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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3. H. Barry III, *ibid.* **65**, 349 (1968); R. K. Kubena and H. Barry III, *J. Pharm. Sci.* **58**, 99 (1969).
4. D. A. Overton, *Psychopharmacology (Berlin)*, in press.
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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13. Supported in part by NIMH grant MH25136. The author acknowledges the assistance of W. Keller, E. Hartsfield, and R. Porter in performing this experiment.

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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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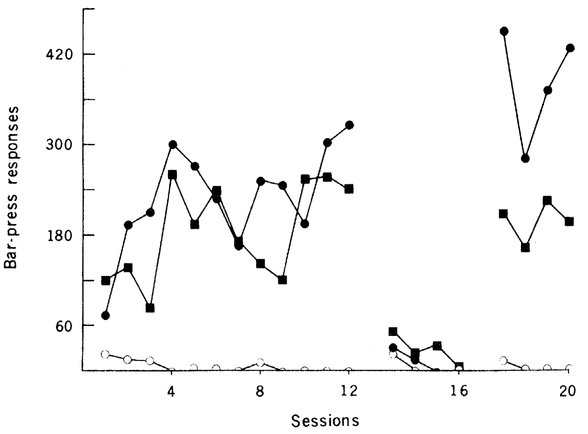

Fig. 1 Median session-by-session bar-press responses for rats with hippocampal (●), medial septal (■), and sham lesions (○). Pellets were dispensed freely every 100 seconds, throughout the first 12 sessions, withheld during the next four sessions, and reintroduced during the last four sessions.

hippocampus prevents the formation of superstitions, five rats with hippocampal and sham lesions (*8*) were prepared. Additionally, since there is evidence to indicate that hippocampal electrical activity is governed by cells in the medial septal nucleus (*9*), five animals with small lesions (*10*) in this area were also observed with the expectation that their performance would parallel that of rats with hippocampal lesions. After the animals recovered from surgery, their weights were reduced to 80 percent by deprivation and maintained by supplemental feeding. They were introduced daily into standard operant chambers (Scientific Prototype), each equipped with a food cup, lever, and pellet dispenser, which delivered 45-mg pellets (Noyes) every 100 seconds according to programming circuitry and without regard to subject behavior. Twelve daily sessions consisting of 50 pellet deliveries spread across 84 minutes were followed by four sessions in which no pellets were dispensed and four sessions with pellets dispensed as before. In no case were the animals trained in any way. All behavior was spontaneous in the sense that it was not controlled by experimental contingencies. Besides visual observation, bar presses were recorded on cumulative counters and periodically on a cumulative recorder. Bar pressing, although presumably representative of the trend of many other possible responses, was specifically chosen for analysis as it is not emitted superstitiously by normal rats and meets the criteria (*1*) for potential superstitious responses.

Unlike animals with sham lesions, those with hippocampal and septal lesions did not attenuate their responding during pellet delivery sessions (Fig. 1). Total hippocampal ($U = 0, P < .01$) and septal ($U = 0, P < .01$) bar pressing in the first sessions not only exceeded that of the sham controls, but in early sessions (one through four) was accelerating while that of shams was decelerating ($U = 0, P < .01$). Suspending pellet delivery greatly decreased hippocampal ($U = 0, P < .01$) and septal ($U = 1, P < .05$) responding as compared with sham controls, which, like normal rats (*5*), tended to briefly increase responding after noncontingent reinforcement ended. Resuming pellet delivery instantly drove responding of each group to approximately its former position [total responding of hippocampal and septal rats exceeded that of controls ($U = 0, P < .01$; $U = 1, P < .05$, respectively)].

The process observed to weaken responsiveness in the presence of free pellet delivery was absent in animals with afunctional hippocampi. Rats with lesions withheld responding during sessions without pellets. In view of this, their deficit cannot lie in a general inability to inhibit responding (*11*).

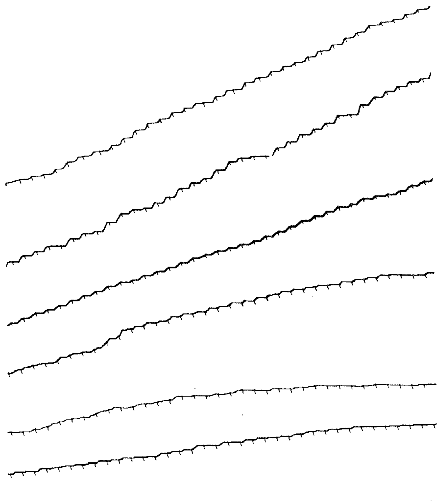

Fig. 2 Sample cumulative bar-press recordings obtained from rats with hippocampal (upper three curves) and septal lesions during sessions 19 or 20. Vertical hatchmarks indicate free pellet deliveries. The hippocampal curves are representative of the entire group. The septal records depict those animals with the most exaggerated bursts of responding after pellet delivery.

Among animals with lesions, activities were much more diverse than bar pressing. All animals exhibited repetitive sequences of stylized, often incomplete, behaviors directed toward virtually all parts of the chamber during reinforcement sessions. In later pellet sessions this responsiveness progressively increased as the probability of pellet delivery approached unity. Cumulative bar-press recordings (Fig. 2) depicted the tendency as successive scallops across 100-second intervals, a phenomenon characteristic of response-dependent interval schedules of reinforcement. A noteworthy difference between septal and hippocampal animals was the tendency of some of the former to emit a burst of responses shortly after pellet delivery. This pattern is also characteristic of septal response-dependent performance (*12*).

As nearly as is possible, the behavior of the animals with lesions corresponded to the descriptions of superstitious behavior in pigeons. It could be argued that the lesions have the paradoxical effect of enhancing learning to such an extent that associations are formed even in the absence of external dependency. This interpretation would be in keeping with Skinner's explanation of the superstitious phenomenon in terms of adventitious response-reinforcer conjunctions (*2*). Yet one must wonder why the learning in every case consisted of positive correlations between some active response and pellet delivery as opposed to an equally erroneous association between not responding and reinforcement, or between responding and nonreinforcement.

Alternatively, and in accordance with more recent analyses of superstition (*13*), the pigeon and the rat may both emit responses induced by the schedule of reinforcement, but the presence of well-developed hippocampi may modulate this behavior with respect to its consequences. Whatever these consequences consist of, it is important as a first step to note the instances in which a normally functioning hippocampus does not permit the weakening of performance—response-dependent situations. The presence or absence of this dependency or some component of it may govern hippocampal function (*14*).

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References and Notes

1. To be described as superstitious, behavior should meet several criteria: It should be skeletal behavior that topographically and temporally resembles operant behavior, and that could in fact be an operant response (that is, be sensitive to reinforcement contingencies). But unlike operant behavior, it must have no programmed relation to reinforcer delivery. This definition excludes "adjunctive" activities [J. L. Falk, *Physiol. Behav.* **6**, 577 (1971)] on temporal grounds. Adjunctive behaviors usually occur after reinforcement, whereas operant responses occur before reinforcement. The definition also disqualifies activities which, like grooming, are refractory to ordinary operant conditioning procedures [S. J. Shettleworth, in *Constraints on Learning*, R. Hinde and J. S. Hinde, Eds. (Academic Press, New York, 1973)]. The criterion of nonnecessity eliminates from consideration activities in or near the area of reinforcement delivery, as at least some of this behavior is necessary for the discovery and ingestion of the reinforcer. Finally, on a logical basis, superstition is not implied merely because some observed response is not part of an experimental contingency. Such a definition rests on the premise that all behavior is either operant or superstitious; its use is certain to spuriously reveal superstitions in all animals in all reinforcement situations.
2. B. F. Skinner, *J. Exp. Psychol.* **38**, 168 (1948).
3. J. E. R. Staddon and V. L. Simmelhag [*Psychol. Rev.* **78**, 3 (1971)] have concluded that the emergence and persistence of superstitious activities result from nonspecific inducement by the schedule of reinforcement.
4. J. E. R. Staddon and S. L. Ayers, *Behaviour* **54**, 26 (1975).
5. L. D. Devenport, paper presented in an animal learning session of the meeting of the Western Psychological Association, San Francisco, Calif., 19 to 22 April 1978.
6. Although mammalian and avian brains are difficult to compare, the area described by those who recognize an avian hippocampal homolog is vestigial or rudimentary in relation to the rat's massive structure [C. J. Herrick, *Neurological Foundations of Animal Behavior* (Holt, New York, 1924), p. 212; J. W. Papez, *Comparative Neurology* (Crowell, New York, 1929), p. 410; E. C. Crosby, B. R. DeJonge, R. C. Schneider, in *Evolution of the Forebrain*, R. Hassler and H. Stephan, Eds. (Plenum, New York, 1967)].
7. If superstitious behavior is induced by a schedule (*3*), the hippocampus may be implicated, as at least one type of schedule-induced rat behavior, polydipsia, is modulated by the hippocampus [L. D. Devenport, *J. Comp. Physiol. Psychol.* **92**, 651 (1978)].
8. Female Sprague-Dawley rats weighed about 250 g at time of surgery. Hippocampal lesions were made by placing a No. 1 stainless steel insect pin insulated with epoxylite, except for 0.5 mm at the tip, at eight sites. With the skull horizontal the stereotaxic coordinates were as follows (in centimeters); 0.25 posterior to bregma, 0.15 and 0.25 lateral to the left and right of the midsagittal suture, 0.34 and 0.30 below the surface of the skull. The remaining four lesions were at 0.45 posterior, 0.45 lateral, 0.7 and 0.36 deep. Anodal current (1.5 mA) was passed for 30 seconds at each of the four anterior placements and for 40 seconds at each of the posterior sites. Three animals with sham lesions were treated identically, but no current was passed. Histological analysis (*7*) revealed lesions that destroyed from 55 to 88 percent of total hippocampal volume. Extrahippocampal damage was minimal and involved the corpus collosum and neocortex overlying the dorsal hippocampus. Some thalamic damage (lateral nucleus and lateral geniculate) was present in two animals but was unrelated to their behavior.
9. J. D. Green and A. Arduini, *J. Neurophysiol.* **17**, 533 (1954).
10. With the skull horizontal, stereotaxic coordinates for the 250-g females were 0.85, 0.90, 0.95, and 1.0 cm anterior to interaural line. Placements were made on the midline by gently displacing the midsagittal sinus. The electrode tip was lowered in each case to 0.5 cm below the surface of the skull. Anodal current (1.5 mA) was passed for 10 seconds at each site. Two animals had sham operations. Histological analysis revealed discrete lesions within the medial septal nuclei. Laterally, they extended to the border of, and in three cases damaged, the medial aspect of the lateral septal nuclei. In two animals the lesions extended about 0.5 anterior to the tip of the medial nucleus.
11. Other research has corroborated this finding (*5*). As it is frequently reported that rats with hippocampal lesions extinguish more slowly than shams, this tendency might have a parallel with superstitiously maintained responses. Recent findings from yoked-control experiments, in which the effects of previous response-reinforcer dependencies can be properly compared across hippocampal and sham groups, have shown that superstitious responses also persevere during extinction. This study also demonstrated, however, that the perseverative tendency is attributable to lesion-induced deficits in response variability rather than an overall inability to withhold behavior (L. D. Devenport and F. A. Holloway, in preparation).
12. P. E. Gay, *Behav. Biol.* **20**, 534 (1977).
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14. The findings presented here have now been obtained with male subjects and variable-interval schedules (L. D. Devenport, paper presented at the Annual Meeting of the American Association for the Advancement of Science, Houston, Tex., 3 to 8 January 1979). The rate of superstitious responses under these conditions was more than twice that observed for the fixed-interval schedule used here. Also, animals with lesions and sham lesions that were trained to bar press for pellets on a variable-interval 100-second schedule have been shifted to the same rate of response-independent reinforcement. Animals with sham lesions stopped responding, but those with lesions maintained steady rates (L. D. Devenport and F. A. Holloway, in preparation).
15. I thank the Department of Biology, Southern Oregon State College, for lending histological equipment, and J. Falk, R. Isaacson, L. Jarrard, and A. Zeiner, for their thoughtful comments on the manuscript. Supported by a grant from the Institutional Research Committee, Southern Oregon State College, Ashland.

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Metabolic Mapping of Functional Activity in the Hypothalamo-Neurohypophysial System of the Rat

Abstract. *Physiological stimulation of the hypothalamo-neurohypophysial system by salt loading of rats resulted in a dramatically increased glucose utilization in the posterior pituitary but not in the paraventricular or supraoptic nuclei. The good correlation between glucose utilization and neural activity in the posterior pituitary (that is, nerve terminals) contrasted with the lack of correlation in the paraventricular and supraoptic nuclei (that is, the sites of the cell bodies of the same neurons). This difference in the metabolic response to functional activity between the two regions of these neurons can be explained by the differences in surface-to-volume ratios of these regions.*

Under most normal circumstances the brain is almost entirely dependent on the utilization of glucose for its biochemical energy (*1*). Studies with the recently developed $[^{14}C]$deoxyglucose method (*2*) for measuring rates of glucose utilization in discrete structural and functional components of the central nervous system have demonstrated a close correlation between levels of local functional activity and local glucose utilization (*3, 4*). Experimentally induced increases or decreases in functional activity in specific motor and sensory systems resulted in corresponding increases or decreases in glucose utilization in specific structural components of the appropriate pathways (*3, 4*). The mechanisms underlying the relationship between functional activity and energy metabolism remain, however, essentially unknown. In which of the cellular compartments are the alterations of glucose utilization localized—glia, perikarya, axons, axonal terminals, dendrites? With which of the numerous energy-consuming processes is the functionally related component of energy metabolism associated—electrical activity; ion transport; storage, release, and reuptake of neurotransmitters; membrane and macromolecular synthesis?

The mammalian hypothalamo-neurohypophysial system appears particularly appropriate for investigation of these questions. It is a neural pathway that is anatomically well defined (*5–7*) and can easily be stimulated physiologically (*8*), and its output can be measured at a site separate and distinct from that of its input. Its perikarya are located in the supraoptic and paraventricular nuclei of the hypothalamus, whereas its axon terminals are situated in the posterior pituitary. We applied the $[^{14}C]$deoxyglucose method to study the metabolic responses of this system to osmotic and pharmacological stimulation. The results demonstrate that metabolic activity varies with functional activity in this system and that this relationship is most prominent in the axonal terminals of the neural pathway.

The studies were carried out in adult male Sprague-Dawley rats weighing 300 to 400 g. Each animal was prepared for the experiment by surgical catheterization of one femoral artery and vein under light halothane anesthesia. While still under anesthesia, the animals were immobilized by application of a loose-fitting plaster cast over the abdominal and pelvic regions, and then at least 2 hours were allowed for complete recovery from the effects of anesthesia. The period of measurement of glucose utilization was initiated by the administration of a