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FACILITATION OF HUMAN TOBACCO SELF-ADMINISTRATION BY ETHANOL: A BEHAVIORAL ANALYSIS[1]

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The effect of ethanol on the cigarette smoking of alcoholic subjects was studied in a residential laboratory. During daily 6-hr sessions, cigarettes were obtained either by request to the ward staff or by operation of a lever (fixed-ratio 5 or 10). In a mixed sequence across days, sessions involved ingestion of either vehicle (orange juice) alone or vehicle plus ethanol (133.7 g). During ethanol sessions, the rate of cigarette smoking increased from 26% to 117% of vehicle levels. A series of control studies eliminated a number of potential behavioral mechanisms for the observed effect and indicated that the ethanol-induced increase in cigarette smoking occurred under a variety of experimental conditions: (1) when smoking could not occur concurrently with ethanol or vehicle consumption; (2) when subjects were not allowed to socialize; (3) when ingestion of ethanol or vehicle was scheduled for a number of consecutive days; (4) when various doses of ethanol were administered under blind conditions. In control experiments, weighing unsmoked tobacco and counting the number of puffs per cigarette indicated the effect was not due to smoking less of each cigarette. The effect was not limited to the experimental sessions alone, since total daily smoking was higher on ethanol days than vehicle days.

Key words: tobacco, ethanol, drug self-administration, cigarette smoking, alcoholics, humans

A number of studies using interviews or questionnaires have demonstrated that people who drink heavily also tend to smoke heavily (Brown and Campbell, 1961; Cartwright, Martin, and Thompson, 1959; Dreher and Fraser, 1967; Heath, 1958; Maletzky and Klotter, 1974; McArthur, Waldron, and Dickinson, 1958; Walton, 1972). Maletzky and Klotter (1974) noted that even among alcoholics there is a high positive between-subject correlation between the amount alcoholics drink and the amount they smoke.

Attempts to explain the determinants of the observed correlation between ethanol consumption and cigarette smoking have resulted in a number of hypotheses involving ill-defined and generally unmeasurable constructs assumed to underlie excessive smoking and drinking, including addictive personalities, oral drives, anxiety states, and general neuroticism (Dreher and Fraser, 1967; Maletzky and Klotter, 1974; McArthur *et al.*, 1958). There are, of course, alternative explanations—a more direct causal relationship may exist between ethanol ingestion and cigarette smoking. The present set of studies explored this possibility by experimentally evaluating the effect of ethanol on the cigarette smoking of volunteer alcoholics in a residential laboratory. A within-subject experimental methodology was used to assess the influence of ethanol ingestion on cigarette smoking. The first experiment was the initial observation that ethanol ingestion may increase cigarette smoking. The subsequent six experiments involved a series of systematic replications under alternative behavioral-pharmacological conditions. These experiments involved an analysis of various behavioral mechanisms that were considered *a priori* to constitute probable mechanisms of action.

EXPERIMENT I: EFFECT OF ETHANOL *versus* VEHICLE CONSUMPTION ON RATE OF CIGARETTE SMOKING

Experiment I was the first of a series that examined the effect of ethanol on cigarette smoking.

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GENERAL METHOD

Five male volunteers referred from the emergency room of Baltimore City Hospitals participated. All were chronic alcoholics, 37- to 48-yr old, with histories of cigarette smoking (20 to 39 yr). All reported histories of problem drinking (14 to 27 yr), repeated hospitalization for alcoholism (two to 40 times), and having experienced symptoms of physical dependence on ethanol. Volunteers were detoxified and their informed consent obtained in writing before participation. The experiments were conducted on an eight-bed behavioral pharmacology research ward. Subjects participated in the research successively in independent replications, rather than simultaneously (the one exception was that Subjects RUM and MI participated simultaneously in Experiment VI). Other ward residents participated in different behavioral studies involving self-administration of various drugs. There was unsystematic variation both within and between subjects with respect to the number of additional residents on the ward (three to six) at any time, and with respect to the experiments in which these other residents participated. A pool table, television set, cards, various games, and reading and craft materials were continuously available to subjects in the dayroom. General ward behavior was maintained via a point economy system that specified the conditions under which points could be earned or spent. Point fines were imposed for violation of certain ward rules. If a subject's total point earnings fell below zero, the subject was detoxified and discharged. Two or three subjects participated in each of seven experiments. Table 1 shows the sequence of exposure to different experiments for each subject. Details of experimental procedures were described to the subjects when they were implemented. However, the nature or purpose of the experiments were not described and subjects were given no instructions or explanations of what they were "supposed" to do, or of what outcomes might be expected.

Scheduling of ethanol or vehicle drinks. Between 9:00 a.m. and 3:00 p.m., except for using the bathroom, each subject was required to remain in the ward dayroom area. Starting at 9:00 a.m. the subject was required to consume a 90-ml drink every half-hour (12 drinks total). On a given day, the 12 drinks were either orange juice (vehicle) or a mixture of ethanol and orange juice. Vehicle drinks consisted of 90 ml of orange juice. Ethanol drinks consisted of 30 ml 95-proof ethanol (11.14 g ethanol) in 60 ml orange juice. Individual drinks were dispensed by the research ward staff and the subject could consume the drinks at whatever rate he chose (provided he finished within 30 min) and while participating in other ward activities. Staff recorded the duration of each drink. The subject was informed immediately before the beginning of each session (9:00 a.m.) whether ethanol or vehicle drinks were available. The scheduling of ethanol *versus* vehicle drinks was determined from a mixed sequence in which no more than three ethanol or three vehicle days occurred successively. The experiment was terminated when the minimum number of days in each condition was 10 (the one exception was Experiment VI, which was terminated after five or six days in each condition). Between 6:00 p.m. and 9:00 p.m. daily, six ethanol drinks were available to the subject, independently of whether ethanol or vehicle had been scheduled between 9:00 a.m. and 3:00 p.m. Blood ethanol levels were assessed (Model 900A Breathalyzer, Stephenson Corp.) at 12:00 noon and 3:00 p.m. daily (the

Table 1

Sequence of exposure to different experiments. Detoxification (Detox) indicates subject had received no ethanol for a minimum period of five days. Weight of individual subjects indicated in parentheses.

Subject (kg)	*Sequence of Experiments*						
MO(81.8):	Detox;	Exp I;	Exp II;	Exp III			
MI(96.4):	Detox;	Exp I;	Exp II;	Detox;	Exp VII;	Detox;	Exp VI
RUT(70.5):	Detox;	Exp I;	Exp V;	Detox;	Exp IV		
RUM(79.5):	Detox;	Exp VII;	Exp III;	Exp IV;	Detox;	Exp VI	
SU(85.5):	Exp V						

one exception was Subject MI in Experiment I for whom blood ethanol levels were not assessed.) During ethanol sessions, Breathalyzer readings ranged from 20 to 70 mg ethanol/100 ml at 12:00 noon and from 80 to 130 mg ethanol/100 ml at 3:00 p.m.

Availability of cigarettes. Between 9:00 a.m. and 3:00 p.m. daily, the subject could obtain cigarettes to smoke from a cigarette dispenser located near the nurses' station (the one exception was Subject MI in Experiment I, who received all cigarettes on request from research ward staff). Only the designated subject was permitted to use the cigarette dispenser. Two independent cigarette dispensers were used during Experiment VI, which involved the simultaneous participation of two subjects. The automatic cigarette dispenser avoided possible confounding effects of having staff dispense cigarettes. Single cigarettes were dispensed on completion of a low fixed-ratio requirement on a standard Lindsley operandum (the fixed-ratio requirement was arbitrarily set at FR 5 or 10). As each cigarette was delivered, control equipment sounded a tone and recorded the delivery on an internal counter that could not be seen by the subject. For a 1.5-min period after operation of the dispenser, additional responding was ineffective. This prevented the subject from obtaining multiple cigarettes. After delivery of each cigarette, staff terminated the tone by manual operation of a switch at the nurses' station, verified that the correct subject received the cigarette, and noted the time on a record sheet. The subject was required to smoke the cigarettes dispensed and no others; he was not permitted to save, give away, or borrow cigarettes. All cigarettes placed in the cigarette dispenser for the 9:00 a.m. to 3:00 p.m. session were marked with a colored pen for identification before the session. This permitted staff to verify that cigarettes were smoked by the correct subject. Throughout the experiments, there were no occasions between 9:00 a.m. and 3:00 p.m. on which a subject was found to be smoking an unmarked cigarette, nor were other patients ever found with marked cigarettes. At times other than during the session, cigarettes were freely available and were given to the subject by the ward staff. The brand of cigarette dispensed was determined by individual subject preference (MI and RUM smoked Camels; MO and RUT smoked Pall Mall; SU smoked Chesterfield). All cigarettes dispensed were 7 cm long (the length of a Camel regular); cigarettes exceeding this length were cut to 7 cm before being placed in the dispenser.

Reliability of staff recording was confirmed by comparing staff records and daily cigarette totals recorded by the dispensing equipment. The total number of cigarettes dispensed each session as recorded by the staff virtually always matched that recorded by the internal counter of the dispenser. Furthermore, informal spot checks undertaken by the authors also indicated that staff virtually never made recording errors.

Results

As shown in Table 2, all three subjects smoked more cigarettes during sessions in which ethanol was consumed than during sessions in which vehicle solution was consumed. The effect was quite stable, with visual inspection of the daily data revealing a clear difference between ethanol and vehicle sessions within all three subjects. This effect is shown in Figure 1, which includes the daily data of each subject under these experimental conditions.

Differences in the total number of cigarettes smoked during ethanol and vehicle sessions appeared to be correlated with different patterns of consuming ethanol *versus* vehicle drinks. For all three subjects (MO, MI, RUT, respectively) the average duration for consuming the ethanol drinks (mean in seconds 333.6, 342.5, 70.9) exceeded the duration for consuming the vehicle drinks (8.6, 17.2, 20.5). Although the duration for consuming drinks was quite variable within subjects, observation revealed that subjects generally tended to gulp the vehicle drinks while standing at the nurses' station; in contrast, subjects often sipped the ethanol drinks over a longer period of time while concurrently participating in other ward activities.

Comparison between ethanol and vehicle conditions of the temporal distributions of cigarette smoking within sessions indicated that ethanol produced relatively uniform increases in the distribution of smoking throughout the session. Despite the fact that the cumulative ethanol dose increased throughout the session, ethanol did not produce a selective increase in cigarette smoking toward the end of the session.

Table 2

Average number of cigarettes dispensed between 9:00 a.m. and 3:00 p.m. (mean ± S.E.M.) under conditions during which ethanol (ETOH) or vehicle (V) solutions were consumed. Number of days in each condition is indicated in parentheses. All doses of ethanol were 133.7 g except in Experiment VII as indicated. Blanks indicate subject did not participate in that experiment. All differences between vehicle and 133.7-g ethanol conditions were statistically significant using a two-tailed matched-paired t test ($p < 0.01$; consecutive vehicle sessions matched with consecutive ethanol sessions) with the exception of Experiment IV, where this statistic is not appropriate.

Subject	*Exp I*	*Exp II (Uniform Intake)*	*Exp III (No Socializing)*	*Exp IV (Chronic Exposure)*
MO	V:9.70 ± 0.37(10) ETOH:12.18 ± 0.42(11)	V:9.60 ± 0.65(10) ETOH:12.50 ± 0.50(10)	V:9.60 ± 0.54(10) ETOH:13.00 ± 0.54(10)	
MI	V:13.82 ± 1.00(11) ETOH:20.70 ± 0.72(10)	V:14.70 ± 0.88(10) ETOH:20.91 ± 0.84(11)		
RUT	V:14.10 ± 0.28(10) ETOH:18.00 ± 0.68(10)			V_1:15.90 ± 0.48(10) ETOH:20.30 ± 0.67(10)
RUM			V:9.30 ± 0.58(10) ETOH:20.20 ± 1.18(10)	V_1:12.44 ± 0.88(9) ETOH:23.70 ± 0.75(10) V_2:13.33 ± 1.07(9)
SU				

Table 2 (continued)

Subject	*Exp V (Cigarette Weight)*	*Exp VI (Cigarette Puffs)*	*Exp VII (Multiple Doses)*
MO			
MI		V:11.17 ± 0.48(6) ETOH:17.00 ± 0.32(5)	V:19.10 ± 0.80(10) 33.4 g ETOH:21.10 ± 0.72(10) 133.7 g ETOH:24.90 ± 0.88(10)
RUT	V:14.30 ± 0.37(10) ETOH:18.10 ± 0.48(10)		
RUM		V:11.00 ± 0.52(6) ETOH:15.60 ± 0.51(5)	V:13.20 ± 0.55(10) 33.4 g ETOH:12.20 ± 0.87(10) 133.7 g ETOH:22.20 ± 0.92(10)
SU	V:9.10 ± 0.75(10) ETOH:12.70 ± 0.73(10)		

EXPERIMENT II: UNIFORM INTAKE–CONTROL FOR CIGARETTE SMOKING AS AN ADJUNCT TO ETHANOL SELF-ADMINISTRATION

Experiment I demonstrated that more cigarettes were smoked under a condition in which ethanol was consumed than under a condition in which vehicle drinks were consumed. Experiment II explored one possible behavioral mechanism for this observed effect.

Falk (1971) observed that the intermittent scheduling of certain stimuli may ". . . induce extra, concurrent phenomena which are strong enough to sustain schedule behavior in their own right". Such observations have led to the recognition of a class of behavior termed "adjunctive" (Falk, 1971). It is possible that the increased cigarette smoking observed in Experiment I represented an instance of adjunctive behavior. Smoking may have been partially maintained as an adjunct to the behavior of drinking, with the increased smoking in ethanol sessions being due to the different pattern of subjects' drinking ethanol as opposed to vehicle. Ethanol consumption was characterized by a larger number of sips distributed over a longer temporal interval than the ingestion of the vehicle solution. Analysis of the durations for consuming individual drinks revealed that ethanol drinks were consumed more slowly (249.0 sec average) than vehicle drinks (15.4 sec average).

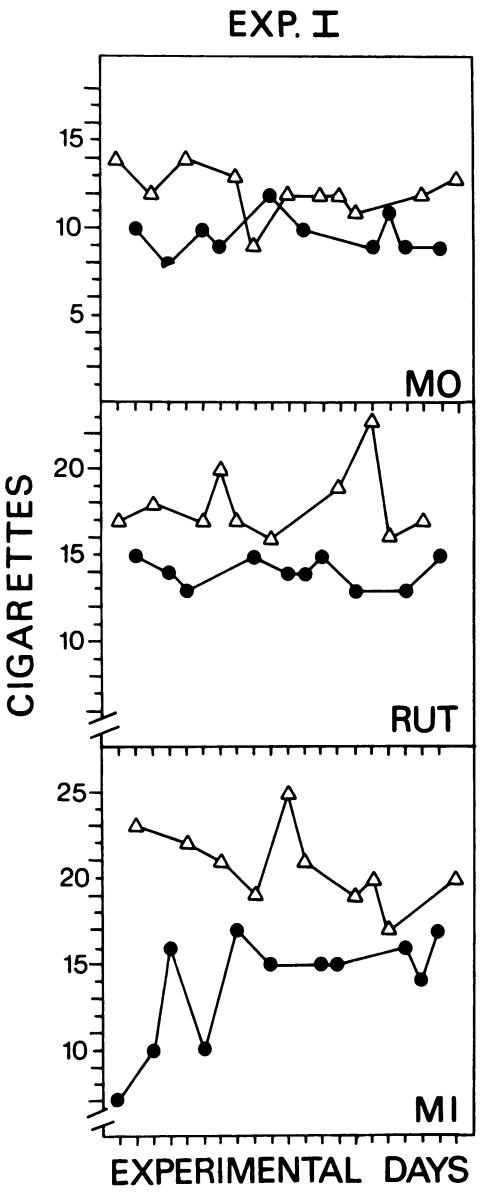

Fig. 1. The number of cigarettes smoked between 9:00 a.m. and 3:00 p.m. daily in Experiment I involving three alcoholic subjects. Subjects ingested solutions containing either vehicle (filled circles) or 133.7 g ethanol (unfilled triangles) on different days.

Experiment II was undertaken to control for the possibility that increased cigarette smoking was maintained as an adjunct to the patterned behavior of ethanol self-administration. Experiment I was systematically replicated under conditions that eliminated the possibility that cigarette smoking would be differentially induced by different patterns of consuming the ethanol and vehicle drinks. Specifically, the opportunity for concurrent smoking and drinking was eliminated.

Method

Two alcoholic subjects participated. The procedure was identical to that described for Experiment I, except that subjects were required to consume the ethanol or vehicle drinks within 30 sec of dispensing and while standing at the nurses station. In addition, subjects were not allowed to have a lighted cigarette while consuming the drinks.

Results

The results were similar to those obtained in Experiment I. As shown in Table 2, both subjects smoked more cigarettes on days on which ethanol was consumed than on those on which the vehicle solution was consumed. As in Experiment I, the stability of the effect was evident from the daily data, which are presented in Figure 2.

EXPERIMENT III: RESTRICTED SOCIALIZING—CONTROL FOR CIGARETTE SMOKING AS AN ADJUNCT TO SOCIAL INTERACTIONS

Experiment II indicated that increased smoking during ethanol sessions was not adjunctively maintained as a consequence of the distinctive pattern of ethanol consumption, because the opportunity for concurrent smoking and drinking was eliminated. Experiment III explored a second possible behavioral mechanism of the observed effect and addressed the question of whether smoking was adjunctively induced by some other distinctive characteristic of ethanol sessions.

A number of observational reports suggest that administration of ethanol produces changes in rates of social interactions (*i.e.*, increased frequency, probability, or duration of human verbal or nonverbal contact) in alcoholics (Diethelm and Barr, 1962; Docter and Bernal, 1964; McNamee *et al.*, 1968). Under conditions of ethanol administration similar to those of Experiment I, Griffiths *et al.* (1974*a*, 1975) have demonstrated quantitatively that ethanol produces increased rates of social behavior in alcoholics. It is possible that the increased smoking observed in Experiments

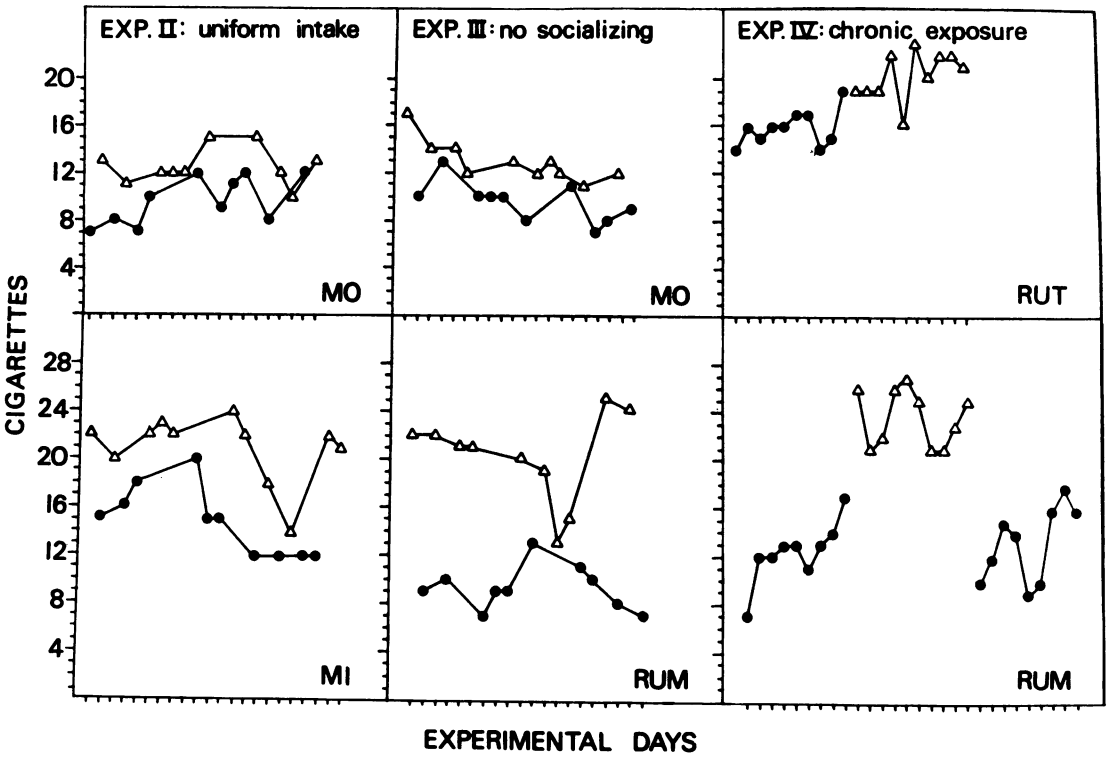

Fig. 2. The number of cigarettes smoked between 9:00 a.m. and 3:00 p.m. daily in three different experiments involving two alcoholic subjects each. Subjects ingested solutions containing either vehicle (filled circles) or 133.7 g ethanol (unfilled triangles) on different days.

I and II was an adjunct to increased social behavior induced by ethanol. Experiment III systematically replicated the prior studies under conditions that eliminated the possibility that cigarette smoking could be maintained as an adjunct to socializing by explicitly restricting all social interactions.

Method

Two alcoholic subjects participated. The procedure was identical to that described for Experiment I, except that during the daily sessions, patients were not permitted to engage in social interactions. Between 9:00 a.m. and 3:00 p.m. a yellow flashing light was illuminated at the nurses' station and while the light was on, the following set of rules was in effect:

"When the light is on, the subject is not allowed to talk, gesture or interact with staff or other patients. A social interaction is any behavior which requires the presence of or involves another person. Therefore, the subject may play pool, cards or games, but only by himself. Also during this time other patients are not allowed to talk or interact with the subject. Finally, staff should keep their interactions with the subject to a minimum. There may, however, be some necessary interactions such as the subject returning an empty glass to the staff; however these interactions should be kept minimal and involve no talking."

Staff explained these rules to the subject and other ward patients. Violation of the rules by the subject or other ward patients resulted in a point fine from the point economy against the violator.

Results

The procedure for restricting socializing eliminated virtually all social interactions between the subjects and other ward residents, and greatly reduced social interactions be-

tween subjects and staff.[2] No subject received any fines for violation of the socializing rules.

As shown in Table 2, differences in smoking comparable to those of the previous experiments were found. Despite the restriction on social interactions, stable increases in cigarette smoking were observed when ethanol days were compared to days on which the vehicle solution was consumed, as shown in Figure 2.

EXPERIMENT IV: SCHEDULING OF ETHANOL OR VEHICLE FOR A PERIOD OF CONSECUTIVE DAYS—A CONTROL FOR SCHEDULING EFFECTS

Experiment III indicated that the increased smoking during ethanol sessions was not a consequence of changes in social behavior during ethanol sessions. Experiment IV was undertaken to determine whether the effect was related to the specific scheduling conditions used in the previous experiments.

Previous experiments demonstrated increased cigarette smoking under ethanol conditions when ethanol or vehicle conditions were presented in a mixed sequence over successive days. It is possible that the observed effect was an artifact of the mixed scheduling procedure. For instance, perhaps the intermittent scheduling of any powerful reinforcer (in this case ethanol) changes the probability of various behaviors (in this case cigarette smoking).

Another possible explanation of the results is that cigarette smoking on days on which no ethanol was scheduled was suppressed by a hangover from ethanol consumed on the preceding day. With all the previous experiments, subjects consumed six ethanol drinks (66.8 g ethanol) in the evenings, independently of whether ethanol or vehicle drinks had been scheduled during their previous 6-hr experimental session. It is possible that subjects were slightly hungover the following morning and that the observed difference in cigarette smoking rate between ethanol and vehicle conditions represents a suppression of cigarette smoking on vehicle days due to discomfort.

Experiment IV was undertaken to eliminate some of the possible artifacts from the mixed scheduling procedure by systematically replicating previous experiments under conditions in which exposure to both ethanol and vehicle was scheduled for a period of consecutive days. This consecutive scheduling procedure also eliminated the possibility that the results on the vehicle days were affected by an ethanol hangover, because subjects did not receive any ethanol during the period of consecutive daily exposure to the vehicle condition. In addition to the measurement of smoking during the standard 6-hr session, the daily total number of cigarettes smoked was estimated to provide a further comparison between ethanol and vehicle conditions.

Method

Two alcoholic subjects participated. The procedure was similar to that described for Experiment I, except that subjects were informed before the experiment that they would initially receive drinks containing no ethanol (V_1:vehicle) for nine (RUM) or 10 (RUT) consecutive days and then subsequently would receive drinks containing ethanol for a 10-day period. In addition, one subject (RUM) was informed that after the period of ethanol availability, he would again receive drinks containing no ethanol for a nine-day period (V_2:-vehicle). On days on which ethanol drinks were scheduled, an additional six ethanol drinks were available to the subjects between 6:00 and 9:00 p.m. These drinks were not available on days on which vehicle was scheduled.

In this experiment, the number of cigarettes smoked was monitored day and night. As in Experiment I, between 9:00 a.m. and 3:00 p.m. daily, subjects could obtain cigarettes from the cigarette dispenser. At other times during the day (8:00 a.m. to 9:00 a.m. and 3:00 p.m. to 9:00 p.m.), subjects could obtain individual cigarettes on request from the ward staff. Each evening at 9:00 p.m. subjects were given an unopened pack of cigarettes, and unused cigarettes were collected at 8:00 a.m. the following morning. Therefore, it was possible to estimate the number of cigarettes smoked throughout the day.

To minimize discomfort upon abrupt withdrawal from ethanol, Subject RUM received doses of chlordiazepoxide at 9:00 a.m. and 9:00

[2]The degree of social restriction achieved with this manipulation was sufficient to have punishing properties under different scheduling conditions. When scheduled contingently, restriction from social interactions suppressed drinking in alcoholic subjects (Griffiths *et al.*, 1974*b*).

p.m. on Days 1 through 5 of the second vehicle period (V_2). Doses were 100 mg twice a day on the first three days and 50 mg twice a day on the remaining two. Administration of the drug did not produce any observable behavioral effects on the subject.

Results

As shown in Table 2, the results were similar to those obtained in previous experiments. Although ethanol and vehicle conditions were scheduled for a period of consecutive days, stable increases in cigarette smoking were observed during the ethanol condition between 9:00 a.m. and 3:00 p.m. (Figure 2). It should be noted that the first five days exposure of RUM to V_2 was confounded with chlordiazepoxide administration. However, the inclusion or exclusion of these data do not alter the interpretation of results. Overall, the study showed that the difference in smoking between ethanol and vehicle days was not due to the mixed scheduling procedure or to a hangover-induced suppression of smoking on vehicle days.

Analysis of the total daily number of cigarettes smoked revealed an effect similar to that observed during the 9:00 a.m. to 3:00 p.m. session, despite the exclusion of several days of incomplete data due to staff recording errors. For RUM, the mean daily number of cigarettes ±S.E.M. was 26.13 ± 2.12 and 32.00 ± 2.15 for the V_1 (eight days) and V_2 (nine days) conditions, respectively, and 50.89 ± 2.31 for the ethanol condition (nine days). Equivalent data for RUT was 45.30 ± 1.54 for the vehicle (V_1) condition (10 days) and 52.67 ± 1.42 for the ethanol condition (nine days).

EXPERIMENT V: WEIGHING CIGARETTE BUTTS—A CONTROL FOR AMOUNT OF CIGARETTE DISCARDED

Experiment IV demonstrated that the increased smoking in ethanol sessions was not an artifact of the mixed scheduling procedure or due to a hangover-induced suppression of smoking on vehicle days. Experiment V considered a further potential behavioral mechanism for the observed effect. Possibly, ethanol affects cigarette consumption by influencing the behavior of extinguishing and discarding cigarettes. That is, it is possible that although a larger number of cigarettes were dispensed during ethanol conditions, the cigarettes were extinguished sooner, and therefore the actual amount of tobacco consumed may not have been different between ethanol and vehicle conditions. Experiment V evaluated this possibility by systematically replicating previous experiments under conditions in which all unsmoked portions of cigarettes were collected and weighed.

Method

Two alcoholic subjects participated. The procedure was similar to that described in Experiment I, except that between 9:00 a.m. and 3:00 p.m. subjects were required to use a designated, portable ashtray while they smoked. All cigarettes dispensed during this time were marked with a colored pen so that the subject's cigarette butts could be differentiated from those of other residents. At 3:00 p.m., the cigarette butts were collected and counted. Subjects received a point bonus from the point economy if the number of butts collected matched that dispensed by the machine, and received a point fine if any cigarette butts were missing. The collected cigarette butts were allowed to dry for at least 48 hr before being individually weighed.

Results

As shown in Table 2, the effect of ethanol on number of cigarettes smoked was similar to that observed in previous studies—an increase in cigarette smoking between 9:00 a.m. and 3:00 p.m.

In one and three sessions, respectively, SU and RUT failed to collect all the cigarette butts they smoked between 9:00 a.m. and 3:00 p.m. These sessions were excluded from further analysis. For SU, ethanol availability did not affect cigarette butt weight (209.1 ± 6.0 mg *versus* 212.6 ± 6.0 mg, mean ±S.E.M. for ethanol and vehicle conditions, respectively). For RUT, cigarette butt weight was less during ethanol sessions than during vehicle sessions (271.4 ± 5.7 mg *versus* 292.4 ± 3.7 mg, mean ±S.E.M. for ethanol and vehicle conditions, respectively).

An estimate of the total weight of the cigarettes burned was obtained by subtracting cigarette butt weight from the average weight of an unsmoked cigarette of the same brand. Figure 3 shows that for both subjects the

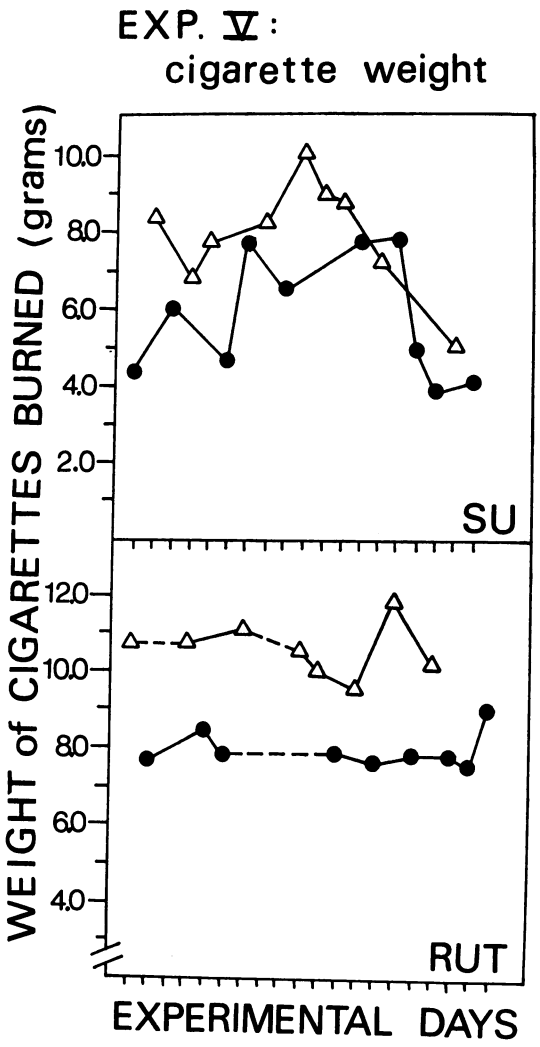

Fig. 3. The estimated weight of cigarettes burned between 9:00 a.m. and 3:00 p.m. daily in Experiment V involving two alcoholic subjects. Subjects ingested solutions containing either vehicle (filled circles) or 133.7 g ethanol (unfilled triangles) on different days. The estimate of the weight of cigarettes burned was obtained by subtracting total weight of all cigarette butts collected between 9:00 a.m. and 3:00 p.m. from the weight of an equivalent number of unsmoked cigarettes of the same brand. Dashed lines indicate missing data.

estimated weight of the cigarettes burned was greater for ethanol sessions than for vehicle sessions. RUT smoked an average (±S.E.M.) of 10.64 ± 0.25 g of cigarettes in ethanol sessions compared to 8.02 ± 0.16 g in vehicle sessions. Similar data for SU were 7.98 ± 0.49 g *versus* 5.85 ± 0.51 g. For each subject, the difference between ethanol and vehicle sessions was statistically significant using a two-tailed matched-pair t test ($p < 0.01$; consecutive ethanol sessions matched with consecutive vehicle sessions).

EXPERIMENT VI: CIGARETTE PUFFS—CONTROL FOR AMOUNT OF CIGARETTE SMOKED

Experiment V indicated that the increased smoking in ethanol sessions was not a consequence of discarding larger portions of cigarettes, since the total weight of cigarettes burned in ethanol sessions exceeded that on vehicle sessions. These results, however, do not necessarily indicate that the subjects actually consumed (*i.e.*, puffed) larger amounts of tobacco under ethanol conditions. If subjects took fewer puffs from each cigarette during ethanol sessions, then the actual amount of tobacco consumed may not have been different between ethanol and vehicle sessions. There are several plausible explanations for this effect. First, it is possible that under conditions of ethanol administration subjects simply held their cigarettes for longer periods of time without puffing, thus allowing the cigarette to burn without being smoked. A second possible explanation is that during ethanol sessions, subjects spent more time walking about the ward, and that this increased movement increased the rate at which the cigarettes burned, thus permitting fewer puffs per cigarette.[3]

Experiment VI evaluated these possibilities by systematically replicating previous experiments under conditions that permitted counting of puffs per cigarette and estimation of total cigarette puffs per session. It was not practical to count every puff of every cigarette; therefore puffs were counted for all cigarettes smoked during the second, fourth, and sixth hours of each experimental session. To minimize between-cigarette variability, and therefore increase the accuracy of the total estimated puffs, cigarettes were marked and subjects instructed to smoke until a predetermined portion of each cigarette had burned.

METHOD

Two alcoholic subjects participated. The procedure was similar to that described in Experiment I, with several modifications. Each

[3]A pilot experiment revealed that the burn time for the 5.5 cm length of a standard Camel cigarette (13.10 ± 0.37 min, mean ±S.E.M.; N = 8) was significantly decreased by walking at a moderate speed (11.51 ± 0.28 min, mean ±S.E.M.; N = 6).

cigarette placed in the cigarette dispenser was marked before the session with two circles that ringed the cigarette, 1.25 and 2.5 cm, respectively, from the inhalation end of the cigarette. After obtaining a cigarette from the dispenser, the subjects were required to smoke the entire cigarette while sitting in a designated chair located in the television area of the dayroom. Subjects were required to sit in the chair before lighting the cigarette, and remain there until the cigarette had burned past the first circle but not past the second circle. Before extinguishing the cigarette, subjects were required to walk to the nurses station and show the staff that the lighted cigarette butt had burned between the two circles. Subjects were not permitted to puff on the lighted cigarette when they were out of the chair, but were permitted to sit in the chair while not smoking.

During the daily session, a video camera and tape-deck (Sony, AV-3600) monitored the television area continuously. The subjects were informed that between 9:00 a.m. and 3:00 p.m. they would be videotaped whenever they sat in the television area; they were not told the nature or purpose of the experiment. After the sessions, a staff member viewed the second, fourth, and sixth hours of the session away from the ward area and counted the number of puffs that the subjects took on each cigarette during these hours. Two staff members participated in this scoring. Reliability was checked by having both staff members separately score the number of puffs taken on 15 cigarettes by each of the two subjects.

Results

Staff agreed on the number of puffs taken from each cigarette on 27 of the 30 cigarettes scored in the reliability check. On each of the remaining three cigarettes, the staff differed by only one puff.

As shown in Table 2, the results were similar to those from previous experiments—ethanol increased the total number of cigarettes smoked.

Ethanol availability did not affect the number of puffs per cigarette for MI (10.26 ± 0.41 *versus* 10.39 ± 0.35, mean ±S.E.M. for ethanol and vehicle conditions, respectively). However, for RUM the number of puffs per cigarette were greater in ethanol sessions than in vehicle sessions (12.95 ± 0.30 *versus* 11.57 ± 0.33, mean ±S.E.M. for ethanol and vehicle conditions, respectively).

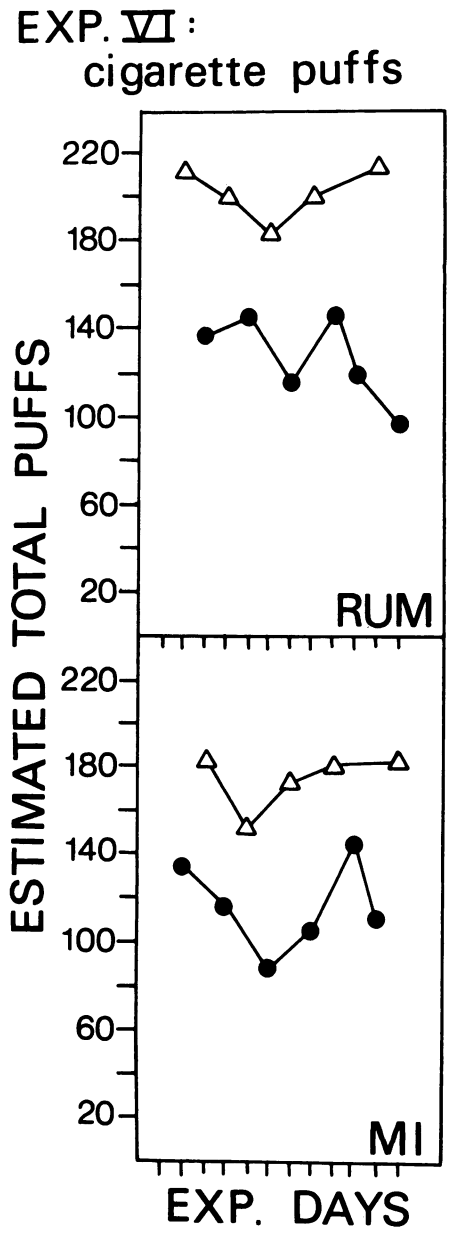

Fig. 4. The estimated total cigarette puffs between 9:00 a.m. and 3:00 p.m. daily in Experiment VI involving two alcoholic subjects. Subjects ingested solutions containing either vehicle (filled circles) or 133.7 g ethanol (unfilled triangles) on different days. The estimate of the total number of cigarette puffs taken per session was obtained by calculating the average number of puffs per cigarette from those scored during the second, fourth, and sixth hours, and multiplying this average by the total number of cigarettes smoked during the session.

An estimate of the total number of cigarette puffs taken per session was obtained by calculating the average number of puffs per cigarette from those scored during the second, fourth, and sixth hours, and multiplying this average by the total number of cigarettes smoked during the session. Figure 4 shows that the daily estimated number of cigarette puffs was consistently higher in ethanol sessions than vehicle sessions for both subjects. For RUM, the mean estimated number of puffs (±S.E.M.) was 201.7 ± 5.3 in ethanol sessions and 126.3 ± 8.1 in vehicle sessions. Similar data for MI were 173.5 ± 5.9 and 116.4 ± 8.2. For each subject, the difference between ethanol and vehicle sessions was statistically significant using a two-tailed matched-pair t test ($p < 0.01$; consecutive ethanol sessions matched with consecutive vehicle sessions).

EXPERIMENT VII: BLIND ADMINISTRATION OF MULTIPLE DOSES OF ETHANOL—CONTROL FOR INSTRUCTIONS

Experiment VI revealed that the increased smoking during ethanol sessions was not due to taking fewer cigarette puffs. Experiment VII was undertaken to determine whether the effect of ethanol on cigarette smoking was dose-dependent, and to evaluate another possible behavioral mechanism for the observed effect. The study sought to control for the possible confounding effect of instruction or knowledge of ethanol consumption. In previous experiments, each morning subjects were informed before their first drink whether they would be receiving ethanol or vehicle solutions. It is possible that these instructions alone may have influenced the frequency of cigarette smoking. Experiment VII controlled for this possibility by examining smoking under conditions in which subjects consumed either vehicle, low-dose ethanol, or moderate-dose ethanol solutions under uniform instructions. Control for the subjects' knowledge of the fact that they were consuming alcoholic beverages was accomplished by dispensing a discriminable dose of ethanol under both low- and moderate-dose conditions, and by verifying that subjects successfully discriminated the presence of ethanol under both dose conditions.

METHOD

Two alcoholic subjects participated. The procedure was similar to that described for Experiment I, except that subjects were not informed whether drinks contained ethanol or of the doses used in the experiment. On a given day, each of the 12 drinks (90 ml each) contained either water alone, a low dose of ethanol (2.79 g) with water, or the standard dose of ethanol (11.14 g) with water. The order of exposure to the three conditions was determined from a mixed sequence in which no more than two days in the same condition were permitted to occur successively. Finally, every day at 9:30 a.m. (after the first drink) and at 3:00 p.m. (after the last drink) the subject was asked, "Do you think that there was alcohol in your drinks today?"

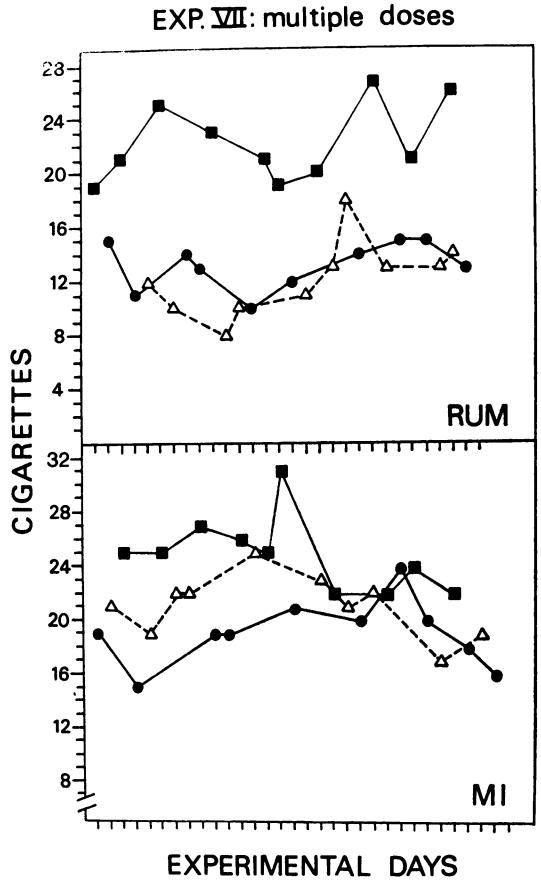

Fig. 5. The number of cigarettes smoked between 9:00 a.m. and 3:00 p.m. daily in Experiment VII involving two alcoholic subjects. Subjects ingested solutions containing either vehicle (filled circles), 33.4 g ethanol (unfilled triangles), or 133.7 g ethanol (filled squares) on different days.

Results

As shown in Table 2 and Figure 5, for both subjects ethanol produced dose-dependent increases in cigarette smoking (*i.e.*, the standard dose of ethanol produced more smoking than the low dose). In one subject (MI), there were statistically significant differences in smoking between vehicle *versus* low-dose conditions and low-dose *versus* standard-dose conditions ($p < 0.01$ one-tailed matched-pair t test; consecutive sessions in one condition matched with consecutive sessions in the other condition). In the other subject (RUM), there was no difference between the vehicle and low-dose conditions; however, the standard dose produced statistically significant increases in cigarette smoking over both of these conditions ($p < 0.01$ one-tailed matched-pair t test; consecutive sessions in one condition matched with consecutive sessions in the other condition). Overall, the study shows that the effect of ethanol on cigarette smoking is not an artifact of instructions and suggests a dose-dependent relationship.

The present study also provides some information about subjects' knowledge of conditions. Both subjects consistently correctly (97.5%) identified the presence or absence of ethanol in their daily drinks at 9:30 a.m. and 3:00 p.m. Since the standard dose resulted in more smoking than the low dose in both subjects, this indicates that the effect of ethanol on cigarette smoking is not an artifact of subjects' knowledge of the fact they were consuming ethanol. It should be noted, however, that since the study did not assess whether the subjects could discriminate between the low and standard doses, there is no information about whether subjects' knowledge of dose contributed to the increased smoking observed in the standard-dose condition.

GENERAL DISCUSSION

The present set of studies indicates that ethanol consumption is a potent determinant of cigarette smoking by alcoholics in a residential laboratory setting. When alcoholics consumed solutions containing ethanol, their cigarette smoking during the 6-hr experimental sessions increased from 26 to 117% of vehicle control levels. The effect was quite robust: it was observed in each of five subjects and replicated a total of 15 times under various experimental conditions. Control studies have ruled out a number of potential behavioral mechanisms for this observed effect. Specifically, the effect was not dependent on: (1) cigarette smoking being adjunctively maintained by a distinctive pattern of ethanol ingestion (Experiment II); (2) cigarette smoking being adjunctively maintained by patterns of social interaction (Experiment III); (3) specific characteristics of the order of scheduling experimental conditions (Experiment IV); (4) alterations in the portions smoked of individual cigarettes (Experiment V); (5) alterations in the number of puffs per cigarette (Experiment VI); (6) instructions to subjects or subjects' knowledge of the fact of ethanol consumption (Experiment VII). Finally, the effect was not limited to the 6-hr experimental sessions alone, since total daily smoking was higher on ethanol days than vehicle days (Experiment IV).

The fact that increases in smoking during ethanol sessions are not adjunctively maintained by patterns of drinking and socializing does not eliminate the possibility that these adjunctive mechanisms might have played historical roles in the etiology of the present effect. For example, Meisch has shown that adjunctive behavior phenomena may contribute to establishing ethanol as a reinforcer in rats, although they are not necessary for the maintenance of that effect.

Mello and Mendelson (1971) also examined cigarette smoking in hospitalized alcoholic subjects given daily access to 32 ounces of 50% ethanol. Their data suggest that ethanol's effects on cigarette smoking are dependent on the response requirements for obtaining cigarettes. In an experiment in which 1000 button-press responses were required for each cigarette, responding for cigarettes was markedly reduced when ethanol was available. However, in a second experiment in which subjects were given 20 tokens daily, which were exchangeable for cigarettes, cigarette smoking occurred at a high level throughout the ethanol-availability phase. Limitations on the number of available cigarettes (*i.e.*, a ceiling effect) may have prevented the appearance of ethanol-induced increases in smoking in this study. Anecdotal evidence cited by the authors lends further support to this interpretation. They indicate that most of the subjects expected to

smoke more during ethanol periods than control periods. They also emphasize that in the first experiment, the subjects' consistent refusal to work for cigarettes during unrestricted access to ethanol did not reflect a decreased interest in cigarettes, since subjects exerted considerable effort trying to get cigarettes from the staff and "complained vociferously" about their cigarette deprivation.

Several behavioral mechanisms could plausibly explain the ethanol-induced increases in cigarette smoking. For instance, although the present studies showed that subjects took more total cigarette puffs under ethanol conditions, the studies did not control for the magnitude or duration of the inhalation. It would be interesting to compare total nicotine and nicotine metabolites in urine under ethanol and vehicle conditions. A second possible explanation is that ethanol may act as a relatively nonspecific behavioral stimulant, increasing the rates of many behaviors under the conditions studied. For instance, it has been demonstrated that under conditions of ethanol administration similar to the present study, ethanol increases the rates of social interactions in alcoholics (Griffiths *et al.*, 1974*a*). A third mechanism is that ethanol might selectively interact with the reinforcing properties of cigarettes. For instance, the observed increase in cigarette smoking during ethanol sessions may be comparable to infrahuman research results that demonstrate that acute administration of a pharmacological antagonist increases rates of drug self-administration (Goldberg *et al.*, 1971; Thompson and Schuster, 1964). A fourth possible behavioral mechanism follows from the suggestions of several investigators that cigarette smoking potentiates the objective and subjective effects of ethanol (Danger, 1938; Elbel, 1938; Linckint, 1956). According to this interpretation, the ethanol-induced increase in cigarette smoking may reflect the ability of cigarette smoking to enhance the effect of ethanol.

Finally, it is instructive to note that a number of investigators using data from interviews and questionnaires have previously observed that people who are heavy alcohol drinkers also tend to smoke heavily (Brown and Campbell, 1961; Cartwright, 1959; Dreher and Fraser, 1967; Heath, 1958; Maletzky and Klotter, 1974; McArthur *et al.*, 1958; Walton, 1972). Attempts to explain this relationship have resulted in hypotheses about underlying addictive personalities, oral drives, anxiety states, and general neuroticism (Dreher and Fraser, 1967; Maletzky and Klotter, 1974; McArthur *et al.*, 1958). There are, of course, alternative explanations involving more direct causal relationships between ethanol ingestion and cigarette smoking. A rigorous experimental analysis involving the systematic manipulation of environmental variables provides the appropriate mechanism for evaluating the determinants of the observed correlations. The present study utilized this methodology to demonstrate that a behavioral-pharmacological variable—ethanol consumption—is a potent determinant of cigarette smoking, and to demonstrate that the effect is not dependent on several behavioral mechanisms that were considered *a priori* to constitute probable mechanisms of action. Using within-subject experimental techniques, the present studies demonstrated and systematically replicated the finding that ingestion of ethanol results in stable increases in cigarette smoking. The results suggest a reasonably direct interaction between ingestion of ethanol and cigarette smoking. Appealing to hypothetical constructs and remote levels of causation (*e.g.*, an oral or addictive personality) does not appear to be a particularly fruitful approach to the analysis of the determinants of drug-behavior interactions. Ultimately, a rigorous experimental analysis of functional relationships is indicated.

REFERENCES

Brown, K. E. and Campbell, A. H. Tobacco, alcohol and tuberculosis. *British Journal of Diseases of the Chest*, 1961, **55**, 150-158.

Cartwright, A., Martin, F. M., and Thompson, J. G. Distribution and development of smoking habits. *Lancet*, 1959, **2**, 725-727.

Danger, W. *Experimentelle studien zur frage der beziehungen zwischen blutalkoholgehalt und alkoholwirkung.* (Experimental studies on the question of the relations between the blood alcohol level and alcohol effect.) Dissertation, Medical Faculty of the University of Göttingen, Germany, 1938. (Interaction of Alcohol and Other Drugs, Addiction Research Foundation, Toronto, Ontario, Canada, 1972, No. 293.)

Diethelm, O. and Barr, R. M. Psychotherapeutic interviews and alcohol intoxication. *Quarterly Journal of Studies on Alcohol*, 1962, **23**, 243-251.

Doctor, R. F. and Bernal, M. E. Immediate and prolonged psychophysiological effects of sustained alcohol intake in alcoholics. *Quarterly Journal of Studies on Alcohol*, 1964, **25**, 438-450.

Dreher, K. and Fraser, J. Smoking habits of alcoholic outpatients. *International Journal of the Addictions,* 1967, **2,** 259-268.

Elbel, H. Trunkenheitsbegutachtung durch blutalkoholbestimmung: Derzeitiger stand unseres wissens. Diagnosis of intoxication by blood alcohol determination: Current state of our knowledge). *Medizinische Welt* (Stuttgart), 1938, **12,** 1667-1671. (Interaction of Alcohol and Other Drugs. Addiction Research Foundation, Toronto, Ontario, Canada. 1972. No. 368.)

Falk, J. L. The nature and determinants of adjunctive behavior. *Physiology and Behavior,* 1971, **6,** 577-588.

Goldberg, S. R., Woods, J. H., and Schuster, C. R. Nalorphine-induced changes in morphine self-administration in rhesus monkeys. *Journal of Pharmacology and Experimental Therapeutics,* 1971, **176,** 464-571.

Griffiths, R. R., Bigelow, G., and Liebson, I. Assessment of effects of ethanol self-administration on social interactions in alcoholics. *Psychopharmacologia,* 1974, **38,** 105-110. (*a*)

Griffiths, R. R., Bigelow, G., and Liebson, I. Suppression of ethanol self-administration in alcoholics by contingent time-out from social interactions. *Behaviour Research and Therapy,* 1974, **12,** 327-334. (*b*)

Griffiths, R. R., Bigelow, G., and Liebson, I. Effect of ethanol self-administration on choice behavior: Money vs. socializing. *Pharmacology, Biochemistry and Behavior,* 1975, **3,** 443-446.

Heath, C. Differences between smokers and nonsmokers. *American Medical Association Archives of Internal Medicine,* 1958, **101,** 377-388.

Linckint, F. Ueber die auslösung abnormer alkoholreaktionen druch medikamente (zugleich eine warnung für verkehrsteilnehmer). (On the precipitation of abnormal alcohol reactions by drugs, and a warning to participants in traffic). *Suchtgefahren* (Hamburg), 1956, **1,** 1-9. (Interaction of Alcohol and Other Drugs, Addiction Research Foundation, Toronto, Ontario, Canada, 1972. No. 783.)

Maletzky, B. M. and Klotter, J. Smoking and alcoholism. *American Journal of Psychiatry,* 1974, **131,** 445-447.

McArthur, C., Waldron, E., and Dickinson, J. The psychology of smoking. *Journal of Abnormal and Social Psychology,* 1958, **56,** 267-275.

McNamee, H. B., Mello, N. K., and Mendelson, J. H. Experimental analysis of drinking patterns of alcoholics: Concurrent psychiatric observations. *American Journal of Psychiatry,* 1968, **124,** 1063-1069.

Mello, N. and Mendelson, J. Drinking patterns during work contingent and non-contingent alcohol acquisition. In N. Mello and J. Mendelson (Eds.), *Recent advances in studies of alcoholism.* Washington, D.C.: U.S. Government Printing Office, 1971. Pp. 647-686.

Meisch, R. A. The function of schedule-induced polydipsia in establishing ethanol as a positive reinforcer. In R. T. Kelleher, S. R. Goldberg, and N. Krasnegor (Eds.), Control of drug-taking behavior by schedules of reinforcement, *Pharmacological Reviews, (in press).*

Thompson, T. and Schuster, C. R. Morphine self-administration food-reinforced and avoidance behaviors in rhesus monkeys. *Psychopharmacologia,* 1964, **5,** 87-94.

Walton, R. G. Smoking and alcoholism: A brief report. *American Journal of Psychiatry,* 1972, **128,** 1455-1459.

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