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BRIEF COMMUNICATION

Response Suppression on a Mixed Schedule of Reinforcement During Alcohol Withdrawal[1]

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DENOBLE, V. J. AND H. BEGLEITER. *Response suppression on a mixed schedule of reinforcement during alcohol withdrawal in rats.* PHARMAC. BIOCHEM. BEHAV. 5(2) 227–229, 1976. – Two groups of rats were maintained on a mixed fixed-ratio, fixed-interval schedule of food reinforcement until performance was stable. The animals were intubated daily with ascending doses of alcohol or water 30 min before each session, starting with 4.0 g/kg and increasing to the final dose of 8.0 g/kg. The results show that withdrawal from alcohol suppresses responding in all components of a mixed schedule and this suppression lasts approximately 14 hours. These results support previous reports which suggest that the duration of the behavioral aberrations produced by alcohol withdrawal are most severe 6 to 14 hours post-withdrawal.

Alcohol Withdrawal Fixed-ratio Fixed-interval

RECENTLY, there have been a number of investigations concerning the role of latent neural hyperexcitability in the genesis of the withdrawal syndrome, specifically, the time course of central nervous system disturbances [3]. The recovery cycle of somatosensory evoked potentials has been used to study changes in brain excitability in human alcoholics during intoxication and withdrawal [2]. More recently, investigators have reported that evoked brain potential changes caused by alcohol withdrawal last for a period of time past the 10 hours previously reported [1, 8, 10]. A recent investigation [9] of the course of central nervous system excitability following alcohol withdrawal indicated that maximum brain hyperexcitability was observed at the visual cortex 7 to 8 hours after alcohol withdrawal. This time course of central nervous system changes closely approximates an earlier result [8] which has shown that the behavioral withdrawal symptoms were most severe 6 to 10 hours postwithdrawal. While several methods have been proposed to observe the behavioral withdrawal syndrome in rodents [4, 7, 10], a need for a more quantitative method still exists. In these studies [6, 7, 8, 10], the overt behavioral signs of withdrawal did not persist past a 10 to 12 hour period, whereas Begleiter and Coltrera [1] have demonstrated that the central nervous system disturbances persist for as long as a 24 hr period.

The purpose of the present study was to access the effects of alcohol abstinence on schedule controlled behavior. Changes in performance under fixed ratio and fixed interval schedules are of particular interest because each produces patterns of responding which are highly reproduceable and should serve as a useful baseline for evaluating labatory therapeutics.

METHOD

Animals

The animals were 14 Long Evans hooded rats, 90 120 days old at the beginning of the experiment. The animals were housed individually and daily weights were recorded for a 2 week period, after which they were gradually reduced to 80 per cent of their free-feeding weights as calculated from the last 5 days of the 2 week period.

Apparatus

Two standard Lehigh Valley rat chambers housed in Lehigh Valley ventilated enclosures were equipped with a response lever, stimulus light, and a reinforcement dispenser. Schedules and data collecting were accomplished by electromechanical and solid state equipment.

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Procedure

Each animal was shaped to barpress for a 45 mg Noyes pellet and allowed to earn 100 reinforcements on a continuous reinforcement schedule for 2 consecutive days. Following this, animals received reinforcements according to a mixed fixed-ratio (FR), fixed-interval (FI) schedule with a time out (TO) following reinforcements in the FI component. During the time out, all lights were extinguished in the chamber and responding had no scheduled consequence.

The schedule contingencies were gradually increased until final schedule values were FR 30, FI 180 sec, TO 90 sec. Daily sessions lasted until 18 reinforcements were obtained and all animals received 45 days of training before baseline data was collected. When the response rates for each component varied less than 20 per cent for 5 consecutive days, daily intubations of ethanol or water were administered. Intubations of ethanol or water (30% w/v solution) were as follows: 4 g/kg for the first 3 days, 5 g/kg for the next 3 days, 6 g/kg for the next 3 days, 7 g/kg for the following 2 days, and 8 g/kg for the final day before total removal of ethanol. Each animal was intubated 30 min before the daily behavioral testing. After 12 days of intubation, alcohol was withdrawn and behavioral testing occurred beginning 6 hr after the last intubation. All animals were run until 18 reinforcements were obtained or until 40 min had elapsed, and were then removed and placed in a holding cage for 20 min. This behavioral testing procedure was repeated every hour until response rates in all components returned to baseline levels. To determine whether the behavioral disruption persisted, animals were tested 24 hr after the last intubation. Four of the animals died during the intubation phase of the experiment, leaving 7 animals in the alcohol group and 3 in the water group.

RESULTS

The 2 graphs in Fig. 1 present the mean response rates for animals in the control group and experimental group. As can be seen, the combined response rates for the fixed interval and the fixed ratio schedules vary less than 20 per cent during the baseline sessions. While there were subject differences in the response rates, each individual animal's baseline response rate varied less than 20 percent from day to day. The baseline data is representative of the last 5 days during which alcohol was intubated. The initial intubations produced a suppression of responding which returned to baseline levels by the sixth intubation. The figure shows that the animals in Group 1 (water intubation) did not exhibit any behavioral disturbances 6 hr after the last water intubation, and when tested every hour for 14 hr from the last water intubation, they did not display any change in responding. When tested 24 hr after the last water intubation, these subjects did not demonstrate any behavioral changes, suggesting that neither the intubation procedure nor the water intubation had any effects on behavior 6 to 14 hr or 24 hr following the cessation of water administration.

The data for Group 2 (ethanol intubation) show that all animals reached a stable level of performance during baseline sessions; however, 6 hr after the last alcohol intubation, the response rate of all animals was largely suppressed. This response suppression gradually decreased and response rates during the fixed interval and fixed ratio components returned to baseline levels between the 11th and 13th hr of testing, whereas the response rates during the time out component returned to prewithdrawal levels between 7 to 8 hr of testing. The data collected 24 hr after the last ethanol intubation show that all components of the mixed schedule are at baseline levels indicating that the

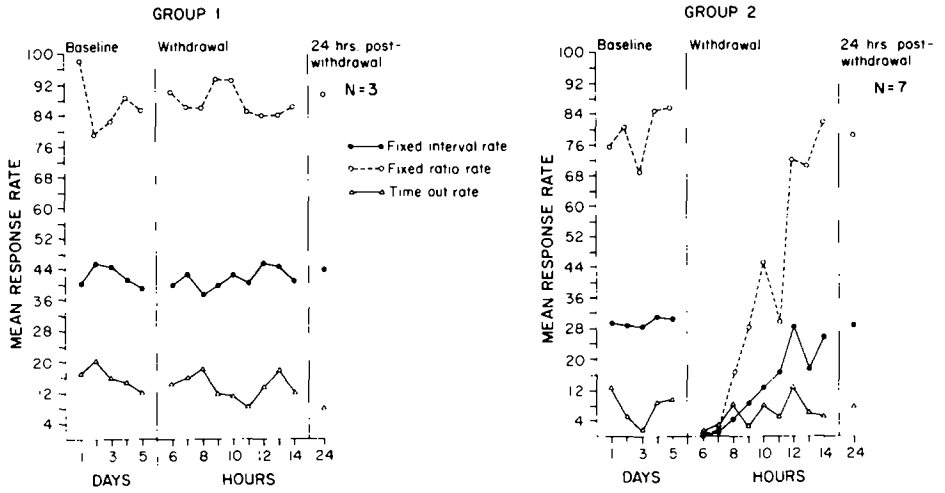

FIG. 1. Responses per min averaged across animals intubated with water (Group 1) and alcohol (Group 2). Each graph contains the data from the 5 days prior to removal of alcohol and the hour data starting with 6 hr postwithdrawal and ending at the 14th hr postwithdrawal. Also included is the data obtained 24 hr after the last intubation.

disrupting effects of alcohol withdrawal observed on a mixed schedule of reinforcement do not last past a 14-hr period. Qbservation of the animals during the withdrawal phase showed that all animals displayed tremors occurring 6–10 hr following the last intubation.

DISCUSSION

The results indicate that withdrawal from ethanol subsequent to chronic intake results in a disruption of the schedule controlled behavior of rats. This disruption is manifested by a suppression of responding in all components of a mixed schedule of food reinforcement for as long as 14 hr following alcohol removal. This suppression cannot be accounted for by an increased caloric intake which occurs during alcohol ingestion because the baseline data was collected during days when ethanol was also intubated and behavioral changes due to the increased caloric value would have been observed during baseline sessions.

The time course of the behavioral disruption obtained in this study, namely 6 to 14 hr after the last alcohol intake, coincides with reports of central nervous system hyperexcitability following alcohol withdrawal [8, 9, 10]. These studies [8,10] found that electroencephalographic and evoked potential changes [9] were most severe from 6 to 10 hr post-withdrawal. These findings, combined with those of the present investigation, suggest that the maximum central nervous system disturbance and the behavioral aberrations that results from alcohol withdrawal occur within the same time interval. Begleiter and Coltrera [1] have reported that abberations of the visual evoked response recorded from the visual cortex caused by alcohol withdrawal last much longer than the 10-hr period previously reported. However, it has been suggested by Hunter *et al.* [8] that the cortex does not play a primary role in the genesis of the behavioral symptomatology observed during alcohol withdrawal. In the present study the behavior of all animals was at prewithdrawal levels 24 hr postwithdrawal, which supports the hypothesis that the cortex may not facilitate the behavioral abnormalities which accompany the onset of withdrawal, but may be of greater importance in relation to the readdicting phenomena.

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