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BRIEF COMMUNICATION

Effect of Chlordiazepoxide on the Partial Reinforcement Extinction Effect

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WILLNER, P. J. AND R. CROWE. *Effect of chlordiazepoxide on the partial reinforcement extinction effect.* PHARMAC. BIOCHEM. BEHAV. 7(5) 479–482, 1977. – Rats were trained to run in a straight alley under conditions of partial or continuous reinforcement. Extinction was slower after partial reinforcement. Chlordiazepoxide, administered during acquisition only, had no effect on acquisition but abolished the partial reinforcement extinction effect. The results support the hypothesis that chlordiazepoxide acts by attenuating the effects of aversive stimuli.

Chlordiazepoxide Partial reinforcement Extinction Frustrative non-reward

RESPONSES acquired under conditions of partial reinforcement are more resistant to extinction than responses acquired under continuous reinforcement [19,27]. The most satisfactory account of this paradox is given by Amsel's theory of frustration [1,2]: during partial reinforcement, approach responses are conditioned to stimuli signalling non-reward; the elicitation of these responses during extinction gives rise to the partial reinforcement extinction effect (PREE). Non-reward is aversive; hence, stimuli signalling non-reward are drive inducing. This explains the partial reinforcement acquisition effect (PRAE), which is that partially reinforced animals run faster during acquisition than continually reinforced animals. This interpretation of the partial reinforcement effects is supported by the finding that the PRAE and the PREE are blocked by barbiturates administered during acquisition [11,16], since these drugs have been shown to attenuate other more overt manifestations of frustrative non-reward [3, 11, 26]. Barbiturates also attenuate responses to punishment [9,25]. This common pharmacological effect on non-rewarded and punished responses has been an important line of evidence in the argument that the effects of both are mediated by a common physiological system: the fear equals frustration hypothesis [10, 12, 32].

Like the barbiturates, the benzodiazepines have often been found to have disinhibitory effects on aversively suppressed behaviour. Thus, response rates may be increased by benzodiazepines (in the dose range 5–25 mg/kg) following their suppression by punishment [5,8], non-contingent shock [15, 18, 23], non-reward [13, 14, 33], or a decrease in reward value [28,31]. These effects could be explained by the hypothesis that the benzodiazepines share with the barbiturates the property of attenuating the effects of aversive stimuli. This hypothesis leads to the prediction that benzodiazepine drugs administered during acquisition should block the subsequent appearance of the PRAE and PREE.

Two alternative hypotheses have been advanced for the action of the benzodiazepines. It has been argued that they exert a disinhibitory effect on any ongoing low-rate behaviour, rather than on behaviour suppressed by aversive stimuli specifically [20,36]; conversely, that the benzodiazepines selectively release behaviour suppressed by punishment, while having little or no effect on behaviour suppressed by non-reward [22,24]. Neither of these hypotheses would predict that the PRAE and PREE would be attenuated by the administration of benzodiazepines during acquisition.

METHOD

Animals

The animals were 32 male Lister hooded rats (Olac, Bicester, England), aged approximately 10 months and weighing approximately 300 g. They were introduced to a 22-hr food deprivation schedule several months prior to the experiment. This schedule was maintained throughout the experiment; animals were tested between 10.00 and 15.30 hr each day, and fed between 16.00 and 18.00 hr approximately. Water was always available in the home cages.

Apparatus

Animals were tested in a straight alleyway, overall length 220 cm, width 15 cm and height 30 cm. The walls and floor

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were of grey perspex, and the roof of transparent smoked perspex. The alley was divided into a 20 cm start box, a 160 cm central section and a 40 cm goal box, separated from each other by grey perspex, hand-operated, guillotine doors. The food cup was 4.4 × 0.6 cm, and made of plastic. The alley was positioned parallel to a strip light in the ceiling, for even illumination.

Procedure

On the first day of pretraining, all animals were introduced for 20 min into the alleyway, in batches of four, with food ad lib in the goal box. This procedure was repeated on the next two days, but preceded by an intraperitoneal injection of 0.9% saline. On the fourth day, animals were injected with saline, and each received two rewarded runs in the alleyway; 15 sec were allowed in the goal box with food ad lib on each of these trials. Animals which did not reach the goal box within two minutes were gently pushed down the runway.

During acquisition proper, the animals were divided into four groups (n = 8). Two groups were trained under conditions of continuous reinforcement (CR), and two groups under partial reinforcement (PR); PR animals were rewarded on 50% of trials (Trials 1, 3, 6, 7, 11, 12, 13 and 16 of each block of 16 trials). Half the animals received injections of chlordiazepoxide hydrochloride (Roche, Welwyn Garden City, England) (15 mg/kg) dissolved in 0.9% saline (Groups C–CR and C–PR), and half received saline alone (Groups S–CR and S–PR). The chlordiazepoxide solution was made up freshly every two days. All injections were given in a volume of 1 ml/kg.

A trial was begun 15 sec after the animal was placed in the start box, by raising the start box door. Running time was measured by stopwatch, starting when the start box door was raised and ending when the animal's back feet entered the goal box. The goal box door was then lowered. On rewarded trials, the food cup was filled with 40 mg food pellets, and the animal was removed 15 sec after it started eating, which after the first few trials, all animals did immediately. On non-rewarded trials, the food cup was empty, and the animal was removed from the goal box after 15 sec.

Animals received four trials on each of the first two days of acquisition (for convenience these eight trials will be considered to constitute Day 1), and eight trials per day thereafter, for a total of nine days. Animals were run in batches of four, one from each treatment group. The inter trial interval was approximately five min, during which the animal was returned to its home cage, and test sessions lasted approximately 40 min. Injections were given 45 min before the beginning of each session. Double blind procedures were employed for drug injection and testing.

At the start of extinction, the order in which animals were tested was randomised, and animals were renumbered, in order that the experiment should be run blind with respect to acquisition performance. Extinction trials were run for 15 days, beginning on Day 10. The procedure was identical to that described for acquisition, except that all animals received saline injections and all trials were non-rewarded. If the animal failed to enter the goal box in 120 sec, it was gently pushed towards the goal box and confined there for 15 sec; a time of 120 sec was recorded. When this happened on three consecutive trials, the animal was dropped from the experiment, and a nominal time of 120 sec was entered for all subsequent trials.

Statistical Analysis

Data were converted to speed scores (1/sec) and the results analysed by 2-way analysis of variance, with two levels of each of the factors drug treatment (drug/saline) and reinforcement history (CR/PR). In the case of a significant overall F-score, the Newman-Keuls procedure [34] was used to test differences between means.

RESULTS

There were no significant differences among the four groups during acquisition; however, Group S–PR were more resistant to extinction than the other groups. The mean running speeds for each day of acquisition and extinction are shown in Fig. 1. Analysis of variance of mean scores on the final day of acquisition found non-significant main effects and a non-significant interaction ($F(1,28) = 0.7$, 1.3, 1.3, all $p>0.25$). However, analysis of variance of mean scores on the first day of extinction found significant effects of drug treatment ($F(1,28) = 16.1$, $p<0.001$) and reinforcement history ($F(1,28) = 4.9$, $p<0.05$) and a significant interaction ($F(1,28) = 4.9$, $p<0.05$). A Newman-Keuls test showed that these effects were brought about by significantly higher scores in Group S–PR ($p<0.01$), with no significant differences among the other groups.

Running speeds on the first trial of extinction were examined for possible effects of the change in drug state between acquisition and extinction. Scores on the first trial of each day tended to be more variable than on subsequent trials; this variability was reduced by subtracting scores on the first trial of extinction from scores on the first trial of the previous day, and analysis of variance was performed on the results. There was a tendency for previously drugged animals to run more slowly than controls, but this was not significant ($F(1,28) = 2.8$, $p>0.1$); the effects of reinforcement history ($F(1,28) = 0.1$, $p>0.25$) and the interaction ($F(1,28) = 0.7$, $p>0.25$) were also insignificant.

DISCUSSION

There was no evidence for a PRAE in this experiment, and therefore the question of the effect of chlordiazepoxide on the PRAE remains unanswered. The failure to find a PRAE was surprising, and perhaps indicates a failure to achieve asymptotic performance. However, it should be noted that the absence of a PRAE makes the PREE easier to interpret. If both are present, then an impairment of extinction in Group S–PR relative to Group S–CR (PREE) could perhaps be explained as being a consequence of their superior performance during acquisition (PRAE). This possibility is ruled out in the present experiment.

The results demonstrate that a PREE was obtained in groups trained under saline treatment but no PREE was seen in groups trained under chlordiazepoxide. The change in state undergone by the groups trained under chlordiazepoxide and extinguished under saline did not appear to make a significant contribution to this effect (although the possibility has not been rigorously excluded). Since all groups received saline during extinction, the difference in the PREE must be explained by a differential effect during acquisition, which only became apparent when reinforcement conditions changed. Hence, there is no way in which the results could be explained by the rate-dependency hypothesis [20,36]; any non-specific rate-increasing effects

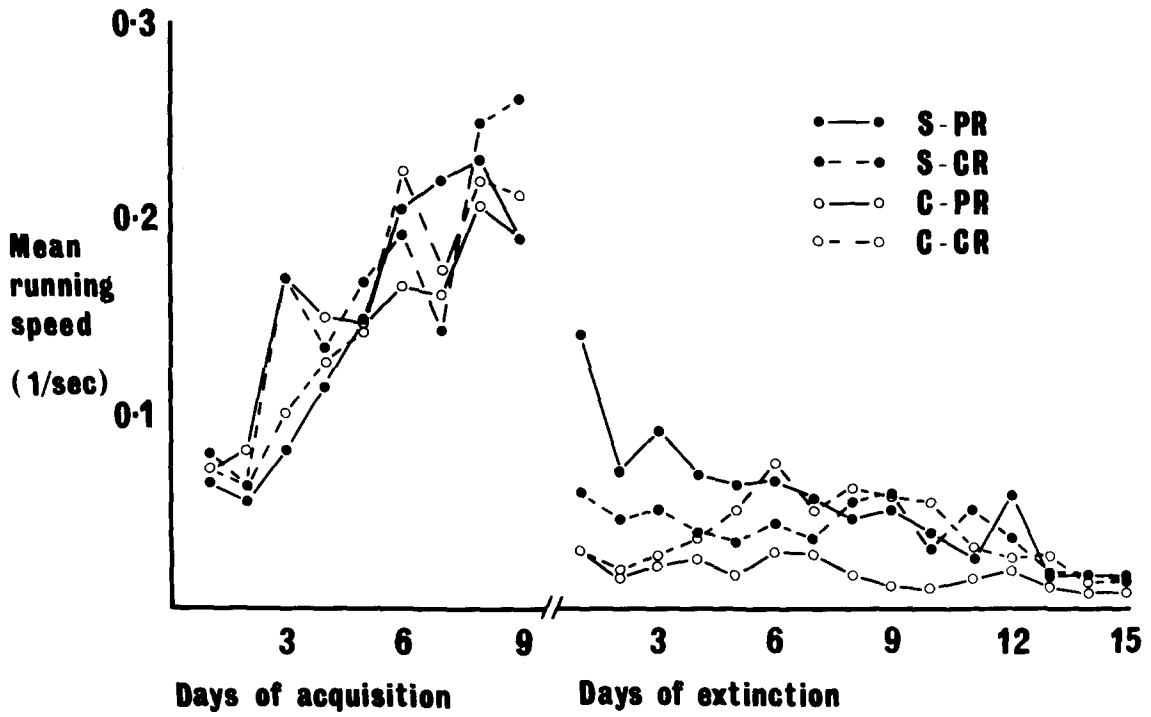

FIG. 1. Running speeds in the straight alley under acquisition conditions of partial (PR) or continuous (CR) reinforcement. During acquisition, animals received saline (S) or chlordiazepoxide (C). All animals were extinguished under saline.

of chlordiazepoxide would have appeared during acquisition. A carry-over effect of the drug from Day 9 of acquisition to Day 1 of extinction is possible, but unlikely, since previously drugged animals ran more slowly than controls, not more rapidly; such an effect would be a facilitation of extinction, which is inconsistent with earlier reports that chlordiazepoxide does not facilitate extinction [13, 14, 22, 24, 33].

The most likely explanation of the results is that chlordiazepoxide blocked the PREE by attenuation of the effects of non-reward during PR training. The results are incompatible with the hypothesis that the effect is specific to responses suppressed by punishment, but spares responses suppressed by frustrative non-reward, i.e., extinction [22,24]. In addition to the present report, there is considerable evidence that chlordiazepoxide does attenuate frustration; effects include increased resistance to extinction [13, 14, 33], decreased suppression by a reduction in reward value [28,31], delaying of breaking point in a progressive ratio reinforcement schedule [30], increased response rate on a DRL schedule [29], the impairment of successive (go/no go) discrimination [17], and the attenuation of the behavioural consequences of insoluble problems [4, 6, 7]. This discrepancy has an important bearing on the fear equals frustration hypothesis, since a differential pharmacological action on punishment and non-reward would argue against common physiological mechanisms. The solution may lie in the specific experimental situations in which chlordiazepoxide did not disinhibit extinguished behaviour. These involved a stable pattern of extinguished non-responding in part of each session, with reward available in another part of the schedule [22,24]. It is possible that under these circumstances, non-reward is no longer aversive. This would allow the suggestion that, like the barbiturates, chlordiazepoxide attenuates the consequences of aversive stimulation, be it punishment or frustrative non-reward, while not affecting non-rewarded responses with non-aversive consequences. The finding that the disinhibitory effects of barbiturates and benzodiazepines on punished behaviour are greatly reduced at low shock intensity [8, 21, 35] would be consistent with this hypothesis. An attenuation of the negative incentive effects of aversive stimulation would not necessarily lead to a disinhibition of behaviour. Thus, in the present experiment, chlordiazepoxide had no acute effect on responding, and it has also been reported that in a schedule in which a preshock stimulus increased response rate, chlordiazepoxide was inhibitory [29].

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REFERENCES

1. Amsel, A. Frustrative nonreward in partial reinforcement and discrimination learning: Some recent history and a theoretical extension. *Psychol. Rev.* 69: 306–328, 1962.

2. Amsel, A. Partial reinforcement effects on vigour and performance. In: *The Psychology of Learning and Motivation*, Vol. 1, edited by K. W. Spence and J. T. Spence. New York: Academic Press, 1967, pp. 2–65.

3. Barry, H., A. R. Wagner and N. E. Miller. Effects of alcohol and amobarbital on performance inhibited by experimental extinction. *J. comp. physiol. Psychol.* **59**: 464–468, 1962.
4. Bremner, F. J., H. D. Cobb and T. J. Nagy. Comparison of the effect of two minor tranquillisers on escape behaviour. *Psychon. Sci.* **17**: 159–160, 1969.
5. Cook, L. and A. C. Catania. Effects of drugs on avoidance and escape behaviour. *Fedn Proc.* **23**: 818–835, 1964.
6. Feldman, R. S. The prevention of fixation with chlordiazepoxide. *J. Neuropsychiat.* **3**: 254–259, 1962.
7. Feldman, R. S. Further studies on assay and testing of fixation-preventing psychotropic drugs. *Psychopharmacologia* **6**: 130–142, 1964.
8. Geller, I., J. T. Kulak and J. Seifter. The effects of chlordiazepoxide and chlorpromazine on a punishment discrimination. *Psychopharmacologia* **3**: 374–385, 1962.
9. Geller, I. and J. Seifter. The effects of meprobamate, barbiturate, d-amphetamine and promazine on experimentally induced conflict in the rat. *Psychopharmacologia* **1**: 484–492, 1960.
10. Gray, J. A. Disappointment and drugs in the rat. *Advance. Sci.* **23**: 595–605, 1967.
11. Gray, J. A. Sodium amobarbital and the effects of frustrative nonreward. *J. comp. physiol. Psychol.* **69**: 55–64, 1969.
12. Gray, J. A. *Elements of a Two-Process Theory of Learning.* London: Academic Press, 1975.
13. Hanson, H. M., J. J. Witoslawski and E. H. Campbell. Drug effects on squirrel monkeys trained on a multiple schedule with a punishment contingency. *J. exp. Analysis Behav.* **10**: 565–569, 1967.
14. Heise, G. A., N. Laughlin and C. Keller. A behavioural and pharmacological analysis of reinforcement withdrawal. *Psychopharmacologia* **16**: 345–368, 1970.
15. Huppert, F. A. and S. D. Iversen. Response suppression in rats: A comparison of response-contingent and noncontingent punishment and the effect of the minor tranquilliser, chlordiazepoxide. *Psychopharmacologia* **44**: 67–75, 1975.
16. Ison, J. R. and E. S. Pennes. Interaction of amobarbital sodium and reinforcement schedule in determining resistance to extinction of an instrumental running response. *J. comp. physiol. Psychol.* **68**: 215–219, 1969.
17. Iwasaki, T., K. Ezawa and S. Iwahara. Differential effects of chlordiazepoxide on simultaneous and successive brightness discrimination learning in rats. *Psychopharmacology* **48**: 75–78, 1976.
18. Lauener, H. Conditioned suppression in rats and the effects of pharmacological agents thereon. *Psychopharmacologia* **4**: 311–325, 1963.
19. Lewis, D. J. Partial reinforcement: A selective review of the literature since 1950. *Psychol. Bull.* **57**: 1–28, 1960.
20. Margules, D. L. and L. Stein. Neuroleptics vs. tranquillisers: Evidence from animal behaviour studies of mode and site of action. In: *Neuropsychopharmacology*, edited by H. Brill, J. O. Cole, P. Deniker, H. Hippius and P. B. Bradley. London: Exerpta Medica Foundation, 1967, pp. 108–120.
21. McMillan, D. E. Drugs and punished responding. III. Punishment intensity as a determinant of drug effect. *Psychopharmacologia* **30**: 61–74, 1973.
22. Miczek, K. A. Effects of scopolamine, amphetamine and chlordiazepoxide on punishment. *Psychopharmacologia* **28**: 373–389, 1973.
23. Miczek, K. A. Effects of scopolamine, amphetamine and benzodiazepines on conditioned suppression. *Pharmac. Biochem. Behav.* **1**: 401–411, 1973.
24. Miczek, K. A. and P. Lau. Effects of scopolamine, physostigmine and chlordiazepoxide on punished and extinguished water consumption in rats. *Psychopharmacologia* **42**: 263–269, 1975.
25. Miller, N. E. The analysis of motivational effects illustrated by experiments on amylobarbitone. In: *Animal Behaviour and Drug Action*, edited by H. Steinberg. London: Churchill, 1964, pp. 1–18.
26. Ridgers, A. and J. A. Gray. Influence of amylobarbitone on operant depression and elation effects in the rat. *Psychopharmacologia* **32**: 265–270, 1973.
27. Robbins, D. Partial reinforcement: A selective review of the alleyway literature since 1960. *Psychol. Bull.* **76**: 415–431, 1971.
28. Rosen, A. J. and R. E. Tessel. Chlorpromazine, chlordiazepoxide and incentive-shift performance in the rat. *J. comp. physiol. Psychol.* **72**: 257–262, 1971.
29. Sanger, D. J. and D. E. Blackman. Effects of chlordiazepoxide, ripazepam and d-amphetamine on conditioned acceleration of timing behaviour in rats. *Psychopharmacology* **48**: 209–215, 1976.
30. Thompson, D. M. Repeated acquisition as a behavioural base line for studying drug effects. *J. Pharmac. exp. Ther.* **184**: 506–514, 1973.
31. Vogel, J. R. and K. Principi. Effects of chlordiazepoxide on depressed performance after reward reduction. *Psychopharmacologia* **21**: 8–12, 1971.
32. Wagner, A. R. Frustration and punishment. In: *Current Research on Motivation*, edited by R. M. Haber. New York: Holt, Rhinehart and Winston, 1966, pp. 229–239.
33. Wedeking, P. W. Disinhibition effect of chlordiazepoxide. *Psychon. Sci.* **15**: 232–233, 1969.
34. Winer, B. J. *Statistical Principles in Experimental Design.* New York: McGraw-Hill, 1971.
35. Witkin, J. M. and J. E. Barrett. Effects of pentobarbital on punished behaviour at different shock intensities. *Pharmac. Biochem. Behav.* **5**: 535–538, 1976.
36. Wuttke, K. and R. T. Kelleher. Effects of some benzodiazepines on punished and unpunished behaviour in the pigeon. *J. Pharmac. exp. Ther.* **172**: 397–405, 1970.