was assigned at random to each of the following six delay conditions: 0.0, 0.5, 1.0, 2.0, 3.0, and 5.0 seconds. This procedure was repeated until eight animals in all had been assigned to each delay-of-reward condition.

In the learning phase of the experiment the center panel was removed from the box to produce a two-bar discrimination situation. The task of the subject was to choose between the two bars, over one of which there was a light (the "discriminative" light). A response on either bar immediately extinguished both the discriminative light and the house lights for a 10-second interval. A response on the lighted bar resulted in delivery of the stimulation after an interval determined by the delay condition to which the animal had been assigned. The side of the box on which the positive stimulus of illumination appeared was varied according to a prearranged order, and each correct response advanced this sequence. With this procedure, a subject was given 500 trials; for the most part these were given in two sessions—300 trials in the first and 200 in the second. In a few cases, especially under the longer delay conditions, an animal would stop responding for 15 minutes or more. When this occurred, training was terminated for that day and continued on the next, for as many daily sessions as were necessary to complete 500 trials.

The reciprocal of the mean number of errors made by each group in the 500 trials was plotted against the delay condition to produce the delay-of-reward gradient shown in Fig. 1. Statistical analysis of these data showed that the differences between the error scores for the six groups were reliable ($p < .001$). Examination of the acquisition curves (not shown) revealed that the first three groups—those subjected to 0.0-, 0.5-, and 1.0-second reward delay—attained a terminal performance level between 90 and 100 percent correct. The curves for the other three groups were still rising at the end of the 500 trials, and it is possible that they would have reached this same performance level had training continued. It is worth noting, however, that an increasing number of animals in the groups where delay was longer failed to show clear evidence of learning over the 500 trials, and three of the animals subjected to 5-second delay responded at what was close to a chance level throughout the experiment. It may be, therefore, that for a visual discrimination the 5-second delay is close to the limit for learning in the rat, as was suggested in an earlier study (*7*).

Much of our present knowledge concerning the relation of delayed reward to the rate of learning in rats is based upon the work of Grice (*7*), who used a food reward. While the work reported here resembles this earlier study in the choice of a visual discrimination task, the two do differ, both with respect to the reinforcing stimulus employed and in the use of a two-bar rather than a two-alley testing situation. In spite of these differences, comparison shows the two sets of data to be remarkably similar. It is possible, of course, that a closer examination of the relation between delayed reward and learning may reveal differences in the responses for food reward and for stimulation reward, perhaps at very short delays where, with food stimuli, the response time of the systems mediating reward may introduce a certain delay that central stimulation eliminates. On the other hand, the close similarity of the present data to those of Grice argues strongly for the essential comparability of food and stimulation as rewards for learning. This, together with the observation that group comparisons of experimental treatments are feasible in spite of the expected variation between subjects in electrode placement, offers considerable encouragement for applying these brain-stimulation techniques to studying the relation between reward and learning.

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References and Notes

1. J. Olds and P. Milner, *J. Comp. Physiol. Psychol.* **47**, 419 (1954).
2. J. Olds, *ibid.* **51**, 675 (1958); R. W. Porter, D. G. Conrad, J. V. Brady, *J. Exptl. Anal. Behavior* **2**, 43 (1959); J. Olds, R. P. Travis, R. C. Schwing, *J. Comp. Physiol. Psychol.* **53**, 23 (1960).
3. J. V. Brady, J. J. Boren, D. Conrad, M. Sidman, *J. Comp. Physiol. Psychol.* **50**, 134 (1957); J. Olds, *ibid.* **51**, 320 (1958); W. Hodos and E. S. Valenstein, *ibid.* **53**, 502 (1960); B. G. Hoebel and P. Teitelbaum, *Science* **135**, 375 (1962).
4. J. Olds, *J. Comp. Physiol. Psychol.* **49**, 507 (1956).
5. J. W. Kling and Y. Matsumiya, *Science* **135**, 668 (1962).
6. R. E. Keesey, *J. Comp. Physiol. Psychol.* **55**, 671 (1962).
7. G. R. Grice, *J. Exptl. Psychol.* **38**, 1 (1948).
8. This report is based upon a thesis submitted to the department of psychology at Brown University for the Ph.D. degree. The research was conducted during tenure of a U.S. Public Health Service predoctoral research fellowship (MF-9865) and was supported by a U.S. Public Health Service research grant [M-2337(C1)] to J. W. Kling. The advice and encouragement of Dr. Kling is gratefully acknowledged.

18 November 1963

Vinblastine Sulfate Treatment of Hodgkin's Disease during a Pregnancy

Ferm has reported [*Science* **141**, 426 (2 August 1963)] that embryocidal and teratogenic effects follow the treatment of pregnant golden hamsters with vinblastine sulfate (VLB) or vincristine sulfate (VCR). In view of this it is perhaps of interest to report the case of a patient with Hodgkin's disease who was treated throughout pregnancy with VLB, before we were acquainted with Ferm's findings.

Prior to pregnancy the woman had been treated with VLB intravenously, but it had become impossible to give further injections when her veins became inaccessible. Fortunately, oral VLB maintained the remission. Treatment with oral VLB commenced 15 August 1962, and has been continued without interruption since then. During most of this time the dosage has been one 5-mg tablet by mouth on each of five consecutive days each week.

For two reasons we believe that the patient absorbed the orally administered VLB. (i) The number of leukocytes per cubic millimeter was reduced on 14 September 1962 to 2300, on 19 October 1962 to 3900, and on 8 March 1963 to 3300. After each leukopenic episode the dosage of VLB tablets was temporarily reduced to permit the leukocyte count to return to normal. (ii) Prior to pregnancy, only 3 weeks after intravenous VLB dosage had been temporarily discontinued, the patient had an acute relapse, with signs of generalized Hodgkin's disease. If the oral preparation had not been absorbed systemically, we would therefore have expected another relapse. Further, we had previously not merely maintained but actually induced remission with oral VLB in other patients suffering from Hodgkin's disease.

On 15 July 1963, after 11 months of oral VLB treatment, the patient spontaneously gave birth to a full-term, normal male infant weighing 3570 g (7 lb 14 oz). Physical examinations of the infant have failed to reveal any abnormalities. As this is written he is 3 months old and thriving.

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21 October 1963