late postshift intervals*[a]

Parameter	Group	Baseline	Early postshift	Late postshift
Amplitude[b], A[c], B	Middle-aged	1.5 ± 0.1	0.9 ± 0.1	1.3 ± 0.1
	Young	1.8 ± 0.2	1.4 ± 0.2	1.5 ± 0.2
Time of minimum[d], A, B	Middle-aged	4.0 ± 0.4	1.0 ± 0.6	−2.1 ± 1.7
	Young	5.3 ± 0.2	1.2 ± 0.5	0.6 ± 0.5

[a] Capital letters indicate significant ($p < 0.05$) results for the comparisons below: A = between groups; B = baseline period vs. early postshift interval. See text for significance levels. All values are means ± SEM.
[b] Degrees Fahrenheit.
[c] $p = 0.08$.
[d] Time of temperature minimum expressed as hours after the baseline bedtime. Negative values represent times of minima preceding baseline bedtimes. Complete adjustment to the 6-hour phase advance would occur at −2.0 hours in the middle-aged group and at −0.7 hours in the young group.

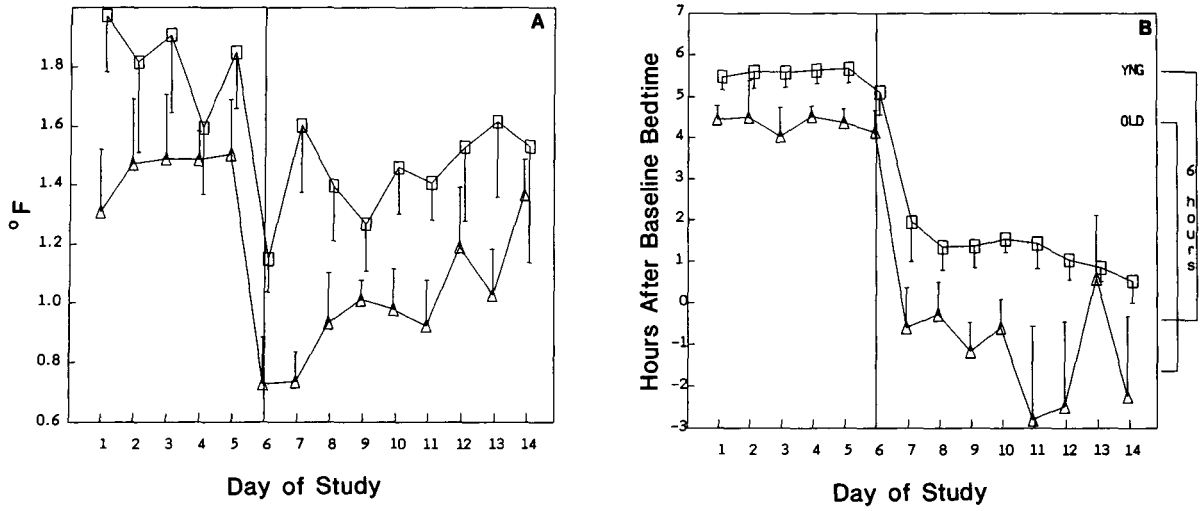

FIG. 4. Temperature parameters in middle-aged and young groups. Each point represents the daily means ± SEM of the parameter. Boxes: young subjects; triangles: middle-aged subjects. A: amplitude; B: phase of temperature minima. Amplitude is defined as the difference in degrees Fahrenheit between the maximum and minimum of the smoothed temperature waveform. Phase is represented as hours before or after the original baseline scheduled bedtime (time 0). Two 6-hour intervals are plotted on the right side of the figure to denote where the phases in each group would be if the temperature minima adjusted completely to the shift. Days of the study are plotted along the x-axis.

In both groups the temperature minima shifted to earlier times in response to the 6-hour shift in schedule (main effect of condition, $p < 0.001$). Most of the change occurred during the early postshift interval (contrast $p < 0.01$). The minima continued to shift more slowly in the same direction through the late postshift interval. By the end of the study, 8 days after the shift, the times of the temperature minima had not fully adjusted to the 6-hour schedule shift in the young subjects. The time of the minima in the middle-aged subjects, on the other hand, appeared to have shifted by more than 6 hours in the late postshift interval, which can be attributed to two subjects as described below. However, the variances were much larger for the middle-aged group, indicating that the adjustment was less uniform overall, especially during the late postshift interval.

The temperature minima of two middle-aged subjects did not shift in the same way as the other members of that group or the six young subjects (Fig. 5). Most subjects showed a single daily decrease in temperature, which presumably reflected the phase of the circadian timing system as well as the evoked effect of sleep. In contrast, daily temperature patterns of the two atypical subjects showed both a decrease in temperature that was synchronous with sleep and a prominent second trough that presumably represents the phase of the circadian timing system (27). The latter component occurred later each day so that it approached (but did not reach) the baseline phase position by the end of the study. None of the young subjects showed this separate component.

Subjective alertness and affective state

Subjective alertness

There were no between-group differences in subjective alertness across the study (Table 4 and Fig. 6A). Subjective alertness decreased following the shift (main effect of condition, $p < 0.01$), especially in the middle-aged subjects. Middle-aged subjects rated themselves as 25% less alert than during their baseline on the day after the short sleep, compared to a 14% decrease in

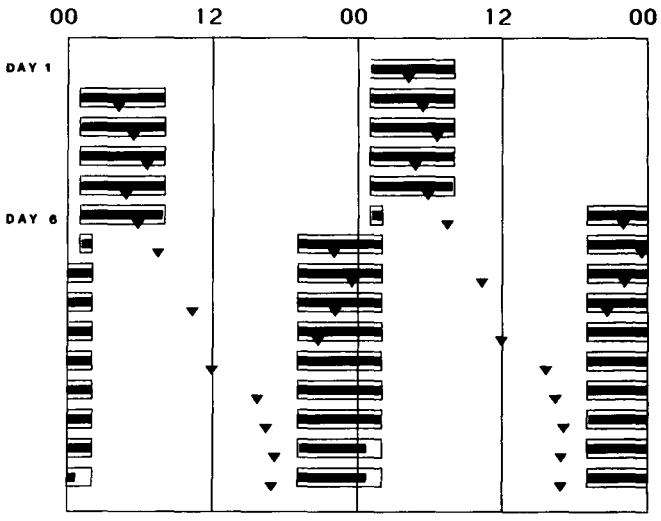

FIG. 5. Double raster plot of sleep and temperature patterns in a middle-aged subject. Black rectangles denote the sleep period, and black bars represent actual time spent asleep. Triangles depict the times of the smoothed temperature minima.

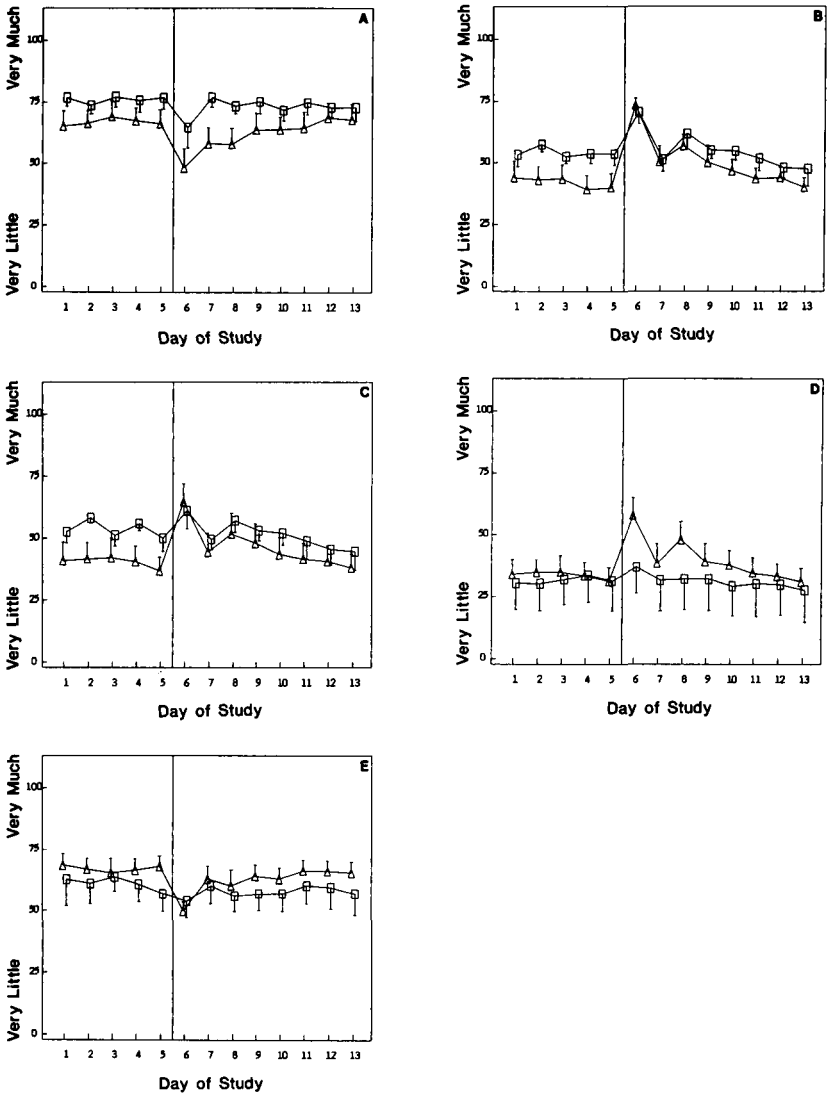

FIG. 6. Subjective alertness and mood ratings across the study. Each point represents the mean ± SEM of the parameter. Boxes: young subjects; triangles: middle-aged subjects. A: alertness; B: sleepiness; C: weariness; D: effort required for daily tasks; E: overall well-being. Values on each y-axis are in units from 0 to 100, with 0 corresponding to "very little" and 100 to "very much" of the parameter.

the young men. Alertness then increased but remained slightly below baseline levels. The young subjects returned to their baseline mean more quickly. The delayed return in the middle-aged subjects may be explained by their more disrupted sleep, especially on night 8 (cf. Fig. 2A and B).

Sleepiness

Subjective ratings of sleepiness increased significantly in both groups in the early postshift interval (main effect of condition, $p < 0.001$; Fig. 6B and Table 4), especially on the first day after the abbreviated night of sleep. By the late postshift interval, sleepiness ratings had returned to baseline levels in both groups. An increase in sleepiness was observed on the day following the second night after the shift (day 8 on Fig. 6B), which was the night of poorest sleep in the middle-aged group.

Weariness

The ratings of weariness (Fig. 6C and Table 4) resembled those of sleepiness in the middle-aged subjects. Subjective ratings of weariness increased following the shift (main effect of condition, $p < 0.01$), an effect that was accounted for by an increase in weariness in the middle-aged subjects during the early postshift interval (condition by group interaction $p < 0.06$). It is also worth noting that weariness, like sleepiness, increased in the middle-aged group on day 8, which followed a night of decreased sleep.

TABLE 4. *Subjective ratings of alertness and mood during the baseline and early and late postshift intervals*[a]

Parameter[b]	Group	Baseline	Early postshift	Late postshift
Alertness, A[c], B, C	Middle-aged	67.5 ± 5.6	57.2 ± 6.4	66.4 ± 5.8
	Young	76.1 ± 3.9	72.8 ± 4.4	73.3 ± 4.4
Sleepiness, B, C	Middle-aged	41.4 ± 5.6	57.8 ± 4.2	43.6 ± 3.9
	Young	54.2 ± 2.5	59.7 ± 3.1	50.3 ± 4.7
Weariness, A[c], B, C	Middle-aged	40.3 ± 6.4	52.2 ± 6.7	40.0 ± 5.6
	Young	53.9 ± 2.8	55.3 ± 1.9	47.8 ± 6.4
Effort, A, B, C	Middle-aged	33.6 ± 5.6	45.8 ± 6.4	34.2 ± 5.3
	Young	31.9 ± 10.8	33.3 ± 11.9	29.2 ± 12.5
Overall, B, C	Middle-aged	66.7 ± 4.4	59.2 ± 4.7	65.3 ± 4.2
	Young	60.6 ± 6.9	56.7 ± 6.4	58.3 ± 7.8

[a] Capital letters indicate significant results ($p < 0.05$) for the following comparisons: A = condition (baseline, early postshift, late postshift) × group interaction; B = baseline vs. early postshift interval; C = early vs. late postshift interval. See text for significance levels. All values are means ± SEM.
[b] Expressed on a scale of 0–100 (very little to very much).
[c] $p < 0.07$.

Effort

The two groups showed a different response to the schedule shift in their ratings of the amount of effort required for daily activities (condition by group interaction, $p < 0.05$). The effort ratings increased significantly in the middle-aged subjects in the early postshift interval (post hoc comparison, $p < 0.05$; Fig. 6D and Table 4), while remaining stable in young subjects. In the middle-aged group, ratings of effort increased on day 8 following the night of poor sleep.

Happiness

Middle-aged subjects rated themselves as happier than the young men across the entire study ($p < 0.01$; Table 4). There were no significant effects of the schedule shift on this parameter.

Overall well-being

This scale reads "Overall, how do you feel?" and serves as an inverse measure of malaise. Ratings decreased during the early postshift interval (main effect of condition, $p < 0.001$) in both groups (Fig. 6E and Table 4).

DISCUSSION

This study employed a unique experimental model of jet lag to study the acute and long-term effects of a single 6-hour advance in schedule. A sustained effect on sleep continuity and architecture and a transient increase in sleepiness and malaise were produced by this change in schedule. In general, the effects were more severe in middle-aged subjects.

Sleep

The schedule shift produced a reduction in total sleep time and sleep efficiency for both groups. The reduction was greater in the middle-aged subjects in the early postshift interval, mostly due to impairment of sleep continuity. A smaller decrease in total sleep time in the young subjects was due largely to increased sleep latency. The amount of REM sleep also decreased after the shift in both groups. By contrast, the amount of SWS increased in the early postshift interval in both groups. In the middle-aged subjects, the increase in SWS persisted through the late postshift interval, while SWS returned to normal in the young subjects.

Previous studies of the effects of eastbound schedule changes on sleep parameters have involved actual travel or acute phase advances without prior sleep deprivation. The short-term, naturalistic studies have produced inconsistent results. Sasaki and colleagues (11) reported an increase in SWS and decrease in REM sleep as in our studies, but no values for sleep efficiency were reported. Dement and colleagues (28) and Wegmann and colleagues (29) reported decreased sleep efficiency but no changes in SWS or REM. In addition, Wegmann's group reported that age was negatively correlated with sleep efficiency following arrival at the destination. Roehrs and colleagues (30) studied alert and sleepy young subjects after an acute 4-hour phase advance and found a significant decrease in sleep efficiency with no change in sleep stages. Unlike the present study, there was no sleep deprivation component to the protocol; thus subjects were put to bed before a full waking day had elapsed. Walsh and colleagues (31) also employed an acute phase advance of 3 hours to study sleep in young subjects. Total sleep time (TST) significantly decreased as did sleep efficiency compared to baseline. REM parameters did not change. As with the previous study (30), there was no sleep deprivation

aspect to their paradigm. Thus, it cannot be directly compared to the present study.

Because the schedule shift included both a change in timing of the sleep period as well as sleep deprivation, the literature on both topics may help explain the pattern of sleep changes in response to a schedule advance. There are at least three possible explanations that are not mutually exclusive. The first involves the effect of sleep deprivation. In studies of sleep deprivation, sleep loss has usually been accomplished by depriving subjects of sleep for one or more nights, and then by allowing them to sleep at their usual time (32–34) or at a later time (35–37). These studies showed that sleep deprivation results in increased TST and sleep efficiency, increased SWS and increased REM (33). Middle-aged subjects were able to respond as young subjects did. In addition, REM latency decreased in older subjects. Of these effects, our subjects showed only the increase in SWS, implying that the schedule shift strongly influenced their response to sleep deprivation. One might conclude from our data that only SWS is relatively free to vary in response to sleep deprivation produced by phase shifts, whereas total sleep and REM are constrained by circadian factors from responding as they would to sleep deprivation alone. These constraints might be stronger in middle-aged subjects.

There has also been a study of subjects sleeping at earlier phases of the day, accomplished by 12–20 hours of sleep deprivation (38). This study did not find robust changes in TST, %SWS or %REM when subjects were sleep deprived for 16 hours (sleeping 8 hours earlier than their usual bedtimes). Because their study involved much more sleep deprivation than the current work, it may be that the significant changes in %REM that we observed are related more to the phase advance per se and less to the sleep deprivation effects.

Sleep deprivation studies have shown that a single dose of sleep deprivation leads to SWS rebound only on the first recovery night. The persistent increase shown by our middle-aged subjects supports the hypothesis that there is a continuing source of pressure for SWS beyond the initial sleep deprivation incurred by the schedule shift. This source could be the continued poor sleep efficiency shown by both groups, leading to cumulative sleep deprivation and continued pressure for SWS. The problem with this hypothesis is that the increase in SWS would come from loss of stage 1, stage 2 and/or REM sleep. Sleep deprivation studies have not provided enough information to predict an increase of SWS from the selective loss of other stages.

A second explanation is that the decrease in REM is a primary and direct effect of the schedule shift. This is consistent with the report by Czeisler and colleagues (39) on free-running subjects, who showed a decrease in the percent of REM sleep during the part of the circadian day spanned by the schedule shift in our study. Zulley (40) also reported that the amount of REM sleep is reduced when temperature minima occur later in a sleep episode, as is the case in our study just after the schedule shift and before the temperature rhythm has resumed its baseline phase relationship to sleep. There might be an inverse interaction between SWS and REM sleep such that SWS increases passively to fill the gap left by decreased REM sleep (41), thus accounting for the increase in SWS shown by our subjects.

A third explanation is suggested by the reported positive correlation between absolute core temperature and amount of SWS (42). In the study by Horne and Shackell, passively elevating the core temperature beginning 2.5 hours before bedtime resulted in increased SWS and decreased REM sleep. To investigate the possibility that the sleep changes in our subjects were associated with a rise in core temperature, we calculated the average core temperatures for the 4 hours preceding bedtime for both the baseline period and the early postshift interval. Following the shift, temperatures were higher ($p = 0.051$) than during baseline (early postshift interval: 98.99 ± 0.29 vs. baseline: 98.81 ± 0.20 for the middle-aged subjects and 98.73 ± 0.02 vs. 98.48 ± 0.10 for the young subjects, respectively). Although produced by a different experimental paradigm, our findings are consistent with their report.

Alertness and mood

Subjective ratings of weariness, sleepiness, well-being and effort required for daily activities worsened just after the schedule shift. In general, the negative effect was greater in the middle-aged subjects. The difference between groups could not be explained by a greater tendency of middle-aged subjects to report more negative symptoms (43), as it was the young subjects who rated themselves higher on the scales assessing sleepiness and weariness and lower on the scales of happiness and overall well-being.

Temperature patterns

The amplitude of the temperature rhythm decreased significantly in both groups after the phase advance. This can be explained by incomplete adjustment of the phase of the endogenous components of the temperature rhythm, which were therefore out of phase with the faster adjusting sleep and activity-related components (44).

Temperature minima occurred earlier in the middle-aged subjects across the whole study. Earlier temperature minima with respect to the sleep–wake cycle have

been reported in older subjects during free-running (12, for example). The rate at which the temperature minima responded to the shift did not differ between the two groups. The middle-aged subjects showed a larger variance between subjects, which can be accounted for in large part by the two subjects who apparently delayed in response to the schedule advance. The mean time of the minimum in the middle-aged subjects actually overcompensated on some days as a result of the two subjects who phase delayed. The phenomenon of overcompensation has also been reported in animals (45).

Mechanisms of jet lag and effects of age

Under our conditions, it takes longer than 8 days for sleep and temperature to adjust to a 6-hour advance in schedule. It is notable, therefore, that daytime symptoms from our simulated jet lag occurred for the most part only during the early postshift interval. During this time, the symptoms appeared to be worse in the middle-aged group. This is also the time that sleep efficiency differed most between the two groups. Though still lower than baseline, sleep efficiency had become nearly identical in the groups by the late postshift interval. The daytime symptoms had also abated by this time.

In general, the patterns of response in the variables measured appeared similar in direction in the two age groups. The middle-aged subjects were characterized by a greater negative response in each parameter, with the exception of sleep efficiency and total sleep time. Whereas the young group showed increases in both parameters on the one night immediately following the shift, presumably because of the sleep deprivation involved, the middle-aged group showed decreases.

There were hints that the middle-aged group had a tendency to respond to the shift in a qualitatively different manner from the young group. First, there were the two middle-aged subjects who apparently showed a phase delay in a component of their temperature rhythm. Second, there appeared to be an increasing probability of short REM latencies following the shift in the middle-aged group. Third, on many different parameters, the middle-aged group seemed to show more day-to-day intrasubject variability of response than the young subjects. This has previously been described by our group in middle-aged subjects as a zig-zag pattern (2). There may be boundaries to how much phase advance middle-aged subjects can tolerate, as shown by an increased likelihood of sleep onset REM periods, multiphasic temperature rhythms and increased intrasubject variance.

In exploring the mechanisms by which jet lag symptoms are produced, and the reasons they are worse in middle-aged persons, we have considered three alternative hypotheses. The first, and perhaps simplest, is that jet lag symptoms are produced when one begins to live on the new time zone, and the myriad biological rhythms controlled by the circadian timing system have not yet fully adjusted to the sudden shift in schedule. It is possible that symptoms remit when the discrepancy between the social schedule and the circadian timing system falls below a certain threshold that might be dependent upon age. If this were the case, a middle-aged subject could theoretically be better adjusted than a young one but be more symptomatic. Alternatively, the circadian timing system might adjust more quickly in young persons, and therefore symptoms would be shorter lasting and less severe than in middle-aged persons.

Another hypothesis is that sleep deprivation produces many of the symptoms of jet lag, and the severity of symptoms depends on the ability to obtain recovery sleep and thereby recover from the effects of sleep deprivation. Middle-aged persons may not respond as fully to sleep deprivation as young persons. The third hypothesis is a combination of the above two. It would require the presence of both a circadian timing system that has not fully adjusted to a change in schedule and of sleep deprivation which directly produces some of the symptoms of jet lag. Having to sleep at the abnormal phase might prevent complete recovery from sleep deprivation, and perhaps even produce further sleep deprivation as a cumulative effect. Such cumulative sleep deprivation would then be predicted to lead to better sleep efficiency on a night following a poor sleep episode, leading to the zig-zag pattern of poor followed by good sleep efficiencies as we observed primarily in the middle-aged subjects (cf. Fig. 2B) (2).

The results of the present study support the third explanation. The amplitude of the temperature rhythm remained lower than baseline, and the time of the minima had either not completely adjusted (young subjects) or was markedly variable (middle-aged subjects) at the end of the study, suggesting that the circadian timing system had not fully adjusted to the new schedule. However, the jet lag-like symptoms are only seen in the early postshift interval. Moreover, there is no clear difference in the rate of adjustment between the two age groups. It is therefore unlikely that the abnormal phase of the circadian timing system is directly responsible for the symptoms or the differential response between the two groups.

The more severe symptoms of jet lag in our middle-aged subjects moreover do not appear to be due to their inability to respond to sleep deprivation with SWS rebound. On the contrary, our middle-aged subjects had both SWS rebound and more intense symp-

toms of jet lag. Inability to recover lost SWS therefore could not be directly responsible for the symptoms.

Because the subjective effects were more pronounced in the middle-aged subjects on those days when they were sleeping more poorly than the young men, differences in the severity of jet lag symptoms may be due primarily to the decreased ability of middle-aged people to sleep during the scheduled sleep period during the first few days following the shift. The subjective symptoms may be directly attributable to the sleep difficulty. We therefore suggest that the symptoms of jet lag (and perhaps shiftwork) increase in severity with age as a result of difficulties in sleeping at an unusual phase of the circadian day, which in middle-aged subjects seems to block the ability to compensate for sleep deprivation. However, it should be noted that simply increasing the duration of sleep with benzodiazepines may not solve the problem, as daytime sleepiness may persist (20).

It should also be noted that subjects may sleep perfectly well (for their age group) under normal conditions and similarly respond as expected to simple sleep deprivation. Only the challenge of sleep deprivation combined with an advance in the timing of sleep periods may produce a differential response according to age. From a longitudinal perspective, a single schedule shift such as the one employed here seems to be a useful probe of sleep–wake mechanisms in aging. Our data suggest that decreased ability of these mechanisms to respond to acute shifts may be an effect of aging, which follows age-related declines in baseline SWS but which occurs before deterioration of baseline sleep efficiency.

It is possible that the pattern of results we observed are dependent upon the magnitude of the schedule change. Our subjects began their shifted sleep periods in what had been the forbidden zone (wake maintenance zone) (46). On the first night, the sleep deprivation associated with the schedule change apparently outweighed the antagonistic effect of the forbidden zone. Therefore, the competition between these two forces was less one-sided as evidenced by the data from the middle-aged subjects. With larger phase advances, subjects would initially begin their sleep periods in the siesta zone. As those subjects adjusted, however, their sleep episodes would presumably pass through the forbidden zone, possibly leading to reemergent difficulties in sleep several days after the schedule change. Whether this pattern really does occur remains to be tested.

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