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Ethanol as a Hypnotic in Insomniacs: Self Administration and Effects on Sleep and Mood

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The purpose of this study was to assess the effects of low ethanol doses on sleep and mood and to assess its reinforcing effects used as a hypnotic. Twenty healthy adults, aged 21–45 yrs, all moderate social drinkers, were studied: eleven subjects had insomnia and nine were normal sleepers, as documented by clinical polysomnography. On two sampling nights each, ethanol (0.5 g/kg) or placebo was administered before sleep in color-coded cups presented in three doses (0.2, 0.2, and 0.1 g/kg) separated by 15 min. On three subsequent nights subjects chose their preferred pre-sleep beverage (0.2 g/kg ethanol or placebo) based on cup color and were given an opportunity for 3 additional refills (0.2 g/kg each) of the chosen beverage at 15 min intervals, yielding a total possible dose of 0.8 g/kg. Insomniacs chose ethanol 67% of nights and normals 22%. Insomniacs chose significantly more ethanol refills than normals for an average nightly dose of 0.45 g/kg and normals took significantly more placebo refills. On the sampling nights 0.5 g/kg ethanol reduced REM sleep for both groups for the 8-hr sleep period and in insomniacs increased stage 3-4 sleep and reduced stage 1 sleep during the first half of the night to the level seen in the normals. Other sleep variables were not altered in either group or halves of the night. Pre-sleep improvements in the Profile of Mood States tension and concentration factors were also associated with ethanol administration. Thus, acutely, both sleep and mood effects appear to be associated with the reinforcing effects of ethanol as a hypnotic for insomniacs.

[Neuropsychopharmacology 20:279–286, 1999]

KEY WORDS: *Ethanol; Hypnotic use; Self administration; Insomnia; Mood effects*

There is a significant population of people with sleep complaints who report using alcohol as a hypnotic. In a recent representative population survey, 28% of those who complained of insomnia reported using alcohol to help them sleep and 67% of those felt it was effective (National Sleep Foundation 1991; Costa et al. 1996). However, no data are available on the effects of ethanol on the sleep of persons with insomnia, nor are there studies of the reinforcing effects of ethanol when used as a hypnotic (i.e., ethanol consumed before sleep).

The effects of ethanol on the sleep of healthy normals and alcoholics has been reported. First regarding ethanol effects in healthy normals, doses from 0.16 to 1.0 g/kg, yielding breath ethanol concentrations (BEC) as high as 105 mg%, have been studied (Gresham et al. 1963; Yules et al, 1966; Yules et al. 1967; Rundell et al. 1972; Williams and Salamy 1972; Stone 1980; Prinz et al. 1980; MacLean and Cairns 1982; Williams et al. 1983; Roehrs et al. 1991). A few studies found reduced sleep latency (Rundell et al. 1972; Williams and Salamy 1972; MacLean and Cairns 1982; Williams et al. 1983) and a single study found increased sleep time at the low dose, 0.16 g/kg, but no effect at 0.32 and 0.64 g/kg (Stone 1980). When analyzing the sleep period by halves, some

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Received January 15, 1998; revised April 21, 1998; accepted May 22, 1998.

Published by Elsevier Science Inc.
655 Avenue of the Americas, New York, NY 10010

0893-133X/99/$–see front matter
PII S0893-133X(98)00068-2

studies report increased wake or light stage I sleep in the second half of the sleep period (Williams et al. 1983; Roehrs et al. 1991). In contrast to these variable effects on sleep induction and sleep maintenance, consistent effects of ethanol on sleep staging are found. Most studies find suppression of REM sleep at least in the first half of the sleep period (Gresham et al. 1963; Yules et al. 1966; Prinz et al. 1980; Williams et al. 1983; Roehrs et al. 1991) and some studies find increased stage 3/4 sleep in the first half of the sleep period (Williams and Salamy 1972; MacLean and Cairns 1982; Williams et al. 1983; Roehrs et al. 1991). Studies have assessed effects over repeated nights of administration and clear tolerance to sedative and sleep stage effects develops within three nights (Rundell et al. 1972; Prinz et al. 1980). However, a healthy normal population sleeping at their usual bedtime is not adequate for assessing hypnotic effects. Sleep latency and sleep efficiency are already optimal and further improvement in sleep is difficult to demonstrate. Furthermore, the doses used in these studies are generally much larger (i.e., yielding >50 mg% BEC) than insomniacs typically report using (i.e., 1–3 drinks).

The effects of ethanol on the sleep of alcoholics has been assessed in a number of studies. The sleep of sober alcoholics is extremely disturbed; sleep latency is prolonged, sleep is fragmented and light, and shortened overall (Williams and Salamy 1972; Gillin et al. 1990; Allen et al. 1980). The administration of ethanol improves the sleep of the alcoholic, but only acutely (Allen et al. 1980; Wagman and Allen 1975). Again, these results do not generalize well to an insomnia population. Taken together these findings in normals and alcoholics suggest that ethanol may have minimal sedative effects and more likely causes a sleep disturbance. But, the important fact is that insomniacs report using ethanol as a hypnotic and 67% report it is effective. Thus, the question is what are the objective sleep effects in insomniacs and are these effects the stimulus properties that are important for any reinforcing effects of ethanol used as a hypnotic.

Studies have shown that the reinforcing effects of ethanol can be studied systematically in the laboratory (de Wit and Johanson 1987; de Wit et al. 1987, 1989). In the de Wit et al. method nonalcoholic healthy normals are given an opportunity to choose between previously experienced color-coded ethanol or placebo beverages. The laboratory preferences observed are consistent with self-reported drinking histories. When given the opportunity to self administer multiple doses of ethanol, consistent individual differences are found. These differences relate to the individuals' drinking histories and to the subjective "mood-altering" effects of ethanol. Those with high intakes experience ethanol as increasing vigor, elation, and positive mood and those with low intakes experience it as increasing fatigue and reducing vigor.

As the data indicate, the effects of ethanol on mood differ among individuals based on drinking history and the effects may also differ in insomniacs versus normals. We are not aware of systematic studies of the mood effects of ethanol in the context of its use as a hypnotic (i.e., prior to sleep). Beyond individual differences in mood effects, is the potential of time-of-day difference in the mood effects of ethanol. The performance disruptive effects of ethanol vary as a function of the time-of-day and the same may be the case for its mood effects (de Wit et al. 1987). Ethanol may have a more perceptible sedative-relaxant mood effect when the level of alertness is high for insomniacs, (i.e., prior to the usual bedtime). Thus, the "mood altering" effects of ethanol before sleep may be the prominent mechanism for its reinforcing effect when used as a hypnotic.

This study was conducted to evaluate whether or not ethanol is a reinforcer used as a hypnotic and whether insomnia enhances the self administration of ethanol as a hypnotic. In addition, this study assessed the effects of ethanol on the sleep and mood of insomniacs relative to that of normals to evaluate possible mechanisms for ethanol's reinforcing effects.

METHODS

Subjects

Twenty healthy men and women, aged 21–55 yrs, 9 without sleep complaints and with normal sleep (sleep latency ≤20 min and ≥7 of 8 hrs sleep time) on a screening polysomnogram (PSG) and 11 with sleep complaints and with disturbed sleep (sleep latency ≥25 min and <6.5 of 8 hrs sleep time) on the PSG participated. Physical and psychiatric exams, drug use histories, laboratory test results, and urine drug screens were negative. The study protocol was approved by the Institutional Review Board. All subjects signed written informed consents and were paid for their participation.

Procedures

Medical and Psychological Screening. Each subject received a physical examination, the Cornell Medical Index, the MMPI, and standard clinical laboratory analyses of blood and urine samples for hematologic, hepatic, renal, and other major system functions. Subjects with clinically significant positive laboratory findings were excluded with special attention paid to the analyses of liver function to exclude any subjects with liver disease. Subjects with MMPI elevations (i.e., T scores >2 SD) on the clinical scales were also excluded.

Alcohol and Drug Use History. Subjects were interviewed to quantify their drug and alcohol use history. No subject reporting greater than 300 mg of caffeine use

per day was admitted. No subject reported smoking, although this was not an exclusion criteria. No subject reporting a current or past history of illicit drug use or alcoholism was admitted (the urine drug screen was used to verify the absence of current drug use). The DSM-III-R criteria were used to define any psychoactive substance (including alcoholism) dependence or abuse. Subjects were selected for their moderate social ethanol drinking (i.e., 1–14 drinks per wk and 6 drinks or less per occasion). SeIf-reported previous use of ethanol as a hypnotic was noted.

Sleep Evaluation. Following the initial screening described above, each subject then underwent additional evaluation to validate their insomnia complaints. A sleep disorders evaluation including a sleep history and a PSG was done. For the sleep history, each subject completed a two-week sleep diary of their usual sleep habits and a detailed questionnaire regarding any sleep-wake complaints. Those subjects with insufficient ($<$6.5 hrs bedtimes) and irregular sleep-wake schedules (i.e., bedtimes and risetimes varying $>$2 hrs) on two-week sleep logs or other evidence suggestive of a circadian rhythm disorder were excluded (American Sleep Disorders Association 1990).

The PSG obtained from each subject included the standard central (C3-A2) and occipital (Oz-A2) electroencephalograms (EEGs), bilateral horizontal electrooculograms (EOG), submental electromyogram (EMG), and electrocardiogram (ECG) recorded with a V5 lead (Rechtschaffen and Kales 1968). In addition airflow was monitored with oral and nasal thermistors and leg movements with electrodes placed over the left tibialis muscles. The recordings, made at a 10 mm/sec paper speed with polygraphs located in a separate monitoring room, began at 2300 hr and continued for 8 hrs. The respiration and tibialis EMG recordings were evaluated by a clinical polysomnographer and subjects having any evidence of apneas (10-sec cessations of air flow) or of clinically significant leg movements (i.e., $>$5 per hr of sleep) were excluded. All recordings were scored in 30-sec epochs according to the standards of Rechtschaffen and Kales (1968). Subjects qualifying as insomniacs had their complaint for 1 yr or more and estimated their nightly sleep time as less than 6.5 hrs. On the PSG, they were required to have a sleep efficiency (sleep time versus time in bed) of 85% or less [(American Sleep Disorders Association (ASDA) 1990)]. All insomniacs received an ASDA diagnosis of psychophysiological insomnia (307.42–0). Those subjects admitted as healthy normals had no sleep complaints and a sleep efficiency $>$85% on the screening PSG.

Ethanol Administration. Subjects were told that the effects of different alcohol beverages on their sleep and their preferences for those beverages were being evaluated. On 4 sampling nights 1 hr before bedtime subjects received ethanol (0.5 g/kg) and placebo (two nights each) in color-coded cups (a 0.2, 0.2, and 0.1 g/kg dose every 15 min). The ethanol was prepared in a 1:4 ratio with 80 proof vodka (Absolut) added to tonic water and the placebo consisted of the tonic water (in equal volume to the ethanol) with three drops of ethanol floated on the surface for gustatory and olfactory cues. The cup colors associated with ethanol and placebo were counterbalanced among subjects and the order of placebo and ethanol on the exposure nights was randomly determined. Subjects were told to attend to the cup color because they would be given a choice of the two beverages on the subsequent nights. On those 3 subsequent evenings they were asked to choose which of the color-coded cups they would prefer and then they were given the opportunity to choose up to 3 refills for a total potential dose of 0.8 g/kg (a 0.2 g/kg dose every 15 min). Once a beverage choice was made on a given evening the refill beverage could not be switched. On both sampling and choice nights ethanol or placebo consumption was completed by 2245 hrs and at that time a breath ethanol concentration (BEC) measurement was made. The same BEC measurement was made at 2200 hrs, prior to the session, and subjects were told they would be dismissed if ethanol was detected (none had to be dismissed). BEC was measured with Alco-Sensor II (Intoximeters Inc, St. Louis) breathalyzers which are calibrated weekly.

The ethanol drinking was done individually in the bedroom, comfortably seated at a table. Movement about the room, except as necessary to void (each room had a bathroom) and go to bed (bed and bathroom are within 10 ft of the table), was restricted in order to minimize any ethanol-related kinatestheic cues.

Subjects went to bed (2300 hrs) and remained in bed for an 8-hour sleep period. During the sleep periods standard PSGs were obtained. The PSGs included continuous monitoring of the central and occipital EEGs, the horizontal EOGs, and the submental EMG as described above. The airflow and leg movement recordings of the screening night were not included.

Subjective Sleep and Mood Effects Assessment. Each evening and morning subjects completed assessments of sleep and mood. For the sleep assessment, a post sleep questionnaire was completed in the morning inquiring as to the quality and quantity of the previous night's sleep. For the mood assessment, subjects completed the Profile of Mood States (POMS) before the drinking began, after the drinking was completed, and the next morning. The POMS is a standard mood measure with six factors (McNair et al. 1971).

Study Restrictions. Subjects were asked to refrain from drinking alcohol throughout the study except that given during the study. The BEC testing prior to each evening drinking session was used to confirm their

compliance. In the evening (after 6 pm) they were asked to refrain from using caffeinated beverages. They were also asked to refrain from eating after 6 pm in order not to retard the absorption of ethanol at the 2200 hr evening drinking session. Throughout the study they were cautioned to maintain their regular exercise habits and sleep-wake schedule and avoid meals after 6 pm.

Analyses. The ethanol choice and refill data were compared between insomniacs and normals by means of t-tests. The sleep and mood variables were analyzed for group (insomniac vs normal) and ethanol (ethanol vs placebo) effects by means of mixed design MANOVAs (SAS Institute, Cary NC) with placebo vs ethanol nights as a within subject variable and groups as the between subject variable. To correct for possible violations of the homogeneity of covariance assumption, the within subject comparisons were made using Greenhouse-Geiser corrections.

RESULTS

The demographic characteristics of the insomnia and normal subjects are outlined in Table 1. The groups were relatively comparable in age (insomniacs were slightly older) and in gender distribution. More insomniacs than normals (27% vs. 11%) reported previous use of alcohol to sleep. The groups did not reliably differ in the average number of drinks per week by social drinking history (insomniacs drank less numerically).

Reinforcing Effects of Ethanol

Table 2 presents the ethanol and placebo choices of the groups. The insomniacs chose ethanol, on average, a significantly greater number of the nights ($t = 3.54$; $df = 18$; $p < .002$) than the normals did and more of the insomniacs chose ethanol (91% vs. 55%) on at least one of the three nights. Five of the insomniacs choose ethanol every night, while no normals did so; one normal chose it 2 of the 3 nights. After the original choice on a given night, refills of the chosen beverage (4 total each night and a total of 12 on the 3 nights) were offered and thus the total number of ethanol or placebo doses for all 3 nights were tabulated. The insomniacs chose a greater total number of ethanol doses ($t = 2.80$; $df = 18$; $p < .01$) and a fewer total number of placebo doses ($t = 2.56$; $df = 18$; $p < .03$) than the normals. On average the insomniacs took a total 0.45 g/kg dose each night (i.e., 2–3 drinks).

Table 1. Demographic and Drinking Histories of Insomniacs and Normals

	Age (yrs)[a]	Gender	Previous Use of Ethanol to Help Sleep	Social Ethanol Drinking
Insomniacs	34.1 (8.8)	5F/6M	3/11	3.3 (1.8)
Normals	26.1 (3.7)	3F/6M	1/9	5.8 (4.9)

[a] Data are means (±SD). Social Ethanol Drinking = standard drinks (1 oz) per week reported.

Table 2. Number and Percent of Ethanol and Placebo Choices by Insomniacs and Normals

		Nights Ethanol Chosen[a]	Subjects Choosing Ethanol	Total Ethanol Doses[a]	Total Placebo Doses[a]
Insomniac	#	2.08 (1.04)	10	6.69 (4.48)	2.54 (3.32)
	%	67	91	56	21
Normal	#	0.67 (0.71)	5	2.00 (2.69)	5.56 (3.33)
	%	22	55	17	46

[a] Data are means (±SD).

The self-reported previous use of ethanol before sleep did not totally account for the differential likelihood of choosing ethanol by the groups. Three of the insomniacs and 1 normal reported a history of previous hypnotic ethanol use. When dropping the previous hypnotic ethanol users from the groups, the mean (± SD) number of nights ethanol was chosen for the remaining 8 insomniacs was 1.63 (1.06), which still differed from the mean number of nights ethanol was chosen [0.63 (0.74)] by the 8 normals ($t = 2.19$, $df = 14$, $p < .046$). The three insomniacs with the previous history of ethanol use as a hypnotic all chose ethanol on each of the three nights.

Effects of Ethanol on Sleep during the Sampling Phase

For the sampling nights, the mean BEC of all subjects on the first ethanol night was 0.044 ± 0.02% and on the second night it was 0.039 ± 0.02%. For the healthy normals on night 1 the BEC was 0.040 ± 0.02% and 0.043 ± 0.02% on night 2. For the insomniacs these measures were 0.045 ± 0.02% and 0.037 ± 0.02% on nights 1 and 2, respectively.

The effects of this dose of ethanol on the sleep of the normals and the insomniacs for the whole 8-hr recording is presented in Table 3. The data are presented as means of the two placebo and the two ethanol nights. As might be expected based on the screening criteria, the insomniacs slept more poorly than the normals as seen in sleep efficiency ($F = 5.62$; $df = 1,18$; $p < .03$), latency to stage 1 sleep ($F = 4.29$; $df = 1,18$; $p < .05$), and a trend toward a greater number of awakenings ($F = 3.50$; $df = 1,18$; $p < .08$). Relative to placebo, effects of ethanol were seen in min of REM sleep ($F = 5.50$; $df =$

Table 3. Effects of Ethanol on the Sleep (8 Hrs) of Insomniacs and Normals During Sampling Nights[a]

	Normals		Insomniacs	
	Placebo	Ethanol	Placebo	Ethanol
Sleep efficiency %[b]	91.5 (3.25)	91.1 (4.18)	86.7 (8.98)	83.3 (9.10)
Latency stage 1 (min)[c]	11.9 (11.8)	10.1 (7.22)	20.9 (20.2)	25.6 (21.0)
Wake during sleep (min)	15.8 (9.57)	12.0 (16.2)	27.3 (24.1)	38.6 (39.6)
Number awakenings	3.50 (3.43)	3.33 (1.87)	5.55 (2.86)	6.30 (3.86)
Stage 1 (min)	55.8 (21.0)	52.8 (15.4)	69.7 (35.1)	71.2 (31.7)
Stage 2 (min)	238 (36.1)	242 (55.2)	217 (53.7)	207 (42.2)
Stage 3–4 (min)	53.0 (36.5)	53.4 (39.6)	33.1 (26.7)	41.5 (31.0)
Stage REM (min)[d]	92.5 (23.1)	89.1 (26.9)	96.1 (36.0)	79.9 (30.7)
Latency to REM (min)	88.1 (20.8)	102 (36.4)	85.6 (34.4)	105 (45.8)

[a] Data are means (±SD). Sleep efficiency % = percent of sleep time per time in bed; Latency Stage 1 = latency to first epoch of stage 1 sleep; Wake during sleep = wake time after sleep onset and before the final awakening; Number awakenings = number of >1 min awakenings. Main effect of group, [b]$p < .03$, [c]$p < .05$; Main effect of ethanol, [d]$p < .03$, [e]$p < .05$.

1,18; $p < .03$), which was reduced in both groups. No other ethanol effects were observed over the 8-hr recording for either group.

Given the elimination rate of ethanol at this dose, analyses by quarters and halves of the night were also conducted to tease out any within the night changes in the effects of ethanol. The half night data for each group are presented in Table 4. Again the data are presented as means of the two placebo and ethanol nights. Stage 3–4 sleep was increased in both groups in the first half of the night ($F = 4.79$; $df = 1,18$; $p < .04$) and this stage 3–4 increase was greater in the insomniacs than in the normals ($F = 4.83$; $df = 1,18$; $p < .04$). In the analyses of sleep by quarters (data are not included) there was an overall reduction in stage 1 sleep in the first quarter of the night ($F = 4.79$; $df = 1,18$; $p < .04$). On placebo nights the mean (±SD) stage 1 percent was 14.36 (9.81) and on ethanol it was 11.28 (6.57). There were no significant half two effects of ethanol or groups.

Correlations were calculated between the total number of ethanol doses taken over the 3 choice nights and the change in a given sleep measure from placebo to ethanol on the two sampling nights (mean change over the two sampling nights). Among all subjects the total ethanol dose chosen was positively related to an ethanol-induced increase in stage 3–4 sleep ($r = 0.55$; $df = 19$; $p < .02$). There was a trend for an ethanol-induced decrease in stage 1 sleep predicting total ethanol dose chosen ($r = 0.44$; $df = 19$; $p < .07$).

Ethanol Effects on Mood during the Sampling Phase

Presented in Table 5 are the change scores (i.e., post minus pre) for each of the six POMS scales. A negative

Table 4. Effects of Ethanol on Sleep by Halves of the Night During Sampling Nights

	Normals		Insomniacs	
	Placebo	Ethanol	Placebo	Ethanol
Half one (hrs 1–4)				
Sleep efficiency %	90.0 (5.40)	90.4 (6.43)	85.4 (9.12)	81.8 (9.84)
Number awakenings	1.16 (1.17)	1.38 (0.96)	3.31 (2.31)	3.65 (2.76)
Stage 1 (min)	23.0 (7.65)	20.8 (5.68)	35.7 (24.6)	28.9 (17.6)
Stage 3-4 (min)[b,c]	44.3 (28.8)	45.3 (31.1)	31.0 (24.9)	40.5 (30.5)
Stage REM (min)	27.2 (7.82)	22.0 (7.1)	30.5 (15.6)	23.1 (9.23)
Half two (hrs 5–8)				
Sleep efficiency %	92.9 (2.87)	92.0 (3.11)	87.8 (13.2)	85.4 (17.1)
Number awakenings	3.11 (2.70)	2.00 (1.39)	3.81 (2.20)	4.54 (3.37)
Stage 1 (min)	32.8 (14.3)	32.1 (11.0)	41.6 (19.8)	41.8 (15.9)
Stage 3-4 (min)[b,c]	8.67 (10.3)	8.1 (9.62)	2.17 (4.52)	1.0 (9.1)
Stage REM (min)	65.3 (17.1)	69.1 (22.8)	65.6 (26.1)	56.8 (25.5)

[a] Data are means (±SD). Sleep efficiency % = percent of sleep time per time in bed; Number awakenings = number of >1 min awakenings. Main effect of ethanol, [b]$p < .04$; interaction effect of ethanol by group, [c]$p < .04$.

Table 5. Effects of Ethanol on Mood (POMS) During Sampling Nights[a]

	Normals		Insomniacs	
POMS scales	**Placebo**	**Ethanol**	**Placebo**	**Ethanol**
Vigor	−2.83 (3.17)	−0.33 (4.08)	−1.90 (6.21)	−1.36 (3.05)
Fatigue	2.11 (3.10)	0.66 (4.77)	0.13 (1.65)	1.54 (3.51)
Concentration[b]	−0.11 (1.96)	0.94 (1.23)	−0.54 (2.65)	0.64 (3.02)
Depression	0.11 (0.54)	0.17 (0.75)	−0.91 (1.68)	−0.59 (0.92)
Tension[c]	−0.61 (2.27)	−0.67 (1.75)	−0.32 (1.47)	−0.54 (1.29)
Anger	−0.17 (0.50)	−0.39 (0.82)	−0.05 (1.15)	0.68 (1.68)

[a] Data are means (±SD) of change scores (i.e., pre minus post) for each of the six POMS scales. A negative change score reflects a reduction in the mood scale dimension and a positive score an increase in that scale.
Main effect of ethanol, [b] $p < .05$; interaction effect of ethanol by group, [c] $p < .02$.

change score reflects a reduction in the mood scale dimension and a positive score an increase in that scale. Again the scores are presented as means of the two ethanol and the two placebo nights. Overall there was a significant increase in concentration with ethanol ($F = 4.16$; $df = 1,18$; $p < .05$) and as shown on the table the groups did not differ in this effect of ethanol. The insomniacs showed a greater reduction in tension with ethanol than the normals ($F = 7.22$; $df = 1,18$; $p < .02$). There were no significant effects on the other scales. The morning mood and subjective sleep evaluations did not reveal consistent effects.

Correlations were calculated between the total number of ethanol doses taken over the 3 choice nights and the change in the six POMS mood factors on the sampling ethanol nights 1 and 2 and on the mean of nights 1 and 2. There were trends with increased ethanol intake related to concentration improvement on night 1 ($r = 0.40$; $df = 19$; $p < .08$) and depression reductions on night 2 ($r = 0.39$; $df = 19$; $p < .09$) and on the mean of nights 1 and 2 ($r = 0.39$; $df = 19$; $p < .09$).

DISCUSSION

These data show that insomniacs are more likely to self administer ethanol before bedtime than are noninsomniacs. It is evident that there were individual differences in hypnotic ethanol self administration. For example, those who reported previous use of ethanol as a hypnotic also had higher nightly laboratory self administration [i.e., 3.00 (0) vs. 1.60 (1.06)], which it should be noted serves as a validation of this laboratory assessment. The critical question is what are the risks for insomniacs who do not have previous experience using ethanol as a hypnotic? Additionally, what stimulus properties of ethanol are associated with its reinforcing effects when used as a hypnotic? Possible stimulus effects fall into two general categories: sleep effects and mood effects.

As to sleep effects, the data show that a low ethanol dose does have pharmacological effects on sleep as evident by the overall REM suppression in both groups. While there was no consistent reduction in sleep latency or increase in sleep time, particularly in the insomniacs, there may have been some subtle improvements in sleep structure. For the insomniacs stage 3–4 sleep was increased and stage 1 sleep was decreased. The sleep of the insomniacs was normalized in terms of stages 3–4 and 1 sleep. In three studies of the self administration of benzodiazepine hypnotics by insomniacs the best predictor of the number of placebo or active drug capsules chosen over the three studies was the patients' percentage of stage 3–4 sleep on the diagnostic-screening night (Roehrs et al. 1995). The self administration of ethanol by insomniacs and its beneficial effect on stage 3–4 sleep is consistent with these earlier data on the self administration of benzodiazepine hypnotics.

Importantly, the second half of the night disruption of sleep found in the studies of normals using higher doses was not consistently seen in these data. As seen in Table 4 sleep efficiency was not differentially affected by ethanol in the second half versus the first half of the night. There was no reduction in sleep efficiency and also no increase in stage 1 sleep with ethanol in the second half of the night. The dose used in this study on the two sampling nights was close to the average dose (0.45 g/kg) that the insomniacs subsequently self administered in the second phase of this study. It appears to have improved the insomniacs' sleep without disturbing their sleep in the second half of the night.

The importance of mood changes in insomniacs consuming ethanol before sleep is also highlighted in these data. The effects of ethanol that are reported in healthy normals with low self-reported social drinking histories during daytime administration of similar ethanol doses (i.e., increased fatigue and reduced vigor) on the POMS are not consistently evident when ethanol is administered before sleep by the insomniacs (de Wit and Johanson 1987; de Wit et al. 1987; de Wit et al. 1989). The POMS data in the insomniacs of this study suggest that

other "mood-altering" effects of ethanol are important. The POMS scales showing ethanol effects were the tension and concentration scales; improvements on these scales correlated with total ethanol dose chosen. Thus, the stimulus properties of ethanol in the domain of mood effects that function to reinforce its use as a hypnotic may not be its sedative effects.

As to the risks associated with hypnotic use of ethanol, while low ethanol doses may acutely have beneficial effects on the sleep of insomniacs, the effects of repeated nightly use, both on sleep and ethanol self administration, is not known, but of concern. The data in normals show that tolerance to the stage 3–4 sleep enhancement develops within 3–5 nights of repeated use (Rundell et al. 1972; Prinz et al. 1980). In these high dose studies of normals, sleep disturbance then follows. But, what of low doses in insomniacs? One would predict tolerance development. But, with tolerance development, is the ethanol use abandoned or is the dose increased in search of improved sleep? The latter may occur without there being the clear perceptible negative consequences (i.e., sleep disturbance) found with higher doses. Another question is what then happens to daytime social use of ethanol by insomniacs. To the extent that the "mood altering" effects are, or become, important in the hypnotic ethanol self administration, daytime social use may also increase.

The persistence of insomniacs' search for good sleep has become evident in a series of studies of insomniacs' self administration of benzodiazepine hypnotics. Given the option to self administer a previously sampled color-coded capsule or no capsule before sleep (a single-choice methodology), insomniacs self administered capsules on about 70% of nights and self administered placebo as frequently as triazolam 0.25 mg (Roehrs et al. 1992; Roehrs et al. 1997; Roehrs et al. 1996). In one of the studies the option of administering multiple capsules (a total of three) nightly was given, again in a single-choice methodology and insomniacs administered an average triazolam dose of 0.27 mg, but double the number of placebo capsules (Roehrs et al. 1996). When forced to chose between triazolam and placebo on a given night (i.e., a forced-choice methodology), insomniacs prefer active drug (Roehrs et al. 1997). But, the point is that when their treatment options are limited (the available capsule or no capsule), insomniacs will pursue ineffective treatments (placebo), at least acutely. Given that ethanol's sedative effect may have diminished due to tolerance development, the concern is how the insomniac responds when ethanol is the only perceived available option.

ACKNOWLEDGMENTS

Supported by NIAAA # RO1-AA07147.

REFERENCES

Allen RP, Wagman AM, Funderburk FR, Wells DT (1980): Slow wave sleep: a predictor of individual differences in response to drinking? Biol Psychiatry 15:345–348

American Sleep Disorders Association (1990): The International Classification of Sleep Disorders. Lawrence, Kansas, Allen Press, Inc

Costa E, Silva JA, Chase M, Sartorius N, Roth T (1996): Special report from a symposium held by the World Health Organization and the World Federation of Sleep Research Societies: An overview of insomnias and related disorders—recognition, epidemiology, and rational management. Sleep 19:412–416

de Wit H, Johanson CE (1987): Choice procedures in human drug self-administration. In Bozarth MA (ed), Methods of Assessing the Reinforcing Properties of Abused Drugs. Berlin, Springer-Verlag, pp 559–572

de Wit H, Uhlenhuth EH, Pierri J, Johanson CE (1987): Individual differences in behavioral and subjective responses to alcohol. Alcohol Clin Exp Res 11:52–59

de Wit H, Pierri J, Johanson CE (1989): Assessing individual differences in ETOH preference using a cumulative dosing procedure. Psychopharmacology 98:113–119

Gillin JC, Smith TL, Irwin M, Kripke DF, Schuckit M (1990): EEG sleep studies in "pure" alcoholism during subacute withdrawal: Relationships to normal controls, age, and other clinical variables. Biol Psychiatry 27:477–488

Gresham SC, Webb WB, Willianms RL (1963): Alcohol and caffeine: Effect on inferred visual dreaming. Science 140:1226–1227

MacLean A, Cairns J (1982): Dose-response effects of ethanol on the sleep of young men. J Stud Alcohol 43:434–444

McNair D, Lorr M, Droppleman LF (1971): Manual for the Profile of Mood States. San Diego, Educational and Industrial Testing Service

National Sleep Foundation (1991): Sleep in America. Princeton, NJ, Gallup Organization

Prinz P, Roehrs T, Vitaliano P, Linnoila M, Weitzman E (1980): Effect of alcohol on sleep and nighttime plasma growth hormone and cortisol concentrations. J Clin & Endocrin Metab 51:759–764

Rechtschaffen A, Kales A (1968): A Manual of Standardized, Techniques and Scoring System for Sleep Stages of Human Sleep. Los Angeles, Brain Information Service/ Brain Research Institute, University of California at Los Angeles

Roehrs T, Yoon J, Roth T (1991): Nocturnal and next-day effects of ethanol and basal level of sleepiness. Human Psychopharm Clin & Exper 6:307–312

Roehrs T, Merlotti L, Zorick F, Roth T (1992): Rebound insomnia and hypnotic self administration. Psychopharmacology 107:480–484

Roehrs T, Rosenthal L, Pedrosi B, Papineau K, Roth T (1995): Predictors of hypnotic self administration. Sleep Res 224:49

Roehrs T, Pedrosi B, Rosenthal L, Roth T (1996): Hypnotic self-administration and dose escalation. Psychopharmacology 127:150–154

Roehrs T, Pedrosi B, Rosenthal L, Zorick F, Roth T (1997): Hypnotic self-administration: Forced-choice vs. single-choice. Psychopharmacology 133:121–126

Rundell JB, Lester BK, Griffiths WJ, Williams HL (1972): Alcohol and sleep in young adults. Psychopharmacology 26:201–218

Stone BM (1980): Sleep and low doses of alcohol. Electroenceph Clin Neurophysiol 48:706–709

Wagman AM, Allen RP (1975): Effects of alcohol ingestion and abstinence on slow wave sleep of alcoholics. Adv Exp Med Biol 59:453–466

Williams H, Salamy A (1972): Alcohol and sleep. In Kissin B, Beghleiter H (eds), The Biology of Alcoholism. New York, Plenum Press, pp 435–483

Williams D, MacLean A, Cairns J (1983): Dose-response effects of ethanol on the sleep of young women. J Stud Alcohol 44:515–523

Yules RB, Freedman DX, Chandler KA (1966): The effect of ethyl alcohol on man's electroencephalographic sleep cycle. Electroenceph Clin Neurophysiol 20:109–111

Yules RB, Lippman ME, Freedman DX (1967): Alcohol administration prior to sleep. Arch Gen Psychiat 16:94–97