in the control of smooth pursuit eye movements by providing the oculomotor system with target velocity information.

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14. Activity reflecting target velocity has been reported for Purkinje cells of the flocculus (*13*), but the experimental situation employed was not sufficient to allow the conclusion that a visual component was dissociated from vestibular and oculomotor components.
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Drug Discrimination Training with Progressively Lowered Doses

Abstract. *Rats were trained to discriminate drug from no-drug conditions in a two-lever operant task. Moderately high dosages were used initially. Whenever the discrimination was learned, training was continued with progressively reduced dosages. Eventually the rats discriminated extremely low doses of phenobarbital, chlordiazepoxide, cyclazocine, and fentanyl.*

Drug discrimination (DD) procedures are used as tools for investigating the actions of psychoactive drugs. In most DD studies, rats are trained to discriminate between the presence and the absence of a particular drug and dosage. The utility of the resulting discriminations is influenced by a variety of factors including the duration of training required to establish the discriminations, the stability and accuracy of the discriminations, and the dosage used during training.

The earliest DD studies used highly intoxicating doses (*1*). The development of more sensitive procedures permitted training doses to be somewhat lower (*2, 3*). However, these procedures required 30 to 40 sessions of training before DD's were learned, and the duration of training increased if dosage was decreased. These drawbacks discouraged investigators from using low training doses. Recently we identified further methodological improvements that allowed DD's to be learned with moderate doses in 10 to 15 training sessions (*4*). As it appeared that these methods should make it feasible to establish DD's with lower training doses than had been used previously, we have now attempted to find the lowest dose at which each of several drugs could be discriminated. To determine this "threshold" dose, we started training with a moderately high dose and then reduced the dosage whenever performance indicated that a DD had been learned (*5*).

Rats were deprived of water for 24 hours and trained to bar press in a compartment that contained two bars (*6*). Reinforcement was 0.1 ml of 1 percent saccharin solution. In order to obtain reinforcement, the rats were required to press bar 2 on days when they were drugged and to press bar 1 when undrugged (*7*). An interlocking fixed ratio–fixed interval (FR-10–FI-90 seconds) schedule of reinforcement was used (*8*). After initial shaping was completed, training consisted of daily 15-minute sessions (*9*).

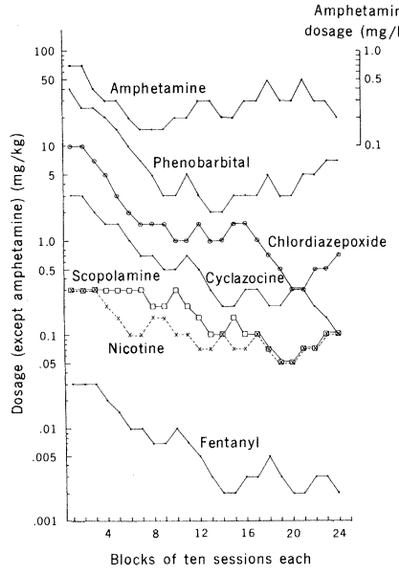

Fig. 1. Rats were required to press bar 1 when drugged and bar 2 when not drugged. Training dosage was decreased whenever this discrimination was learned and increased whenever the discrimination was not learned for 20 consecutive sessions. The plots show training dosages for seven individual rats during successive blocks of ten sessions. Note the displaced ordinate for amphetamine.

At the beginning of each training session, no reinforcement was delivered until the rat had accumulated ten presses on one bar or the other. Presses on both bars before the first reinforcement of each session were used to indicate the accuracy with which the rat could select the currently correct bar on the basis of the imposed drug state (that is, the degree to which the drug and no-drug conditions had acquired discriminative control). Criterion performance was five or fewer presses on the incorrect bar prior to completion of ten presses on the correct bar during eight out of ten consecutive sessions.

The drugs used for training were all known to be discriminable. Initial training dosages, selected on the basis of pilot experiments, ranged from 60 to 90 percent of the maximum doses that could be used without severely disrupting bar pressing. As training proceeded, performance was reviewed every ten sessions, and the training dosage of each drug was altered according to the following rules: (i) If performance was at criterion level during the ten sessions, the dosage was reduced by about 30 percent. (ii) If criterion was not achieved, the dosage was not changed. (iii) Whenever criterion was not achieved during 20 consecutive sessions of training with a particular dosage, the dosage was raised by 30 percent. To avoid behaviorally toxic effects, doses were never raised above the original training dosages.

During successive 10-day blocks of training sessions, all drugs were discriminated, and these discriminations were maintained during reductions in dosage ranging from 60 to 95 percent (Fig. 1). With some drugs, dosage reductions occurred as rapidly as the procedure allowed (30 percent every ten sessions), whereas with other drugs, dosage was reduced more slowly. The number of training sessions before the beginning of criterion performance with the initial training dosages ranged from one with phenobarbital (40 mg per kilogram of body weight) to 51 with scopolamine (0.3 mg/kg); this index of the discriminability of the initial training dose was not highly correlated with the amount of reduction

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in training dosage that was subsequently found to be possible ($r = -.36$). After the threshold dose was reached, substantial variations in the discriminated dose occurred with some of the drugs. Although these variations may have reflected real changes in the discriminability of the drugs, some dosage reductions may also have been based on spuriously achieved criterion-level performance, with dosage subsequently returning upward to the actual threshold dose. Possibly the use of a more stringent criterion would reduce the size of such oscillations.

The results leave several questions unanswered. One of the most useful properties of high-dose DD's is their specificity. This specificity is great enough so that after drug versus no-drug discrimination training with a particular drug, rats appear to disregard the stimulus effects of most other drugs, except those that are pharmacologically related to the training drug (*10*). It is not yet known whether rats trained with very low doses will exhibit greater or less specificity than is observed after training with high doses. Additionally, the threshold doses determined in this experiment, which are probably specific to the particular training procedures that we followed, were obtained in only a single animal for each drug. Further studies might attempt to replicate the threshold dose obtained with each drug, and could determine thresholds for discrimination with other types of psychoactive drugs and with various schedules of reinforcement.

With some of the drugs tested, the final training doses were comparable to the lowest doses that can produce observable effects in any other behavioral test paradigm. This result indicates that DD's provide a test procedure that can be as sensitive as behavioral tests specifically developed to respond to the effects of individual classes of drugs. Such sensitivity might be useful in a variety of contexts. For example, the use of low training doses might increase the sensitivity of DD studies designed to investigate agonist-antagonist interactions or changes in drug effects caused by manipulating neurotransmitters or precursors. Also, many instances of drug abuse (such as tobacco smoking) involve repeated self-administration of doses too low to produce obvious behavioral consequences (other than self-administration); low-dose DD's might provide a method for investigating the effects of drug doses comparable to those used during such drug abuse.

The results appear to have theoretical significance. State-dependent learning (SDL) and DD's are probably controlled by the same mechanism (*2*). A variety of mechanisms have been hypothesized to be responsible for SDL and DD's (*11*); Bliss has divided these models into two general classes—sensory mechanisms and central state or neurological mechanisms (*12*). It has thus far been impossible to experimentally verify any of these models. The present results are easily explicable under most sensory models by postulating that the animals learned to discriminate the effects of increasingly low doses of drug as training progressed. However, few of the "neurological" models for SDL would operate over a 10:1 dosage range with sufficient strength to maintain discriminative control. By inference, the results support sensory interpretations of SDL and of DD's.

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5. The idea of training with progressively lowered doses has been previously suggested by many investigators and was partially implemented with *d*-lysergic acid diethylamide by I. Greenberg, D. M. Kuhn, and J. B. Appel [*Psychopharmacologia* **43**, 229 (1975)]. More recently, both F. C. Colpaert and A. Weissman obtained discrimination of progressively lowered doses of narcotic drugs (personal communications), which led me to test whether low-dose discriminations could also be obtained with other types of drugs.
6. The training compartment was 50 cm wide, 45 cm deep, and 25 cm high. Two operant bars were mounted side by side on one wall 6 cm above the floor. The reinforcement spout was mounted on the same wall directly between the two bars.
7. Drug injections were intraperitoneal except for fentanyl which was administered subcutaneously. Isotonic saline was injected before no drug sessions.
8. With this interlocking schedule, a counter is set to 10 immediately after reinforcement, whereupon the rat must make ten presses in order to earn another reinforcement. One press is subtracted from the required ratio every 10 seconds, until only a single press on the correct bar is required to earn reinforcement after 90 seconds. Because the required number of responses decreases whenever the rat slows down for any reason, this schedule is more lenient than a simple FR schedule.
9. Rats were shaped to bar press, and brought up to an FR-30 schedule of reinforcement in a compartment that contained only one bar. Subsequently, all training was conducted in the two-bar box described. This training began with seven sessions of no-drug shaping with bar-1 presses reinforced. The durations of these sessions were 15 hours, 8 hours, 1 hour, and 30, 15, 15, and 15 minutes. The ratio requirement was incremented every tenth reinforcement, and at the beginning of these sessions, it was 2, 5, 2, 5, 10, 10, and 10. Next the rats received four shaping sessions preceded by drug injection, with reinforcement for presses on bar 2. The durations of these sessions were 15 hours, 30, 30, and 15 minutes, and the initial ratio requirements were 2, 5, 5, and 10. On session 12, discrimination training was begun with the drug state and correct bar alternating during successive sessions.
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Superstitious Bar Pressing in Hippocampal and Septal Rats

Abstract. *Unlike normal animals or those with sham lesions, rats with hippocampal and septal lesions behaved in an operant chamber as if a dependency existed between pellet delivery and their behavior, despite the fact that reinforcement was based on time, not behavior, and was therefore free. This superstitious behavior did not result from a general inability to inhibit responding, as responding rapidly ceased when the pellets were discontinued. These findings suggest that the hippocampus integrates information regarding response-reinforcer relations, which in the normal rat permits superfluous operant behavior to be eliminated.*

Most "superstition" (*1*) experiments have used birds as subjects. The superstitious pattern emerges when reinforcement is independent of response (*2*); it is characterized by sequential responses repeated stereotypically, including the much studied instrumental response—pecking (*3*). The rat, although continuing to emit a wide variety of consummatory and other (*4*) responses in the presence of free reinforcement does not persist in bar pressing. This response begins at moderately high rates but is dynamic; by the third or fourth session it is virtually absent from performance (*5*).

Perhaps the rat does not possess the associative or motivational mechanism responsible for the avian pattern. More likely, a mechanism may have evolved whereby mammals can eliminate some of their superfluous, energy-consuming responses. Neuroanatomical (*6*) and neurobehavioral (*7*) evidence point to the hippocampus as a likely candidate for the performance of this function.

As a test of the hypothesis that the rat

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