istered subcutaneously 30 minutes before training (*5*), we sought to determine whether such injections of amphetamine also antagonize the effects of cycloheximide on activity. Mice were first injected with cycloheximide; 3 hours and 45 minutes later, they were injected subcutaneously with amphetamine (1 mg/kg) or saline. This interval between drug injections is the same one employed in memory studies, where amphetamine, but not saline, was found to antagonize the effect of cycloheximide. Activity was measured continuously during the 1st hour after amphetamine or saline injection. Mice given cycloheximide and saline ($N = 8$) exhibited marked inhibition of activity during this period; their activity was significantly less than that of mice given only saline (Fig. 1) before activity ($P < .01$). Amphetamine ($N = 8$) did not antagonize the depression of activity. Thus, the effect of amphetamine on memory in cycloheximide-treated mice (*5*) is not correlated with a measurable increase in activity.

We conclude from these studies (i) that cycloheximide affects activity by acting on the brain, (ii) that this action is unrelated to its inhibition of protein synthesis, and (iii) that these effects of cycloheximide on activity do not appear to be responsible for its amnesic action. It is possible, of course, that cycloheximide has some other property, unrelated to inhibition of cerebral protein synthesis, that is responsible for its amnesic effect.

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6. Activity was measured in a soundproof chamber 45.72 cm by 45.72 cm and 27.94 cm high. The floor of the chamber was divided into quadrants, and an index of gross activity was obtained from the number of times each animal crossed from one quadrant to another. In addition, an index of rearing was obtained from touch plates that were placed along the walls of the chamber at 5.08 cm above the floor. All data were automatically recorded.
7. A 12-mg sample of isocycloheximide was provided by Francis Johnson, Dow Chemical Company, Wayland, Mass. The small amount of the drug limited our study to effects of intracerebral injections. In accordance with previous observations (*1*), we determined that this sample had a negligible inhibitory effect (12 percent) on cerebral protein synthesis.
8. For training, a mouse was placed in the stem of the T maze; after 5 seconds, shock (0.4 ma) was applied through the grid floor. The shock was terminated when the mouse entered the dark limb of the maze. The mouse was removed 5 seconds later. Training was continued with an intertrial interval of 30 seconds and a criterion of five out of six correct responses. Savings was calculated as described by S. H. Barondes and H. D. Cohen [*Science* **151**, 594 (1966)]. Mice that required more trials to reach criterion on retest than on original learning were scored as having zero savings. The savings of mice given cycloheximide were significantly less than the savings of mice given saline ($P < .02$) or isocycloheximide ($P < .02$).
9. Supported by PHS grant MH-18282.

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## Models for the Transport of DDT: Verification Analysis

In their article Harrison *et al.* (*1*) presented interesting models for the transport of DDT (*2*) through several trophic levels. Their models essentially represent a series of mass transfer equations in a homogeneous spatial medium. Harrison *et al.* claim that the models they propose are "sufficiently descriptive to yield the general nature of population response, and to make possible the prediction that a significant variation of a predator population would cause upsets throughout the entire system, some of which might be of sufficient magnitude to create 'out-of-control' conditions." However, nowhere in the article does there appear a verification analysis of the models proposed which would lend even minimum support to such a contention.

A verification analysis should compare the analytical model to observed data from the real world. Such an analysis is basic to a systems analysis of any phenomenon. The presentation of a model without some indication of how well the model does in "independent" test predictions represents only part of the systems analysis. One must always be prepared to demonstrate the utility of the model for decision-making. For this reason it is necessary to go substantially beyond mere structuring of the analytical model. Numerous changes in the model may be necessitated by such a verification analysis. Certainly this step must be carried out before any claim is made about the ability of the model for prediction purposes.

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2. DDT, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)-ethane.

17 December 1970

## Activity Change as the Cause of Apparent Aversiveness during Prolonged Hypothalamic Stimulation

Mendelson (*1*) reported that rats in the presence of relevant goal objects (for example, food for a stimulus-bound eater) while receiving rewarding hypothalamic stimulation turn off the stimulation less frequently than rats do when there are no relevant goal objects. The rats could switch the stimulation ON by moving into one half of a shuttle box and switch it OFF by running into the other half. Mendelson states that the phenomenon is due to a suppression of the normally aversive effects of long lasting stimulation by consummatory behavior. He then proposed that the aversive effects of the brain stimulation (*2, 3*) are due to the excessive arousal of drive, and that the opportunity to engage in consummatory behavior reduces the drive and makes the stimulation less aversive. However, a much simpler hypothesis can account for his result. During hypothalamic stimulation, the rat shows a high level of activity such as sniffing, searching, and moving, but if the relevant goal object is supplied during stimulation, such activity is reduced because the rat becomes engaged in eating, drinking, or gnawing (*4*). This simple "activity" hypothesis can account for Mendelson's finding that the rat would prefer a longer duration of brain stimulation with a goal object than without one. Such a sim-

Table 1. The number of movements from one end to the other in a shuttle box during a trial of 47 seconds of hypothalamic stimulation. E/F is the ratio of the mean score of condition of an empty box to that of the condition of the floor covered with food. See text for details.

| Subject | Condition | Crossings during ON (Mean ± S.D.) | Ratio E/F |
|---|---|---|---|
| N-6 | Food | 1.75 ± 0.829 | 2.68 |
| | Empty | 4.7 ± 1.59 | |
| L-9 | Food | 0.7 ± 0.537 | 4.87 |
| | Empty | 3.35 ± 0.555 | |
| M-9 | Food | 0.65 ± 0.345 | 5.00 |
| | Empty | 3.25 ± 0.303 | |

ple hypothesis can be tested by measuring the movement of the rat from one side of the shuttle box to the other when such movement does not lead to a change in the hypothalamic stimulus. The following experiment was performed to test this hypothesis.

Three rats were used. One or two monopolar electrodes were implanted in the lateral hypothalamic area (de Groot coordinates : H-2.3, L 1.7, and A 5.8) of each animal (*5*). Each rat was shown to be a good self-stimulator and a reliable stimulus-bound eater. A sine-wave stimulator (60 hz) at 4.5 volts (peak to peak) was controlled by a timing circuit and a relay. A regular alternation of 47 seconds stimulation-ON time and 47 seconds stimulation-OFF time, was controlled by the timing circuit and connected to the deep electrode and to the indifferent skull electrode. The rats had no way to control the ON-set and OFF-set of the brain stimulation. If the relevant goal object (food in the form of crushed small pieces of Simonsen Laboratory S/L white diet) were provided, the rat showed reliable eating responses on every occasion when brain stimulation was turned on. This crushed food was evenly distributed on the floor of the apparatus when appropriate. For the condition without food, the floor was cleaned carefully beforehand. This was the same arrangement Mendelson used. Each rat served as its own control between two conditions; either (i) the goal object was supplied or (ii) the box was empty. Every condition was run in blocks of five trials, preceded by 5 minutes of free exploratory time and 5 minutes of free exploratory time with the wires and connectors attached to the electrodes. The subjects were permitted free access to food and water throughout the whole experiment, except during testing periods.

The experiment was conducted in a shuttle box identical with Mendelson's (*6*). Two microswitches were attached to the end of each side. To depress a microswitch, the rat had to progress to within 18 cm of one of the ends of the box, and as a result the device recorded the number of crossings from one end to the other. Rat numbers and food availability were assigned randomly to condition A or B. Sequential effects were avoided by the use of an ABBABAAB design. The side of the shuttle box occupied by the rat at the start of each trial was a matter of chance. The score was the number of movements from one end to the other during the 47 seconds of stimulus-ON time of each trial. Each day, the rat would run each pair of AB blocks with a resting interval of 1 hour or more.

The rats are more active in an empty box (Table 1). They go across the center line more often than when they are preoccupied with eating. There are highly significant differences ($P > .01$) in each rat's performance under the two experimental conditions by the Wilcoxon matched-pairs signed-ranks test. The ratio of center crossings between the two conditions is similar to the ratio of the two "preferred" durations of brain stimulation in Mendelson's experiment. In the condition in which food is not available, my experiment indicates an increase in activity of more than 100 percent (range 168 to 400 percent). In one experiment, a similar result was obtained in an open-field test condition which is simpler for measuring activity.

Because of the absence of a suitable control, Mendelson's data do not justify his conclusion; that is, that apparent aversive effects of prolonged stimulation are due to the excessive arousal of a drive. They may simply result from activity changes. My results show that activity change rather than changes in aversiveness can account for Mendelson's data (*7*).

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3. J. Olds, *Physiol. Rev.* **41**, 554 (1962).
4. According to Mendelson's description: "The introduction of appropriate goal objects into the box produced a dramatic change in all the animals' behavior. Instead of the restless searching, rearing, and sniffing, which was characteristic of their behavior on the ON side of the empty box, each rat calmly engaged in feeding, drinking, or gnawing behavior while the current was on in the presence of appropriate goal objects. Their median ON times increased by at least 50 percent and in most cases by more than 100 percent." Our observation was the same as Mendelson's.
5. Histology was not available at the time this report was prepared.
6. Shuttle box measured 30 by 12 inches and was 15 inches high (1 inch = 2.54 cm). The floor of the box was mounted in its center on an axle across the width.
7. J. A. Deutsch and R. D. Hawkins (personal communication) have confirmed an early idea of L. Stein [*J. Comp. Physiol. Psychol.* **55**, 405 (1962)] that "adaptation" is the cause of apparent "aversiveness" of prolonged rewarding brain stimulation.
8. I thank L. Squire and S. K. Roll for discussion. This research was supported by NIH grant MH 12766-04 to J. A. Deutsch, and a predoctoral fellowship from the University of California, San Diego.

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Hu (*1*) has performed a "control" experiment whose results lead him to offer an alternative interpretation of my data (*2*). I found that the duration of hypothalamic stimulation preferred by rats is increased by the opportunity to engage in consummatory behaviors (feeding, drinking, gnawing) facilitated by the stimulation. I considered these data as being consistent with the hypothesis that the aversive effects of prolonged stimulation are due to the excessive arousal of a drive, and that this drive can be reduced by appropriate consummatory activity. Hu attributes this increase in preferred duration to a reduction in the animals' general level of activity, which is brought about by introducing appropriate goal objects into the shuttle box. However, there are a number of important procedural differences between Hu's experiment and mine which should caution us against the use of his data to interpret mine.

First, the nature of the food is an important variable. It is not clear how finely Hu ground the food which he spread on the floor. The pieces may have been large enough to induce the rats to pick them up in order to eat them; this would greatly reduce their activity, as they would not be able to perambulate while eating food being held in their front paws. In my experiment finely powdered Purina chow was used, so that the animals could and did walk around the box while lapping up the food in the same way as they would lap up water.

Second, in Hu's experiment there

was no response available to the animals to turn off the stimulation, whereas in my experiment there was. The decrease in activity produced by introducing food under Hu's conditions by no means proves that activity would decrease in a similar fashion when food is made available to animals given an opportunity to perform a well-practiced response to terminate the stimulation. Lapping up the food could slow down the animals' locomotions toward the OFF side, but reference to table 1 of my report indicates that they could walk over to the OFF side within 12 to 22 seconds while feeding; why then, did two animals spend averages of over 100 seconds on the ON side when food was available? The magnitude of these effects is much too great to be accounted for solely in terms of the slowdown in locomotion produced by feeding.

Third, Hu failed to first measure his rats' preferred durations of stimulation and then use these durations in the main part of the experiment. Rather, he arbitrarily selected a stimulus duration of 47 seconds which corresponds neither to the median duration of 14 seconds selected by my rats while the shuttle box was empty, nor to the median of 31.5 seconds selected when the floor was covered with appropriate goal objects. Similarly he arbitrarily selected an interstimulus interval (OFF duration) of 47 seconds which is much greater than the OFF durations selected by my animals (3 to 5 seconds in each condition).

In Hu's experiment the rats received the same long duration of stimulation both in the presence and absence of food, while in my experiment the durations received were more than twice as long with food as without. In my experiment the animals themselves controlled the durations of stimulation, so that aversive stimulation was minimized. In Hu's experiment it may have been that the aversive quality of long durations of stimulation was responsible for the increase in activity which occurred in the empty-box condition. In fact, it is possible that Hu's rats' activity did not increase during the stimulation received in the empty box until after the intracranial stimulation (ICS) had been on for a period of time that exceeded the durations which the rats would have selected, that is, until after it had become aversive. When Hu produced an increase in activity by removing the food from his box, the increased activity could have been due either to the absence of food or to the extremely long (and presumably aversive) durations of ICS imposed on the animals. Hu confounds these two variables. In my experiment the rats rarely received aversive stimulation under either condition since they themselves controlled the ICS durations. Hu should have determined preferred durations under the food and empty conditions and then programed these durations into the animals, matching each predetermined preferred duration to the appropriate condition.

But even had Hu done this, his "control" experiment would still be unsatisfactory, since programing preferred durations of brain stimulation into rats does not guarantee that they will be rewarding. Indeed, Steiner *et al.* (*3*) have shown that rats will tend to escape from such stimulation. This suggests that to insure that ICS is rewarding we must let the rat itself choose how much stimulation it will receive and when it will receive it. The activity generated by self-selected (rewarding) durations of brain stimulation may be quite different from that generated by (aversive) stimulation which is imposed on the rat by the experimenter.

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3. S. S. Steiner, B. Beer, M. M. Shaffer, *ibid.* **163**, 90 (1969).

4 February 1971

## Saharan Ordovician Ice Age

It is not correct, as I stated (*1*), that visitors to the Algiers meeting of the sedimentology group were invited to "confirm or deny" the existence of a Saharan Ordovician ice age. Under the auspices of the Institut Français du Pétrole of Paris, field workers had laid out the geology of this region and had established the existence of such an ice age. I tried to bring out that there was a convergence of evidence from paleomagnetists, paleontologists, and field workers. To the field geologists S. Beuf, B. Biju Duval, O. de Charpal, and P. Rognon goes the credit for the demonstration under rugged conditions of what previously had only been hinted at. I apologize to these pioneer workers for an unintended slight to their work.

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## Catalyst for Auto Exhaust

Libby's note (*1*) on the potential use of $LaCoO_3$ as a catalyst for automobile exhaust prompts me to report the similar application of $Pr_6O_{11}$ and $Tb_4O_7$. In 1958, at Stanford Research Institute, we used both of these on alumina carriers in the exhaust system of a small engine and monitored the emission by infrared spectrophotometry. Virtually complete breakdown of extraneous gasoline was achieved, and the catalysts were not poisoned by the lead component of the exhaust gases; indeed, we even loaded the system with lead bromide without affecting its function.

Use of rare-earth catalysts in the petroleum industry has been known for many years, but our data on their catalytic function in auto exhaust were never published. Even in the concentrations we used—about 5 to 10 percent on the carrier—the costs of praseodymium and terbium oxides cannot bear comparison with the estimated cost for $LaCoO_3$. But it would seem from our old experiments and Libby's data that the rare earths and particularly those (or their compounds) exhibiting paramagnetism do possess a high potential in this area.

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**Reference**

1. W. F. Libby, *Science* **171**, 499 (1971).

10 February 1971