EFFECTS OF TEMAZEPAM, FLURAZEPAM AND QUINALBARBITONE ON SLEEP: PSYCHOMOTOR AND COGNITIVE FUNCTION

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- 1 The effect of temazepam 15 and 30 mg, flurazepam 15 and 30 mg, quinalbarbitone 100 and 200 mg and placebo were studied in 14 healthy male volunteers according to a Latin-square design. At 14-d intervals subjects received capsules 30 min before bedtime on 2 consecutive nights and were evaluated for objective sleep characteristics, for morning estimates of sleep characteristics, and for cognitive and psychomotor performance and subjective state at 3.5, 10.0 and 22.5 h after ingestion.
- 2 Changes in sleep induction and sleep maintenance were observed with temazepam 30 mg and flurazepam 30 mg. REM sleep was suppressed by quinalbarbitone, and by flurazepam 30 mg.
- 3 Flurazepam 30 mg had the greater effect on cognitive performance, whereas quinalbarbitone 20 mg had the greater effect on psychomotor performance. Subjective assessments of alertness were most affected by flurazepam, and by quinalbarbitone 200 mg.
- 4 The results suggest that temazepam produces less residual effects and is shorter acting than quinalbarbitone and flurazepam.

Introduction

WE have studied the acute effects of temazepam, flurazepam and quinalbarbitone using subjective and objective measures of sleep and waking behaviour. This choice of drugs provides useful information on the comparative effects of benzodiazepines and barbiturates, and on the effect of flurazepam which has an active metabolite of long half-life (Randall & Kappell, 1973) and temazepam with no metabolite of long half-life (Fuccella *et al.*, 1972). A practical assessment was also carried out on the relative effects on sleep and waking behaviour of temazepam, a relatively new hypnotic agent (Nicholson & Stone, 1976), and two well established hypnotic agents.

Methods

Fourteen healthy male volunteers (aged 21-35 yr; mean 25.4 yr) without sleep problems were selected for study. Physical health was determined using the Cornell Medical Index (Brodman *et al.*, 1949), a

routine physical examination, haematology and blood chemistry analyses, urinalysis and electrocardiogram. Psychological health was assessed using the Minnesota Multiphasic Personality Inventory (Dahlstrom *et al.*, 1972). Sleep status was determined using an 18-item questionnaire about sleep habits and problems. Each subject was evaluated in the laboratory in seven conditions; temazepam 15 mg (T15), temazepam 30 mg (T30), flurazepam 15 mg (F15), flurazepam 30 mg (F30), quinalbarbitone 100 mg (Q100), quinalbarbitone 200 mg (Q200), and placebo (P). In each condition, subjects received the scheduled capsules on 2 consecutive nights and underwent evaluations of sleep, subjective state and psychomotor and cognitive function. The 2 drug nights were followed by a 12-d washout period during which the subjects slept at home and received no medication or placebo. Drug and placebo administration was double blind. All capsules were identical in appearance. The sequence of biweekly treatments conformed to a Latin-square design. The subjects were administered the test battery for subjective state and psychomotor and cognitive function twice during the week before the start of the study so that they could achieve asymptotic baseline levels of performance. There were no special sessions for adapting subjects to sleeping in the laboratory;

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we relied on the Latin-square design to control for any "first-night effects". Subjects were instructed not to take drugs or alcohol at any time during the study and not to take naps on the days of laboratory monitoring. Their compliance was monitored by means of a presleep interview and a presleep questionnaire.

Table 1 lists the sequence of events during each 48-h evaluation session. Attachment of electrodes for polygraphic recording followed the standard procedure (Rechtschaffen & Kales, 1968). Subjects slept in sound-, temperature-, and light-controlled private bedrooms. For each subject, time of retiring and total time in bed conformed to his usual routine, but total time in bed had to be at least 7 h; these times were set at the beginning of the study and were held constant for the subject throughout the study.

During the test battery for subjective state and psychomotor and cognitive function (tests 1, 2 and 3) subjective ratings were obtained using the Clyde Mood Scale, the Stanford Sleepiness Scale (Hoddes *et al.*, 1973) and the Bond Sleep Self-Rating Scale (Bond & Lader, 1972). Psychomotor function was assessed with the following tasks: reaction time (Jonsson & Anderson, 1960), Purdue pegboard with both hand and assembly of parts (Lawton & Cahn, 1963), symbol copying (Kornetsky *et al.*, 1959), and platform balance (Veldkamp *et al.*, 1974).

Cognitive function was assessed with these tasks: continuous arithmetic (Epstein & Lasagna, 1968); time estimation (Pfaff, 1968); free recall (short-term memory) (Murdock, 1962); digit symbol substitution (Wechsler, 1944); at tests 1, 2 and 3, recall of a three-digit number memorized before "lights out"; at tests 2 and 3, recall of a trigram memorized before returning to sleep after test 1. The latter two tasks were designed specifically to assess deficits in long-term memory, or the 'amnesia'-provoking properties of the drugs.

Sleep recordings were scored in 30-s epochs according to the standard procedure (Rechtschaffen & Kales, 1968). Scorers were ignorant of the condition in which a given record was made. The resulting data were used to derive values for the variables listed in Table 2. No adjustments were made to compensate for the 90-min awakening for test 1. The self-rating instruments and the tests of subjective state and psychomotor and cognitive function were scored to derive values for the variables listed in Table 3. Two-factor repeated-measure analyses were used to evaluate the effects of drug condition (T15, T30, F15, F30, Q100, Q200 and P) and night of testing (night 1 and night 2) for the polygraphic data and the postsleep questionnaire measures. For the remaining measures, three-factor repeated-measure analyses were used to evaluate the

Table 1 Subject's schedule of activities during each 48-h evaluation session

Night	Time (h)	Activity
1	-1.0	Reports to laboratory; has sensors attached; completes presleep questionnaire and Stanford Sleepiness Scale; has respiration rate, heart rate, blood pressure and temperature measured, standing and supine.
	0.0	Takes two capsules.
	0.5	Memorizes three-digit number; retires to bed; recording begins.
	3.5	Is awakened; takes subjective state, psychomotor function and cognitive function test battery (test 1); has respiration rate, and so on, measured; completes Side-Effect Checklist.
	5.0	Memorizes trigram; returns to bed; recording continues.
	10.0	Is awakened; completes postsleep questionnaire; takes test battery (test 2); has respiration rate, and so on, measured; completes Side-Effect Checklist.
	11.5	Dresses; departs laboratory.
	22.5	Reports to laboratory; takes test battery (test 3); has respiration rate, and so on, measured; completes Side-Effect Checklist.
	2	-0.5 Has sensors attached; completes presleep questionnaire and Stanford Sleepiness Scale.
	0.0	Takes two capsules.
2	0.5	Memorizes three-digit number; retires to bed; recording begins.
	3.5	Is awakened; takes test battery (test 1); has respiration rate, and so on, measured; completes Side-Effect Checklist.
	5.0	Memorizes trigram; returns to bed; recording continues.
	10.0	Is awakened; completes postsleep questionnaire; takes test battery (test 2); has respiration rate, and so on, measured; completes Side-Effect Checklist.
	11.5	Dresses; departs laboratory.
	22.5	Reports to laboratory; takes test battery (test 3); has respiration rate, and so on, measured; completes Side-Effect Checklist.
	24.0	Departs laboratory.

effects of drug condition (T15, T30, F15, F30, Q100, Q200 and P), time of testing (3.5, 10.0, and 22.5 h after drug ingestion) and night of testing (night 1 and night 2). All significant effects were followed by Newman Keuls analyses; for these analyses we report only results that reached significance at the 5% level or beyond.

Results

Average values and results of statistical analyses for objective and subjective indices of sleep effects are shown for the seven conditions in Table 4. Healthy subjects with no sleep problem would be expected to exhibit minimal improvement in sleep induction and sleep maintenance with hypnotic drug administration. This expectation was confirmed in our study. Standard measures of initial sleep induction showed no significant differences among conditions. The special procedures of this study, however, provided a unique measure of sleep induction, the sleep return latency. For this variable there was an overall significant difference among drug conditions. All

drug conditions reduced this measure to an extent, but only the reductions produced by T30 and F30, relative to P, were significant.

Subjects' estimates of initial sleep latency conformed reasonably well with the objective stage 2 latency, and, as with the latter, there were no significant changes. On the other hand, the estimates of sleep return latency were exaggerated, and the subjects failed to perceive the reductions that were documented on the polygraph tracings.

Several objective measures of sleep maintenance, or the relative amounts of sleep and wakefulness after initial sleep onset, were at least somewhat improved relative to P by most drug conditions. The measures wake during sleep and percent stage 1 showed significant overall changes for drug conditions. It will be noted that the measure wake during sleep includes the time awake between return to bed after test 1 and subsequent stage 2 onset, so it is not a pure measure of spontaneous wakefulness. All compounds reduced wakefulness during sleep, but only the reductions produced by flurazepam (F15 and F30) were significant relative to P. Among the active compounds F30 produced a significantly

Table 2 Variables used to assess the effects of temazepam, flurazepam, and quinalbarbitone on sleep

<i>Name</i>	<i>Definition</i>
Objective	
Sleep induction:	
Wake before sleep	Minutes between record start ("lights out") and first epoch of stage 1, 2, 3, 4 or REM.
Sleep latency to stage 2	Minutes between record start and first epoch of stage 2.
Sleep return latency	After sleep interruption for test 1, minutes between return to bed and first epoch of stage 2.
Sleep maintenance:	
Total sleep time	Minutes of stages 1, 2, 3, 4 and REM between record start and final morning awakening.
Number of awakenings	Number of stage wake intervals that lasted at least 30 seconds.
Wake during sleep	Minutes of stage wake between first epoch of stage 1, 2, 3, 4 or REM and the final morning awakening.
Wake after sleep	Minutes of stage wake between final morning awakening and record end.
Percentage stage 1	Minutes of stage 1 as a percentage of time in bed.
Sleep composition:	
Percentage stage 2	Minutes of stage 2 as a percentage of time in bed.
Percentage stage 3-4	Minutes of stages 3 and 4 as a percentage of time in bed.
Percentage stage REM	Minutes of stage REM as a percentage of time in bed.
Latency to stage 3	Minutes between first epoch of stage 2 and first epoch of stage 3.
Latency to stage REM	Minutes between first epoch of stage 2 and first epoch of stage REM.
Subjective:	
Sleep induction:	
Sleep latency	"How long did it take you to fall asleep last night?: ____ minutes".
Sleep return latency	"How long did it take you to return to sleep after the test battery?: ____ minutes".
Sleep maintenance:	
Total sleep time	"How long did you sleep last night?: ____ minutes".
Number of awakenings	"How often did you wake up during the night?: ____ times".

Table 3 Variables used to assess the effects of temazepam, flurazepam and quinalbarbitone on subjective state and psychomotor and cognitive function

<i>Instrument/task</i>	<i>Definition</i>
Subjective state:	
Clyde Mood Scale	Scores on each of six subscales — "Friendly", aggressive", "clear-thinking", "sleepy", "unhappy" and "dizzy".
Stanford Sleepiness Scale	Score on a seven-point scale: 1, very awake; 7, very sleepy.
Bond Sleep Self-Rating Scale	Distance in 10-mm units from "very sleepy" (0) to "very alert" (10).
"Feeling now and feeling on awakening"	
Psychomotor function:	
Reaction time	Mean choice reaction time (s) for 15 trials.
Purdue pegboard (both hands)	Mean number of items placed for two 30-s trials.
Purdue pegboard (parts assembly)	Mean number of parts assembled for two 60-s trials.
Symbol copying	Number of symbols copied in 5 min.
Balance board	Mean amount of time (s) off balance for four 1-min trials.
Cognitive function:	
Continuous arithmetic	Number of problems correctly completed in 15 min.
Time estimation	Mean error of estimate (s) for 10 trials.
Free recall	Number of stimuli correctly recalled from a total of 10.
Digit Symbol Substitution Test	Number of substitutions made in 5 min.
Recall of three-digit number	Correct recall no (0) or yes (1).
Recall of trigram	Correct recall no (0) or yes (1).

Table 4 Effects of temazepam 15 mg (T15) and 30 mg (T30), flurazepam 15 mg (F15) and 30 mg (F30), and quinalbarbitone 100 mg (Q100) and 200 mg (Q200) on sleep

<i>Variable</i>	<i>Results of analyses</i>	<i>Placebo</i>	<i>T15</i>	<i>T30</i>	<i>Drug condition</i>		<i>F15</i>	<i>F30</i>	<i>Q100</i>	<i>Q200</i>
Objective:										
Wake before sleep		18	23	18	19	15	20	18		
Sleep latency to stage 2		23	29	24	25	22	26	14		
Sleep return latency	D [†]	24	16	12	14	12	17	14		
Total sleep time		439	436	441	442	454	432	449		
Number of awakenings		4.5	4.4	4.0	3.9	3.6	6.0	3.7		
Wake during sleep	D [*]	25	13	13	10	8	17	14		
Wake after sleep		0.2	4.9	2.6	0.8	0.3	3.3	0.1		
Percentage stage 1	D [†]	9.2	8.6	6.8	8.5	6.0	8.4	7.6		
Percentage stage 2	D [†] , N [*]	44	46	50	48	52	48	53		
Percentage stage 3-4	DN	14	13	13	14	14	13	14		
Percentage stage REM	D [*]	21	21	20	20	20	19	17		
Latency to stage 3		13	21	14	16	15	15	14		
Latency to stage REM	D [†]	75	91	107	77	87	100	135		
Subjective:										
Sleep latency		25	22	22	22	21	22	17		
Sleep return latency		23	25	24	20	20	22	17		
Total sleep time	D [†]	433	460	464	463	468	458	458		
Number of awakenings	D [‡]	1.5	0.5	0.9	0.5	0.8	0.6	0.4		

D^{*}, D[†] and D[‡], Significant main effect for drug condition at $P < 0.05$, $P < 0.01$ or $P < 0.001$.N^{*}, Significant main effect for night of testing at $P < 0.05$.DN, Significant interaction for drug condition and night of testing at $P < 0.01$.

greater reduction than Q100. We have chosen to include percentage stage 1 as a measure of sleep maintenance because stage 1 is typically associated with arousals. The reductions in percentage stage 1, relative to P, produced by T30 and F30 were significant, and these reductions were also significantly greater than those produced by T15, F15 and Q100.

Subjects' estimates of total sleep time and number of awakenings were exaggerated in the direction of improved sleep in all drug conditions. Interestingly, total sleep time was underestimated with administration of P. In contrast to the comparable objective data, these two estimates underwent significant overall changes with drug administration. Total sleep time was significantly increased relative to P by T15, T30, F15 and F30; there were no significant differences among active drug conditions. Number of awakenings was significantly reduced, relative to P, by each drug condition; again, there were no significant differences among active drug conditions.

Drugs had different patterns of effects on sleep composition. For percentage stage REM, the significant main effect for drug-condition was due to the individual significant suppressive effects of F30, Q100 and Q200, relative to P; none of the active drug conditions differed significantly from any other. The most significant drug condition main effect for latency to stage REM was due to the significant increase, relative to P, produced by T30 and Q200. Note that T30 elevated REM latency but did not significantly suppress total percentage REM.

There was no significant main effect for percentage stage 3-4 nor any significant effects for latency to stage 3. There was, however, a significant

drug-by-night interaction for percentage stage 3-4. This result reflected the fact that in all active drug conditions percentage stage 3-4 decreased from night 1 to night 2, whereas with P it increased. The night 1-to-night 2 changes were significant for T30 and F30. Increases in percentage stage 2 characterized all drug conditions, and the effects were significant relative to P for F30, Q100 and Q200.

Average values and results of statistical analyses for the assessments of subjective state, psychomotor function and cognitive function are shown in Tables 5, 6 and 7. For all variables there was a significant effect due to time of testing; scores improved significantly from test 1 to test 2 and from test 2 to test 3. The fact that such improvements occurred with P as well indicates that they were simply reflections of diurnal variations in the functions under examination.

Analyses of the data for the six subscales of the Clyde Mood Scale failed to reveal any significant effects except that for time of testing; the data have therefore not been included in Table 5. The remaining measures of subjective state focused on the subjects' degree of perceived alertness or sleepiness. In the morning after taking hypnotic medication the previous bedtime, unusual sleepiness contributes largely to the feeling of drug hangover. The significant drug-condition main effect for the Stanford Sleepiness Scale measure reflected the fact that Q100 and F30 produced significantly greater sleepiness than P, and Q200 produced significantly more than T30, F15, and Q100. The drug-by-time interaction derived from the fact that at test 1 T15, F30, Q100 and Q200 all produced significantly greater sleepiness than P, and Q200 produced

Table 5 Effects of temazepam 15 mg (T15) and 30 mg (T30), flurazepam 15 mg (F15) and 30 mg (F30), and quinalbarbitone 100 mg (Q100) and 200 mg (Q200) on subjective state at 3.5 (test 1), 10 (test 2) and 22.5 h (test 3) after drug ingestion

Instrument	Results of analyses	Test	Drug condition							
			Placebo	T15	T30	F15	F30	Q100	Q200	
Stanford Sleepiness Scale	D*, T†, DT†	1	3.0	4.5	4.3	4.0	4.3	4.3	4.9	
		2	2.7	2.9	2.7	2.8	3.2	2.7	2.9	
		3	2.1	2.1	2.0	2.3	2.1	2.2	2.2	
Bond Sleep Self-Rating Scale Feeling on awakening	D†, T†, DT*, DN	1	3.2	3.2	2.7	2.4	2.3	2.5	2.0	
		2	4.4	4.1	4.3	3.1	3.2	4.1	3.1	
		3	4.0	3.8	4.3	3.0	3.2	4.1	3.1	
Feeling now	D†, T†, DT*	1	5.0	4.2	4.2	3.8	3.5	4.2	2.9	
		2	6.5	6.4	6.3	5.2	5.2	6.3	4.9	
		3	7.2	7.4	7.4	6.9	7.4	7.4	7.2	

D*, D†, Significant main effect for drug condition at $P < 0.05$ or $P < 0.01$.

T†, Significant main effect for testing time at $P < 0.01$.

DT* and DT†, Significant interaction for drug condition and testing time at $P < 0.05$ or $P < 0.01$.

DN, Significant interaction for drug condition and night of testing at $P < 0.05$.

Table 6 Effects of temazepam 15 mg (T15) and 30 mg (T30), flurazepam 15 mg (F15) and 30 mg (F30), and quinalbarbitone 100 mg (Q100) and 200 mg (Q200) on psychomotor function at 3.5 (test 1), 10 (test 2) and 22.5 h (test 3) after drug ingestion

Task	Results of analyses	Test	Drug condition						
			Placebo	T15	T30	F15	F30	Q100	Q200
Reaction time	T [†]	1	0.50	0.51	0.54	0.51	0.53	0.52	0.57
		2	0.47	0.46	0.52	0.47	0.48	0.47	0.51
		3	0.47	0.45	0.47	0.48	0.47	0.47	0.46
Purdue pegboard (both hands)	T [†]	1	27.5	26.0	26.3	26.5	25.6	26.0	24.6
		2	28.4	27.9	27.6	28.8	27.4	28.0	27.5
		3	30.5	39.4	30.0	29.5	29.3	29.4	29.3
Purdue pegboard (parts assembly)	T [†] , DT	1	47.9	45.0	43.9	47.4	46.3	47.0	42.5
		2	50.3	49.0	47.9	50.4	49.8	50.1	48.9
		3	55.0	52.6	52.2	53.5	54.5	52.6	54.7
Symbol copying	T [†]	1	457.0	440.2	442.9	445.6	428.8	463.4	425.5
		2	466.0	452.2	456.9	470.8	433.8	451.7	438.8
		3	518.2	520.0	510.9	527.1	509.5	520.9	501.8
Balance board	D [†] , T [†] , DT	1	9.6	9.4	12.8	11.0	11.0	10.7	16.1
		2	8.7	7.9	8.8	8.2	7.9	8.2	10.4
		3	7.7	7.4	7.9	7.2	7.5	7.1	8.6

D[†], Significant main effect for drug condition at $P < 0.01$.T[†], Significant main effect for testing time at $P < 0.01$.DT, Significant interaction for drug condition and testing time at $P < 0.01$.**Table 7** Effects of temazepam 15 mg (T15) and 30 mg (T30), flurazepam 15 mg (F15) and 30 mg (F30), and quinalbarbitone 100 mg (Q100) and 200 mg (Q200) on cognitive function at 3.5 (test 1), 10 (test 2) and 22.5 h (test 3) after drug ingestion

Task	Results of analyses	Test	Drug condition						
			Placebo	T15	T30	F15	F30	Q100	Q200
Continuous arithmetic	T [†]	1	51.4	48.4	46.9	43.3	42.1	50.5	45.0
		2	55.6	54.7	54.8	54.1	49.0	55.1	51.6
		3	61.5	59.5	57.9	58.9	58.9	62.3	61.1
Time estimation	T [†]	1	7.4	5.4	7.4	6.0	7.8	5.5	6.3
		2	6.9	5.8	7.6	5.9	7.8	5.7	5.7
		3	4.9	5.0	6.3	4.2	6.9	3.5	4.0
Free recall	T [†] , DT [*]	1	5.3	5.0	4.6	4.7	4.5	5.5	4.5
		2	5.4	5.1	5.1	5.4	5.4	5.5	5.7
		3	5.4	5.7	5.1	5.9	5.4	5.6	5.7
Digit Symbol Substitution Test	D [†] , T [†] , DT [†]	1	193.2	179.7	167.6	176.6	167.9	187.6	158.6
		2	204.5	206.2	201.3	197.2	186.1	203.3	185.6
		3	223.4	220.9	230.0	226.4	215.3	220.6	222.8
Recall of three-digit number	T [†] , DT [*]	1	0.90	0.97	0.97	0.93	0.75	0.83	0.90
		2	0.82	0.86	0.93	0.90	0.72	0.97	0.82
		3	0.90	0.82	0.83	0.93	0.71	0.97	0.90
Recall of trigram	T [†]	2	0.72	0.68	0.57	0.53	0.50	0.75	0.61
		3	0.75	0.68	0.50	0.56	0.50	0.64	0.61

D[†], Significant main effect for drug condition at $P < 0.01$.T[†], Significant main effect for testing time at $P < 0.01$.DT^{*} and DT, Significant interaction for drug condition and testing time at $P < 0.05$ or $P < 0.01$.

significantly more than F15, F30, and T30. At test 2 only F30 and Q200 continued to produce significantly greater sleepiness than P, and F30 produced significantly more than F15, T30 and Q100. All significant differences among conditions had disappeared by test 3.

The significant drug-condition main effect for the Bond Sleep Self-Rating Scale score of Feeling Now was due to the significantly greater sleepiness produced by F30 and Q200 relative to T15, T30 and Q100 and that produced by F15 relative to T15 and T30. At test 1, T30, F15, F30 and Q200 produced significantly greater sleepiness than P, and Q200 produced significantly more than each other active drug condition. At test 2, the significant effects relative to P persisted with F15, F30 and Q200, and Q200 continued to produce significantly more sleepiness than T15 and Q100. All significant differences among conditions had disappeared by test 3.

The drug-condition main effect for the FEELING ON AWAKENING score of the Bond Scale was due to the significantly greater sleepiness produced by F15 and Q200 relative to P, T15 and T30. There were no significant differences among conditions at test 1, primarily because on night 1 subjects were rating their feelings for the previous morning at home when they were drug free. At test 2, ratings of sleepiness were significantly greater relative to P with F15, F30 and Q200. At test 3 scores were significantly higher with F15, F30, and Q200 relative to T30.

There were few significant changes in measure of psychomotor function (Table 6). The significant drug-by-time interaction for Purdue Pegboard Parts Assembly derived from the fact that at test 1 Q200 significantly impaired performance when compared with P, F15, F30 and Q100. By test 2, this difference had disappeared. The balance board was the most sensitive of the psychomotor tasks for there was a significant effect both for drug condition and for the drug-by-time interaction. At test 1, all conditions except T15 produced increases in time off balance relative to P, but only the increases with T30 and Q200 were significant. Q200 also produced significant increases relative to each other active drug condition. The effect of Q200 persisted into the morning, for at test 2 it produced values significantly greater than those for P, T15, F15, F30 and Q100. This effect had generally disappeared by test 3, although the Q200 performance continued to be significantly worse than with Q100.

Three of the six tasks assessing cognitive function revealed significant changes (Table 7). The significant drug-by-time interaction for free recall (short-term memory) was due to the occurrence of significant decrements at test 1, but not at tests 2 and 3. At test 1, recall was significantly poorer with T30, F30 and Q200 than with P. The digit symbol

substitution test underwent significant changes associated with drug condition and the interaction between drug and time. Overall, F30 and Q200 produced significant decrements relative to P. At test 1, both doses of flurazepam and Q200 produced significant decrements relative to P: the decrements associated with F30 and Q200 were also significantly greater than those for T15 and Q100. At test 2, F30 and Q200 produced significantly worse performance than P, T15, T30 and Q100. At test 3, the decrements associated with F30 relative to P and to Q100 continued to be significant. Recall of the three-digit number memorized at bedtime (long-term memory) showed a significant drug-by-time interaction. At test 1, recall with F30 was significantly worse than with T15, T30 and F15, whereas at test 2 it was worse than that with T30 and Q100. The significant differences had disappeared by test 3.

Discussion

The results of this comparative study of the effects of temazepam, flurazepam and quinalbarbitone on sleep and selected waking behaviours indicate that temazepam may be comparable to flurazepam and quinalbarbitone with respect to hypnotic efficacy and superior to both in terms of effects on daytime function. This study, with its inclusion of normal subjects, did not provide the ideal conditions for assessment of hypnotic efficacy, but the variables used — sleep return latency, wake during sleep, and percentage stage 1 — were improved with drug administration. On two of the three, temazepam produced significant improvements. Temazepam resembled quinalbarbitone in producing a delay in REM onset, but did not resemble either flurazepam or quinalbarbitone with respect to the suppression of REM sleep. Temazepam resembled both drugs in its cumulative suppression of stage 3-4 sleep over 2 nights; it did not have the significant effect on stage 2 that characterized the other drugs.

Subjects' ratings of alertness revealed the drug hangover produced by quinalbarbitone (especially Q200) and flurazepam. The ratings with T30 were never significantly worse than those with P and were at times less severe than those with F30 and Q200. The effects with quinalbarbitone and flurazepam had dissipated by 22.5 h after drug ingestion, but with these data we cannot estimate when this occurred.

Q200 produced the greatest deficits in psychomotor function, but F30 affected cognitive function to the greatest degree. In general, cognitive function was

more impaired with the drugs than psychomotor function. For both systems, the effects often continued into the morning after awakening. To be noted is that T30 never significantly impaired

performance at the morning test (test 2). In contrast to T30 and Q200, F30 seemed to produce amnesia in the morning for material memorized the previous bedtime.

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