Pharmacology Biochemistry and Behavior, Vol. 2, pp. 293–296. ANKHO International Inc., 1974. Printed in the U.S.A.

Alcohol-Induced State-Dependent Learning in Non-Alcoholics

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(Received 25 October 1973)

HINRICHSEN, J. J., M. KATAHN AND R. W. LEVENSON. *Alcohol-induced state-dependent learning in non-alcoholics.* PHARMAC. BIOCHEM. BEHAV. 2(3) 293–296, 1974. – The generality of the dissociative effects of a high dosage (1.40 g/kg.) of rapidly ingested ethyl alcohol in non-alcoholic human subjects was examined. Verbal memory was found to be more susceptible to dissociation than either motor-skills learning or autonomic (heart-rate) control training. The dissociation of the verbal material appeared to be asymmetrical in that subjects who originally learned the material while intoxicated but were tested 48 hr later while sober showed a greater memory decrement than a group which learned the material originally while sober but was tested while intoxicated.

Ethyl alcohol Dissociation Verbal Motor Autonomic Non-alcoholics

THE BASIC notion underlying the concept of state-dependent learning (SDL) is that if an organism learns a response while under the influence of certain centrally-acting drugs e.g., pentobarbital or ethyl alcohol, the newly acquired response will transfer or generalize to a dissimilar i.e., non-drugged, physiological state less well than it would generalize to a similar physiological state and vice-versa. Complete failure of transfer of learning from one state to another is referred to as "dissociation of learning" [10], "habit dissociation" [21] or just "dissociation" [12].

While most studies of SDL have used either rats or mice as subjects, several recent experiments have demonstrated that dissociation also occurs in man. Among the drugs found to produce dissociation in humans are amphetamines and amobarbital [4,5], and ethyl alcohol [11, 17, 20, 21, 22, 23]. Most studies using alcohol have employed verbal learning tasks [11, 20, 21, 22, 23], although some attention has also been given to avoidance learning [11], and to various physiological components of the orienting response [17].

The present study was undertaken in order to further explore the generality of alcohol-induced SDL in non-alcoholics. This objective was realized through the use of 3 types of learning tasks not previously employed. In addition, this study employed the highest dosage of alcohol yet reported in the literature. The purpose of using a very high alcohol dose was to maximize the probability that dissociation would be observed if, in fact, the types of learning in which subjects engaged were subject to dissociation.

METHOD

Subjects

Forty volunteer males having a mean age of 19.7 years (SD = .90) and a modal class standing of sophomore were recruited from the population of Vanderbilt University undergraduates. None of the subjects reported any history of problems with alcoholism, diabetes, or epilepsy. The subjects were informed that they might or might not receive alcohol during one or more of the 2 experimental sessions depending upon their random assignment to a group.

Learning Tasks and Apparatus

The present study employed 3 tasks which can be roughly differentiated in terms of the relative importance of verbal skill, nonverbal motor co-ordination and autonomic sensitivity involved in the acquisition and retention of the skill involved.

Task 1. Verbal learning. As a measure of verbal learning this study employed ten number-word (one-syllable common nouns) pairs. The reason for employing this task, as opposed to a serial learning task which has been used in some prior research, is that the paired-associate learning process is often considered to be more representative of the things people do when they learn verbal material under ordinary conditions e.g., foreign language learning, [8]. From this theoretical point of view, the paired-associate tasks assumes special importance in that it is the model example of the classical associative process i.e., the establishment of S-R bonds.

Task 2. Motor skills learning. The second task employed in the present study had as its most distinguishing feature a greater emphasis on the motor component of learning than Task 1. Task 2 was a mirror-drawing (MD) task (see [19] for a complete description of this task), and was included in order to determine whether a skill characterized by the additional involvement of a significant distal motor compo-

nent would be as susceptible to dissociation as, for example, verbal learning.

Mimeographed 6-pointed starts which were 20.32 cm from point-opposites were used as stimuli. When viewed in a mirror the points were seen to be numbered from 1 to 6. The distance between the inside and outside of the lines was 0.476 cm except at the points of the star where the lines were 1.42 cm apart.

Task 3. Heart-rate control training. This was a psychophysiological task which at the present time cannot be easily characterized in terms of the roles of cognition (central nervous system), the autonomic nervous system, and motor-components (e.g., muscle tension). Thus, this task was included with the others in order to provide further evidence with regard to the generality of dissociation, in spite of the fact that the processes involved in the acquisition of heart-rate control are not yet well understood.

Heart-rate (HR) data were recorded bipolarly using Beckman Biopotential Skin Electrodes attached to the subject's rib cage. The electrocardiograph signal was amplified by a Grass Model 7 polygraph and the amplified signal was connected to an analog input of a Hewlett Packard 2114A digital computer. The computer was used on-line to perform several operations: to determine HR; to provide HR feedback to the subject; and to record the number of heart rate interbeat intervals (IBI's) which met criterion.

Feedback was presented via a digital readout device placed horizontally on a table in front of the subject. The illuminated digit was updated at the end of each heart beat interval. HR feedback was mean contingent, i.e., based on the mean IBI of a 50-beat baseline period which preceeded each control trial. Thus, subjects were always trying to control HR with reference to recently determined baselines. Mean baseline IBI plus or minus 20 msec intervals were established for the digits below and above 4 such that HR increases (IBI decreases) from the baseline level caused higher digits to be illuminated and HR decreases (IBI increases) caused lower digits to be illuminated. The range of possible digits was from 1 to 7 which represented an IBI range of 140 msec.

This feedback system provided subjects with a straightforward task. On HR increase trials subjects were to keep a number higher than 4 illuminated and on decrease trials the object was to keep numbers lower than 4 illuminated.

Procedure

Forty subjects were assigned randomly to 1 of 4 groups of 10 subjects each. The subjects were asked not to eat anything for two hours prior to reporting to the laboratory. They were also asked not to drink any alcoholic beverages for 24 hr prior to reporting. One group (A-A) had alcohol during both experimental sessions. A second group (A-N) had alcohol in the first session but not in the second. The third group (N-A) did not have alcohol in the first session but did have it in the second session. The fourth group (N-N) did not have alcohol in either session. No subject knew in advance of either session whether or not he was to have alcohol in that session.

The subjects who received alcohol were given a dosage of 1.40 g of alcohol per kg of body weight diluted 2:1 in orange juice. Absolute alcohol (Gold Shield 200 proof) was used in order to allow for precise dosage control. The subjects were allowed one hr to ingest the alcohol which was administered in equal portions every 10 min.

Five to 10 min following the completion of alcohol intake (or 5 to 10 min after their arrival for subjects not having alcohol), subjects began work on one of the 3 tasks. The order of task completion was randomized with the exception that all subjects completed the HR task either first or last in a session, never second. This was necessary because the HR task took approximately the same amount of time as the other two tasks combined.

The instructions for the paired-associated, MD and HR control tasks were tape recorded and played for each subject immediately prior to the respective tasks.

The procedure for a typical subject in Session I ran as follows. After having finished consuming his alcohol he was seated at a table and the paired-associates task was completed. Following a few minutes rest, he was seated at a different table above which was suspended a large mirror into which he was to look while carrying out the MD task. A cloth screen prevented the subject from directly observing his hands. Five trials were given on this task. After completing the paired-associate and MD tasks (which took 35 to 40 min), the subject was given a Breathalyzer test to determine the percent alcohol in his blood. Doningan [9] discusses this procedure, its reliability, and validity in detail.

Finally, the subject was escorted to another room and seated in a comfortable reclining chair. The electrodes were then attached to his rib cage and a 5 min adaptation period was begun. HR baselines were determined on the basis of 50 heart-beat periods while control trials were 75 beats long. The order of increase and decrease trials was randomly determined and included 9 increase and 9 decrease trials for a total of 18 control trials in each session. A new baseline was found between each trial.

Forty-eight hr after their first session subjects returned to the laboratory and repeated all of the tasks in the same order that they had completed them in the first session. One difference which occurred in Session II was on the paired-associate task. On this task the first trial in Session II was a test trial and not a training trial as in Session I.

RESULTS

Forty minutes after ingestion, the 4 groups that received alcohol did not differ significantly in blood-alcohol level. Three of the means were 0.15% and one was 0.16%. With these blood alcohol levels subjects were visibly intoxicated in that there was some slurring of speech, gross motor impairment, and verbal reports of feeling quite drunk.

Scores for the MD task were obtained by both the experimenter and an independent rater by counting the number of times a subject either touched or went outside of the lines of the star and adding to this count the time (in seconds) taken to complete each trial [19]. It is important to note that, in general, the number of seconds and number of errors were of the same order of magnitude per trial across subjects. The scores for the 5 trials in each session were then summed to yield an over-all score for each session. Product-moment correlations between the error scores indicated that the interrater reliability of this scoring method was 0.93 for Session I and 0.95 for Session II. Having established that the MD scores were reliable, the scores obtained by the independent rater were used in subsequent analyses.

MD scores were subjected to a square-root transformation in order to bring them into conformity with the homo-

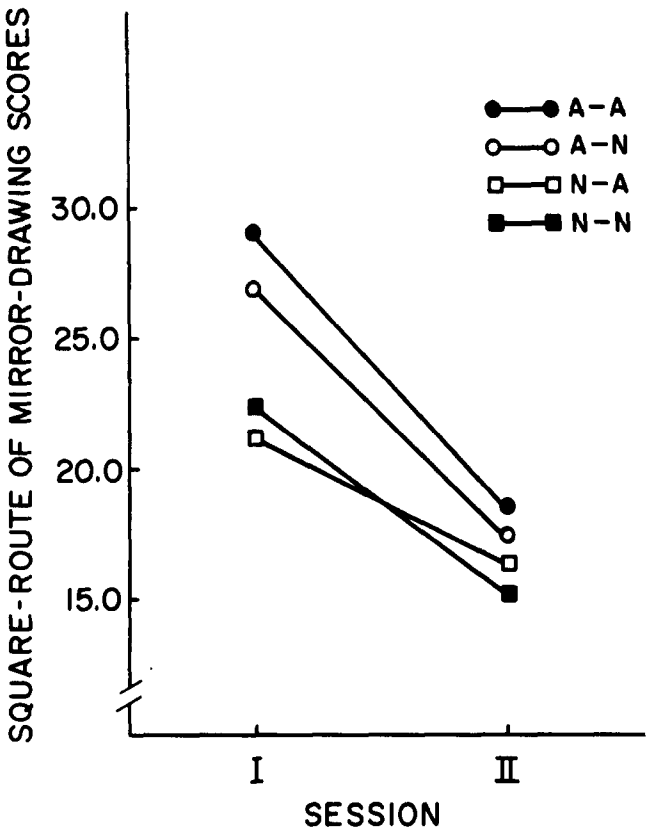

FIG. 1. Mean MD scores as a function of alcohol condition and experimental session.

geneity assumption of the analysis of variance method. These data were subsequently analyzed in a 2 × 2 × 2 (Alcohol Condition at Original Learning × Alcohol Condition at Relearning × Sessions) ANOVA. The 8 means obtained from this analysis are presented in Fig. 1. Groups A-N and A-A performed significantly more poorly, $F(1,36) = 30.49$, $p<0.001$, than groups N-A and N-N during original learning (Session I), but not during relearning (Session II). A significant second-order interaction which would have indicated state-dependence did not obtain, $F(1,36) = 1.88$, $p>0.10$.

Since, unlike MD performance, all subjects were taken to the same learning criterion on the paired-associated task, errors to criterion in Session II for this task were analyzed in a 2 × 2 (Alcohol Condition at Original Learning × Alcohol Condition at Relearning) ANOVA. Mean Session II errors for the groups were: A-A = 3.3; A-N = 6.5; N-A = 8.1; N-N = 6.3. The interaction effect was nearly significant, $F(1,36) = 3.40$, $p = 0.07$, with groups A-N and N-A tending to make more errors during relearning than groups A-A and N-N. A comparison between groups N-N and N-A indicated a non-significant difference ($t = 1.35$; $df = 36$; $0.10<p<0.05$; one-tailed) while a comparison between groups A-A and A-N did yield a reliable difference ($t = 2.40$; $df = 36$; $p<0.025$; one-tailed).

An ANOVA was carried out on the IBI data in order to determine whether subjects were able to significantly change their HRs. This analysis indicated that while subjects were able to significantly, $F(1,36) = 126.40$, $p<0.001$, increase and decrease their HRs, the magnitude of the changes was not dependent upon the number of training trials which subjects had experienced.

The consistency with which subjects were able to produce HR changes was evaluated with an ANOVA on the number of heart beats in the correct direction (i.e., at least 20 msec faster or slower than the baseline mean). This analysis revealed that the consistent production of HR changes was not a function of training.

DISCUSSION

With respect to verbal learning, the present data seem generally consistent with previous research in this area. Of particular interest, however, is the finding that even with the high dosage of alcohol used in the present study, the degree of observed dissociation was greater for group A-N than for group N-A. This phenomenon, known as asymmetrical dissociation, has been observed previously with both animals [1, 3, 6, 7, 15] and man 11,17]. Overton [16] pointed out that the significance of asymmetrical dissociation is not yet clear. He speculated that a summation of dissociative and other drug effects may be responsible for apparent asymmetrical dissociation but he cautioned that the parameters involved have not been carefully investigated. Further research is needed to determine whether asymmetrical dissociation is a real phenomenon or an artifact resulting from a combination of drug effects, task demands, or multifactorial interaction effects.

The data from the MD task showed no indication of SDL. This finding, along with the relatively weak dissociation observed in the paired-associated data, provide empirical support for the suggestion [11,22] that learning tasks on which there occurs considerable overlearning are less susceptible to drug-induced dissociation. This result further reaffirms the contention that the choice of appropriate learning tasks is essential to the furtherance of knowledge about SDL. The identification of characteristics of tasks which are more or less susceptible to dissociation should considerably enhance the possibility of testing alternative theoretical accounts [14, 16, 18] of SDL.

The failure to demonstrate a learning curve (defined as an increase in the number of beats in the correct direction as a function of the number of training trials) for the heart rate control tasks makes an interpretation of the results in terms of a dissociation hypothesis untenable. This finding, while disappointing, is not particularly surprising in view of the lack of conclusive evidence that human subjects actually learn to control their HRs. Much of the evidence to date seems to indicate that subjects adopt a particular strategy e.g., muscle tension, respiratory changes, or mental imagery, to alter HR and then use this strategy with greater or lesser success independent of the number of training trials they have received.

In conclusion, two points concerning the relevance of the present study to future research on SDL need to be made. The first concerns the hypothesized continuous nature of dissociation of learning is at least a partial function of the dosage of the particular drug being used. In the present study subjects were given a very high dosage of alcohol in a very short time yet the dissociative effects of the alcohol on verbal learning were not pronounced. It therefore seems essential that future parametric studies of the continuity issue be carried out using learning tasks, performance criteria, and experimental designs which are

extremely sensitive to the dissociative properites of the drug of interest.

The second point to be made concerns the status of currently existing theoretical explanations of SDL and the future of research in this area. Although several theoretical models of SDL have been offered [14, 16, 18] the evidence related to these models has been equivocal at best. The basic processes underlying SDL are not well understood, nor is it unequivocally clear which drugs, dosages, tasks, and subject populations interact to produce dissociation. Future research should proceed along at least two general paths. First, more research should be devoted to the further examination of potential basic determinants of dissociation. With respect to alcohol, Beard [2] has reported some preliminary evidence which indicates that alcohol alters both the intra- and extra-cellular electrolytic balances in the brain, thus leading to altered firing potentials in the affected neurons. This type of evidence could easily bear upon the exploration of dissociation at the physiological level. Second, research should continue in the direction of a further elaboration of the kinds of agents, dosages of these agents, tasks, and subject populations which interact to produce dissociation. Research along these lines should yield more information about both the effects of various chemical agents on learning and on the basic mechanisms underlying the phenomenon of dissociation.

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