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The Effects of Flurazepam, Lorazepam, and Triazolam on Sleep and Memory

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Abstract. This study evaluated the effects of flurazepam 30 mg, lorazepam 4 mg, triazolam 0.5 mg, and placebo upon sleep and memory in eleven normal male subjects continuously monitored for nighttime EEG, EOG, and EMG recording. Subjects received each drug or placebo for two consecutive nights per week for 4 weeks in a repeated measures, double-blind, Latin Square design. Three hours post-administration, subjects were awakened and presented with a series of tasks. Recall was assessed immediately following task presentation and after the final morning awakening. The results showed that every drug significantly decreased stage 1, increased stage 2, and produced no change in stage 3 – 4 sleep in comparison to placebo. Only lorazepam significantly decreased REM percent. Post-drug recall was significantly decreased in comparison to placebo at night and was further decreased in the morning. Morning recall was significantly poorer when the return to sleep was 2.5 min or less than when the return to sleep was greater than 5 min following the nighttime awakening in all drug conditions. These results indicate that 1. failure of memory consolidation rather than failure of retrieval is the most likely explanation for the morning memory loss and 2. hypnotic drug properties, measured by latency to fall back asleep, affect memory consolidation.

Key words: Amnesia – Flurazepam – Lorazepam – Triazolam – Sleep – Benzodiazepines

Introduction

Benzodiazepines have become the most widely prescribed class of drugs for providing symptomatic relief of insomnia (Anlyan and Solomon 1979). The subjective complaint of disturbed sleep is improved following administration of these hypnotics (Liebowitz and Sunshine 1978; Wang et al. 1976), and laboratory studies have consistently demonstrated improvements in objective sleep parameters such as decreases in latency to sleep onset and increases in total sleep time (Kay et al. 1976). In constrast to the barbiturates, the effectiveness of benzodiazepines is sustained with long term usage, i.e., there is minimal drug tolerance (Kales et al. 1975, 1976a), and there is a wide margin of safety for accidental overdose (Cooper 1977). Since benzodiazepines appear to be relatively effective and safe hypnotics, the question arises as to whether there are any concomitant side effects which would limit their use as sleeping medications in the general population.

One potentially important side effect of some benzodiazepines is that of anterograde amnesia, amnesia for events occurring subsequent to the administration of the drug. Several reports have shown that diazepam (Clarke et al. 1970; Pandit et al. 1971), flunitrazepam (Bixler et al. 1979; Dundee and George 1976), and lorazepam (Dundee et al. 1977; Heisterkamp and Cohen 1975; Pandit et al. 1976) possess anterograde amnesic properties. With the exception of the Bixler et al. (1979) study, these benzodiazepines were given as surgical premedicants. In the hospital setting, amnesia for events leading to surgery is highly desireable. Benzodiazepines are also widely used by non-hospitalized patients, particularly insomniacs, as hypnotics for the purpose of sleep induction. However, the amnesic properties of benzodiazepines have not been extensively studied in relationship to their use as hypnotic drugs, and the self-administration of these drugs in a non-controlled home environment could have potentially serious consequences.

It is not certain whether benzodiazepines as a class possess amnesic properties or whether amnesic proper-

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ties are specific only to diazepam, flunitrazepam, and lorazepam. The mechanism of memory loss is also uncertain. That is, is the amnesic effect due to a failure of memory consolidation or to a failure of memory retrieval? The purpose of this study was to evaluate the effects of three different benzodiazepines – flurazepam, lorazepam, and triazolam – upon sleep and memory functioning in normal adult males and to examine the consolidation vs. retrieval hypotheses as explanations for the memory loss occurring subsequent to drug administration.

Materials and Methods

Subjects

A total of 12 male volunteers 19–30 years old without a history of sleep disturbance served as subjects. All subjects had MMPI profiles within the normal range. Only those subjects with a normal physical examination, a normal clinical electrocardiogram, and normal blood and urine laboratory test values participated in the study. No subject took or received any medication other than the experimental drugs 72 h prior to or during the study. All subjects gave their informed consent. One subject terminated his participation before the study was completed. Data for eleven subjects are included in this report.

Drug Administration

Each of four experimental drug – placebo, flurazepam 30 mg, lorazepam 4 mg, and triazolam 0.5 mg – were administered to every subject for 2 days in a repeated measures, double-blind, Latin Square design. The study was conducted over a consecutive four week period with subjects receiving a different medication for 2 consecutive nights of each week. There were 5 washout days separating each of the 2-day experimental conditions for a total of 8 laboratory nights. With this design, then, each subject served as his own control. All capsules were matched in appearance. The subjects were cautioned against taking medication, alcohol, or naps during the course of the study.

No attempt was made to administer equipotent doses of the three active drugs, and dosages were chosen which have, in addition to well-known soporific effects, effects upon memory loss. Triazolam 0.5 mg has been anecdotally reported to induce anterograde amnesia (Kales et al. 1976b) and several previous studies have shown that lorazepam 4 mg is reliably associated with a similar memory loss (Dundee and George 1976, Dundee et al. 1977; Pandit et al. 1976). No studies have examined the effect of flurazepam upon memory loss; 30 mg was chosen since it is the standard dose in clinical practice (Kales et al. 1976).

Recording Procedures

Subjects reported to the laboratory at 10 p.m. Electrodes were attached for continuous monitoring of the central electroencephalogram (EEG), electroculogram (EOG), and the submental electromyogram (EMG), and each subject completed a presleep questionnaire, Bond Sleep Self-Rating Scale (BSSR), and Stanford Sleepiness Scale (SSS). Thirty minutes prior to lights out, subjects took their medication.

At 2 a.m., 3 h after administration of the capsules, the subject was awakened by having his name called over the intercom. If he did not respond with a waking EEG of at least 15 s in duration accompanied by eye movements, elevated chin muscle tonus, and a verbal response, his name was repeated until these signs of wakefulness appeared. Typically, no more than 20 s elapsed between the time that the subject's name was first called and the actual EEG awakening. The technician immediately entered the bedroom, turned on the room lights, and briefly questioned the subject to verify that he was awake.

Following the nighttime awakening, the subject returned to bed and was instructed to go back to sleep. Each subject spent an additional 5 h in bed. Thus, all subjects were recorded for a total of 8 h.

Tasks

Following the awakening, a series of four tasks, each containing four details, was presented to the subjects. Rather than employing commonly used memory tests, the major consideration which dictated the choice of tasks was to mimic clinically relevant situations that individuals who take benzodiazepine hypnotics for the purpose of sleep induction might encounter during a nighttime awakening. For example, insomniac patients frequently awaken during the night to take sleeping pills. It would be of importance for the medical care of these patients to determine whether these medications affect their ability to remember if additional sleeping pills had been taken.

Prior to the first experimental night, the format of the stimulus presentation was explained, and each subject participated in one practice session.

1. "Pill" task: The subject ingested one to four small candy mints with a fruit flavored drink. The relevant details were the color of the bottle containing the mints, the number of mints ingested, the color of the mints, and the flavor of the drink taken with the mints. Subjects were informed prior to the start of the study that the mints which they ingested during the nighttime awakening did not contain any medications. It is important to emphasize that these mints were different in taste, shape, color and size from real medications.

2. Dressing task: Each subject was given several articles of clothing to put on and take off. The relevant details were the names of two articles of clothing, the sequence of dressing, and the color of one piece of clothing.

3. Time task: Each subject was required to read a pre-set time on a clock and then to reset the clock to a new time. The relevant details were the original time at which the clock was set, the color of the clock, the type of numerals on the clock face, and the time to which the subject reset the clock.

4. Travel task: The subject engaged in a conversation regarding travel reservations on a hypothetical journey. The relevant details were the destination of the trip, the name of the airline, the time of departure, and the flight number of the airline.

There were two additional tasks, a "dream" task in which the subject was asked to fabricate a short story about a specific topic and a five digit span task in which the subject was required to recall a five digit number. The data for the "dream" task will not be further considered.

After the subject had completed all tasks, he completed a 17-item questionnaire which assessed his memory for the four details of each task and for the five digit number. Again, since the intent of these task presentations was to mimic the clinical setting, the subjects were not prompted to remember any of the stimulus material. The order of the tasks was not varied from experimental night to experimental night; that is, the tasks were always presented in the above order. However, the information contained in each task varied on each of the eight laboratory nights. For example, in the "pill" task, there were two mints on night one and four mints on night two. The color of the mint bottle was changed from white to green, the color of the mints was changed from yellow to green and the flavor of the beverage was changed from orange to punch. Although the subjects undoubtedly remembered the order of the four general tasks, nightly changes in the 16 details and in the five digit number precluded any improvement in memory for specific details over the 8 study nights.

Fifteen minutes after the awakening, the subjects returned to bed. In the morning, each subject completed a second memory questionnaire identical to that administered the previous night in order to assess his recall of the previous night's tasks. Each subject also completed a post-sleep questionnaire, the BSSR, and the SSS.

Test-retest and split-half measures of reliability were utilized to evaluate the reliability of the questionnaire in assessing morning memory recall. Test-retest reliability was evaluated by comparing morning recal on placebo day 1 to morning recall on placebo day 2. The mean number of items correctly remembered was 14.1 on day 1 and 14.2 items on day 2. As expected, there was no significant difference in recall between the 2 days. Split-half reliability was assessed by the correlation between recall for odd and even items on the 16 item morning recall questionnaire for 2 days of the placebo condition. This correlation was 0.65 ($df = 10$, $P < 0.05$). Thus, it can be concluded that the questionnaire reliably measured the subjects' memory for test items.

Since the four tasks differed somewhat in the quality of stimulus material, memory for each task was compared to that for the other three tasks in the placebo condition. None of the intra-task comparisons of morning recall produced any significant differences across the 2 placebo days. A day-by-day analysis revealed that there were no significant differences in memory between tasks on placebo day 1. On placebo day 2, there was only one significant difference; the subjects remembered the four details of the time task better than they remembered the four details of the travel task. These findings indicate that the morning memory deficits could not be differentially attributed to any one of the four tasks, and scores for memory recall were summed across all four tasks.

All sleep records were scored for stages waking, 1, 2, 3–4, and REM by the standard Rechtschaffen and Kales (1968) criteria. A night and morning memory score was obtained by counting the number of correct items on both memory questionnaires.

Table 1. F-Ratios

	Drug[a]	Day[b]	Drug × day[a]
Objective measures of sleep efficacy			
Mean latency to stage 2 (min)	0.92	3.38	1.54
Mean latency back to stage 2 (min)	8.06*	2.09	2.37
Mean no. awakenings	4.65*	0.50	0.18
Mean % wake	3.27*	3.50	3.54*
Mean total sleep time (min)	2.56	3.06	2.96*
Subjective measures of sleep efficacy			
Mean latency to stage 2 (min)	4.05*	4.85	1.02
Mean latency back to stage 2 (min)	3.33*	2.68	2.43
Mean no. awakenings	3.88*	2.06	2.41
Mean total sleep time (min)	2.27	0.06	0.53
Sleep quality (mean cm)**	6.37*	0.68	1.48
Sleep stage percentages			
Mean % stage 1	12.86*	0.01	0.89
Mean % stage 2	9.64*	1.72	2.84
Mean % stage 3–4	1.79	2.64	2.19
Mean % REM	4.92*	2.13	1.02
Mean latency to REM (min)	2.07	1.05	2.26
Memory recall			
Mean no. of items recalled immediate	13.94*	2.88	2.41
Mean no. of digits recalled immediate	11.38*	0.89	1.09
Mean no. of items recalled morning	20.38*	0.03	2.27
Mean no. of digits recalled morning	13.03*	1.24	0.84

[a] $df = 3,30$
[b] $df = 1,10$
* $P < 0.05$ or less
** 10 cm visual analog scale ranging from 0 cm (very bad) to 10 cm (very good)

Results

Statistical analyses were performed for each dependent measure with a two factor (drug condition and day) ANOVA. The results of these ANOVAs are presented in Table 1. Post hoc *t*-tests (two-tailed) were used to evaluate all significant ANOVA effects. Unless otherwise stated, all drug comparisons are with placebo.

Objective Measures of Hypnotic Properties. (Table 2)

Since normal subjects rather than insomniacs were used in this study, sleep in the non-drug (placebo) condition was within the normal range for young adults with the exception of stage 3–4 (see below). As a result, the hypnotic efficacy of the three drugs for those persons with sleeping difficulties cannot be fully evaluated in our subject population. Sleep induction and sleep maintenance parameters in normal subjects, however, do reflect hypnotic properties and may be used to predict hypnotic efficacy in insomniac subjects. Sleep induction was measured by two different sleep latencies, the initial latency to fall asleep beginning at lights out $^1/_2$ h after drug ingestion and the latency to fall back asleep after the 2 a.m. memory task awakening. Sleep latency was defined as the time from lights out to the first epoch of stage 2.

Latency to sleep onset at the beginning of the night was decreased following administration of each of the three active compounds. This decrease, however, was

Table 2. Objective measures of sleep efficacy averaged across two consecutive nights

	Mean latency to stage 2 (min)	Mean latency back to stage 2 (min)	Mean no. awakenings	Mean % wake	Mean TST (min)
Placebo	14.7 ± 14.5	22.2 ± 27.3	4.1 ± 4.6	6.5 ± 9.9	413.0 ± 46.6
Flurazepam	12.5 ± 9.9	5.4 ± 5.9**	2.1 ± 1.5	2.4 ± 2.9	431.7 ± 21.0
Lorazepam	12.1 ± 8.2	3.3 ± 3.5**	2.2 ± 1.8	2.2 ± 2.5	426.3 ± 23.1
Triazolam	10.1 ± 5.7	3.2 ± 4.2**	1.8 ± 1.5*	1.6 ± 1.8	433.4 ± 21.4

* $P < 0.05$; ** $P < 0.02$ in comparison to placebo; TST = total sleep time

Table 3. Subjective measures of sleep efficacy averaged across two consecutive nights

	Mean latency to stage 2 (min)	Mean latency back to stage 2 (min)	Mean no. awakenings	Mean TST (min)	Sleep quality (cm)+
Placebo	17.8 ± 12.8	10.0 ± 13.2	0.9 ± 1.0	441.6 ± 33.9	6.7 ± 2.5
Flurazepam	12.9 ± 14.2	3.9 ± 5.0	0.4 ± 0.7**	448.9 ± 24.6	8.4 ± 1.7*
Lorazepam	9.1 ± 5.3**	3.7 ± 4.1	0.2 ± 0.4**	455.7 ± 31.5	8.4 ± 1.4*
Triazolam	7.3 ± 4.2*	2.8 ± 2.6	0.8 ± 1.0	451.8 ± 26.1	8.2 ± 1.7*

** $P < 0.02$; * $P < 0.01$ in comparison to placebo; + 10 cm visual analog scale ranging from 0 cm (very bad) to 10 cm (very good)

Table 4. Sleep stage percentages averaged across two consecutive nights

	Mean % stage 1	Mean % stage 2	Mean % stage 3–4	Mean % REM	Mean latency to REM (min)
Placebo	8.8 ± 4.1	54.4 ± 8.4	6.4 ± 5.9	20.5 ± 5.6	91.7 ± 48.6
Flurazepam	6.6 ± 3.1**	63.7 ± 7.1***	4.3 ± 5.2	19.7 ± 6.7	107.2 ± 61.2
Lorazepam	4.9 ± 2.0***	67.0 ± 9.5***	7.6 ± 7.3	15.2 ± 5.1****	117.8 ± 53.4
Triazolam	6.0 ± 2.54**	62.2 ± 9.3**	8.4 ± 8.4	18.6 ± 5.3	122.3 ± 48.3

* $P < 0.05$; ** $P < 0.02$; *** $P < 0.01$; **** $P < 0.001$ in comparison to placebo

not statistically significant. When sleep latency was measured a second time following the 2 a.m. memory task awakening, there was a significant main effect due to drug condition ($P < 0.001$). Post hoc analyses demonstrated that flurazepam, lorazepam, and triazolam all significantly ($P < 0.02$) reduced the latency to fall back to sleep, but there were no significant differences between the three active drugs.

Sleep maintenance was evaluated by the number of spontaneous awakenings, percent stage wake, and total sleep time. The effect of drug condition on total sleep time was not significant. However, the analysis of variance showed significant ($P < 0.04$) main effects due to drug for percent awake. Each of the three active drugs reduced percent awake; post hoc *t*-tests did not reveal a statistically significant reduction in percent awake between placebo and any other drug. Only triazolam significantly decreased the number of awakenings ($P < 0.05$). (The awakening for memory testing was not counted as an awakening in any condition.) None of the sleep maintenance parameters showed a significant difference between direct comparisons of the three active drug conditions.

In addition to the main effects due to drug, there were significant drug by day interactions for percent awake and total sleep time. Although wakefulness tended to be decreased on placebo day 2 (3.5 ± 4.7%) in comparison to placebo day 1 (9.5 ± 12.1%), this difference was not significant. There were no other significant differences in percent awake between days in any of the three drug conditions nor were there any significant differences between days across drugs and placebo. The difference between mean total sleep time on placebo day 1 (397.4 ± 56.6 min) and placebo day 2 (428.6 ± 28.7 min) was significant at $P < 0.05$ (10 *df*). Total sleep time in the three active drug conditions did not show a significant difference due to days. The only other comparison which was significant ($P < 0.05$, 10 *df*) was the increased total sleep time on triazolam day 1 (434.1 ± 21.1 min) in comparison to placebo day 1 (397.4 ± 56.6 min).

Subjective Measures of Hypnotic Properties. (Table 3)

Sleep induction, measured by the subject's morning estimates of time to fall asleep after lights out, showed a significant ($P < 0.02$) main effect due to drug. Both lorazepam and triazolam administration were associated with a significant ($P < 0.02$) reduction in the subjective latency to sleep onset. Although flurazepam also reduced subjective sleep latency, the effect was not statistically significant. Estimated latency to fall back to sleep after memory testing approached statistical significance ($0.10 > P > 0.05$) only after triazolam administration. Estimates of total sleep time were not significantly different between any of the three experimental conditions. Only flurazepam and lorazepam significantly ($P < 0.02$) reduced the estimated number of awakenings. All three active drugs were judged to significantly improve the "quality of sleep" as measured by a 10 mm visual analogue scale (P values < 0.05 and < 0.01). Like the objective measures of hypnotic properties, the subjective measures produced only minimal differences between active drugs.

Sleep Stages. (Table 4)

Flurazepam, lorazepam, and triazolam all produced significant changes in sleep stages. Percent stage 1 was

Table 5. Memory recall averaged across two consecutive nights

	Mean no. of items recalled immediate	Mean no. of digits recalled immediate	Mean no. of items recalled morning	Mean no. of digits recalled morning
Placebo	14.6 ± 1.2	4.8 ± 0.9	14.1 ± 1.6	4.5 ± 1.3
Flurazepam	13.7 ± 2.7	3.9 ± 1.8**	12.7 ± 2.7*	2.7 ± 2.0***
Lorazepam	9.7 ± 4.3****	2.7 ± 2.0****	8.0 ± 4.7****	1.7 ± 1.9****
Triazolam	11.8 ± 3.6***	3.4 ± 1.7****	9.3 ± 4.2****	2.1 ± 2.0****

* $P < 0.05$; ** $P < 0.02$; *** $P < 0.01$; **** $P < 0.001$ in comparison to placebo

significantly reduced by all three drugs with P values ranging from < 0.02 to < 0.001, and lorazepam administration was associated with a significantly greater reduction in stage 1 than that produced by either of the other two drugs. Percent stage 2, on the other hand, was significantly increased by all three active compounds ($P < 0.01$ or < 0.02). Previous studies have shown reduction in stage 3–4 sleep following administration of flurazepam (Kales et al. 1975), and minimal changes in stage 3–4 following triazolam administration (Roth et al. 1976; Vogel et al. 1975). Globus et al. (1972) have reported an increase in stage 3 sleep with no change in stage 4 sleep following three to four days of lorazepam in normal subjects. In this study, however, stage 3–4 sleep was not significantly altered from placebo levels following administration of any drug. This result could be due to the short-term 2-day drug administration period, or more likely, due to the low percentage of stage 3–4 on placebo nights. Percent REM showed a significant ($P < 0.001$) decrease only in the lorazepam condition in comparison to both placebo and flurazepam. Latency to REM was not significantly changed by any of the drugs.

Memory Functioning. (Table 5)

Recall of the 16 test items was significantly decreased in both the lorazepam ($P < 0.001$) and triazolam ($P < 0.01$) conditions immediately after the test items were presented. The difference in recall between flurazepam and the other two drug conditions was also statistically significant. All three drugs significantly reduced immediate recall of the five digit number ($P < 0.02$ or < 0.001).

Recall of the 16 memory items and five digit number was significantly reduced at morning testing following administration of all active compounds ($P < 0.001$ to $P < 0.05$). Recall following flurazepam administration was significantly better than that following either lorazepam or triazolam administration.

A total night recall score and a total morning recall score for the 16 test items was calculated across all three active drug conditions and all experimental nights. At nighttime testing, 29% of the total number of items presented was not recalled. By morning, however, 38% of the total number of items was not recalled, indicating that the majority of memory loss occurred at the nighttime task presentation. Further analysis showed that of the items which were not recalled at morning testing, 71% were not recalled at night whereas only an additional 29% of these unrecalled items were forgotten between the nighttime and morning testing.

The inability to recall information post drug may be related to hypnotic properties. For each of the active drug conditions, subjects had significantly ($P < 0.05$) poorer recall when they fell asleep within 2.5 min in comparison to when they fell asleep in more than 5 min. Additionally, the correlation between number of items recalled and the latency to fall back to sleep for subjects who took five or less minutes to fall back asleep was 0.74.

Discussion

In confirmation of previous studies, these results show that significant anterograde memory deficits occur following benzodiazepine administration. Although we did not systematically evaluate retrograde amnesia, it was never observed with any of the drugs. Unlike previous studies of memory function which have employed benzodiazepines as surgical premedicants, we have demonstrated that anterograde amnesia is present when these drugs are used as sleeping medications. Although it is not possible to be absolutely certain that all benzodiazepines possess amnesic properties, it is clear from this study that both short acting benzodiazepines such as triazolam with a half-life of 4.5 h (Metzler et al. 1977) and long acting benzodiazepines such as flurazepam with a half-life of 47–100 h (Kaplan et al. 1973) produce similar deficits in memory. This suggests that amnesic properties may be a common side effect of different drugs with widely differing half-lives in this class.

What is the mechanism of the post drug memory loss? There are at least two explantions for the effect. First, amnesia could be the result of a failure of memory consolidation. According to this view, morning recall

for the tasks is impaired because the information is not stored at the nighttime task presentation. If this were the case, recall at night would be at least as poor as morning recall. Alternatively, the amnesia could be the failure of memory retrieval. That is, nighttime recall is intact because the memory has been consolidated, but there is morning memory loss because the memory cannot be retrieved from storage. If this were the case, the majority of the memory loss would be present at morning testing. Our results support the memory consolidation hypothesis. The majority of memory loss occurred at nighttime testing. Therefore, it is unlikely that the decrease in morning recall for the previous night's events could be attributed to the failure of retrieval.

The inability of subjects to consolidate nighttime memory for morning recall is related to the hypnotic properties of the three active drugs. When subjects fell asleep within 2.5 min, they had significantly poorer recall than when they fell asleep in more than 5 min. Also, there was a high correlation between the number of items recalled and the latency of 5 min or less to fall asleep. These findings indicate that a critical period of wakefulness, 2–3 min in duration, is necessary before memories are consolidated. It also suggests that sleep per se may have amnesic properties. In contrast to these findings, a recent study has presented data which indicate that another benzodiazepine, flunitrazepam, does have anterograde amnesic properties (Bixler et al. 1979). However, these investigators did not examine the latency back to sleep following nighttime testing nor did they evaluate immediate recall of test items. In light of our results, it is possible that the amnesic effects of flunitrazepam may also be related to latency to fall back asleep after stimulus presentation.

As mentioned in the introduction, the amnesic properties of benzodiazepines are potentially dangerous. However, our findings indicate that if a critical period of wakefulness in maintained following an awakening, the post drug amnesic effects may be minimized. Under these conditions, the amnesia may not be an important side effect which would preclude the use of these drugs in non-hospitalized patients. The amnesic side effects of benzodiazepines might also be efficacious for those insomniac subjects who experience multiple awakenings during the night, and in fact, these individuals may experience a subjective improvement in their sleep if they are not aware of numerous brief arousals.

The question still remains as to whether amnesia is a specific side effect associated only with benzodiazepines or whether it is a side effect associated with all sleep-inducing compounds. There is evidence, for example, that pentobarbitone, a barbiturate, does not produce anterograde amnesia when administered as an IV surgical premedicant (Heisterkamp and Cohen 1975). However, orally administered secobarbital has been reported to have anterograde amnesic properties (Bixler et al. 1979). Our results do suggest that a critical period of wakefulness, which may be independent of drug class, is essential for memory consolidation. Additional studies are necessary which would 1. systematically vary the degree of vigilance and the amount of wakefulness following a nighttime awakening to correlate these variables with morning memory recall and 2. determine whether non-benzodiazepine hypnotics such as barbiturates produce anterograde amnesia under the experimental conditions which we have employed in this study.

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