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Operant conditioning in forebrain ablated rats by use of rewarding hypothalamic stimulation

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It is well established that cortical and limbic structures subserve an important function in the learning of complex behaviors. It is not clear, however, to what extent these structures are essential for the process of operant learning and reinforcement. The aim of the present study was to determine if simple operant conditioning is still possible in the absence of the major forebrain areas in the rat. In summary, we found that, by use of rewarding hypothalamic stimulation, instrumental conditioning of limb movements and other behaviors was intact after removal of all of the cortex, hippocampus, striatum, septum and other structures. Extinction of the conditioned behaviors, however, was severely retarded or absent in this preparation.

Adult albino rats of the CFN COBS strain were anesthetized with ether, the skulls were trephined and the brain tissue removed by aspiration. Bleeding was controlled by flushing with warm saline and application of hemostatic cotton. After completion of the ablation a bipolar stimulating electrode, insulated except across the 0.2 mm tips, was aimed at the lateral hypothalamic area. The brain cavity was then filled with hemostatic cotton and cemented shut with dental acrylic. The animals were kept alive by daily intraperitoneal injections of isotonic saline and intragastric tube-feeding of 10% glucose solution.

Testing for conditioning was usually begun one day after the operation. Instrumental learning was defined as an increase in the frequency of a defined response as a function of contingent hypothalamic stimulation. The responses which were selectively reinforced were varied, including discrete limb, head and tail movements, foot-shuffling, and gross body movements such as sitting up, rearing and turning. To rule out the possibility that the behaviors to be reinforced were elicited by the electrical stimulation, trains of stimulation were administered at regular intervals on a non-contingent basis prior to training. Reinforcing hypothalamic stimulation consisted of 60–100 Hz sine waves at 0.1–0.5 sec train duration. The currents employed varied from 30 to 80 μA, which is the range known to be rewarding in intact animals.

Operant learning was considered to be successful only when it was possible to condition at least two separate incompatible behaviors in the same animal. For example, one animal was shaped to perform a head movement to the left, then to the

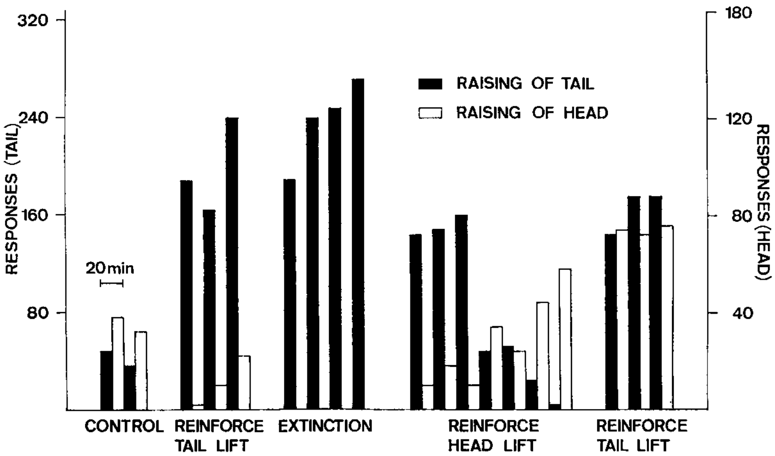

Fig. 1. Total number of responses (head raising and tail raising) emitted over 20 min periods during (a) control session, (b) reinforcement of tail raising, (c) extinction, (d) reinforcement of head raising, and again (e) reinforcement of tail raising. Represents continuous record of rat no. 20.

right, then was reinforced for sitting up. In order to automate the procedure and to quantify the results some animals were partly restrained around the mid-section and suspended in the air. Three photocells were then adjusted to record the frequency of occurrence of various behaviors, such as head and tail movements, on a cumulative recorder. Fig. 1 summarizes the results of such an animal who was initially reinforced for lifting its tail. The position of the photocell was gradually adjusted upward to require a vertical tail position for reward. Notice that this behavior did not undergo extinction when reward was withdrawn. Next, the raising of the head was reinforced. Note the gradual increase in head-raising responses and the concomitant decrease in tail-raising. Finally, the raising of the tail was reinforced again, which led to a linkage of head- and tail-raising behaviors. Fig. 1 represents one continuous testing session. These results are typical for the 9 animals who exhibited operant conditioning. Once a response was established by reinforcement, it showed little evidence for extinction. When a different response was subsequently reinforced it sometimes became linked to the previous response in a behavior chain. In some cases the learned behavior was still emitted with high frequency days after reinforcement was withheld.

Fig. 2 depicts 3 representative brains of animals who exhibited operant conditioning, including rat no. 20 whose data are shown in Fig. 1. The position of the stimulating electrode tips are marked by filled squares, for each rat in the 4th section from the top. The reconstructed brains are conservative estimates of intact structures,

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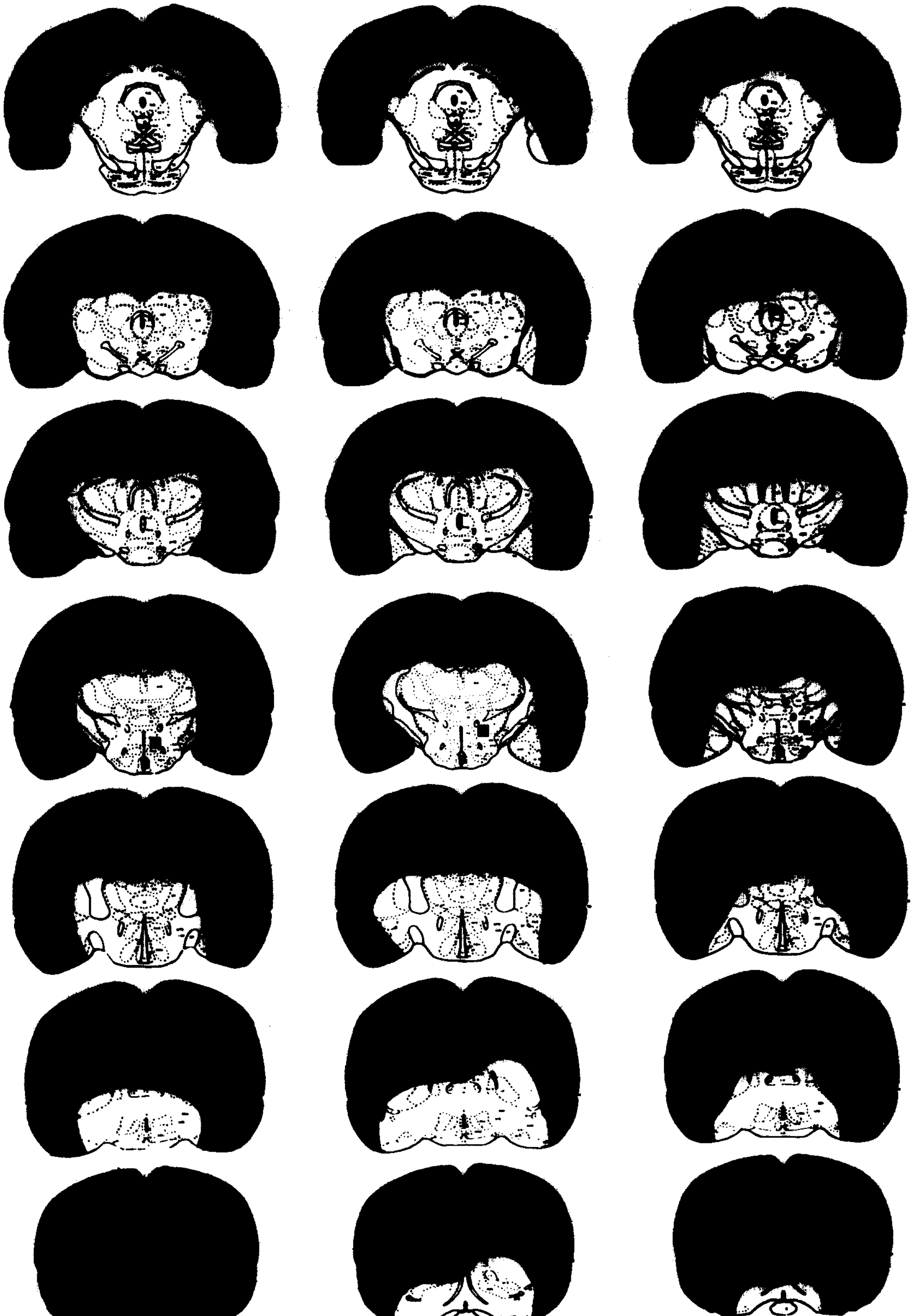
Fig. 2. Extent of brain ablation (dark areas) of 3 representative animals who successfully underwent operant conditioning by use of rewarding brain stimulation. The electrode tip sites in each brain are marked by black squares in the fourth sections from the top. The sections are from the atlas of Pellegrino and Cushman[22], measured —4.6, —3.4, —2.2, —1.0, 0.2, 1.4, and 2.6 mm from the bregma.



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as they are based on the gross outline of histological sections and do not take into account damage due to degeneration. Note that cortex, hippocampus, septum and striatum are largely removed, although the amygdalae are partly intact in two animals. Dorsal thalamus and preoptic region were damaged to varying degrees in different animals.

Histology was performed also on the brains of 6 of the 11 rats who failed to show evidence for operant conditioning. Five of these brains showed damage to the thalamus or hypothalamus in addition to the structures listed above; however, the failure to condition is difficult to interpret in terms of extent of ablation in such a small sample, since it is not known if the electrical stimulation would have been reinforcing in the intact preparation.

In normal rats longer trains of lateral hypothalamic stimulation through electrodes which yield reward or self-stimulation often also result in the elicitation of consummatory behaviors such as eating, drinking, gnawing, etc.[11,12,17,19]. Hence, at the beginning of each testing session the lesioned animals were administered long trains of stimulation to test for elicited behavior. Such continuous stimulation induced forward locomotion in all 9 animals who exhibited conditioning. Stimulation induced *in vacuo* gnawing in one animal and ejaculation in another. Once a behavior was strengthened by operant conditioning and the animal was in a period of quiescence, the longer trains of stimulation, even at very low current levels, were effective in 'priming' the animal to perform the learned response, a phenomenon also common in intact animals[10,13]. Startling by noise or touch was also effective at times in inducing a quiescent animal to perform the learned response.

The finding that the reinforcement system is relatively independent of limbic and other forebrain structures concurs with the results of other studies employing more restricted lesions[1,3,4,16,20,27,28].

Apparently operant learning is possible in the thalamic preparation; however the learning is not adaptive since it does not extinguish readily, *i.e.* negative feedback based on the consideration of non-reinforcement is absent. The relative lack of extinction in this preparation suggests a clear separation between a reinforcement system and a system responsible for extinction. Such a separation is in accord with the results of many studies which have shown that discrete lesions, particularly involving the hippocampus and septum[8,9,14,18,25,26], but also of the frontal cortex, striatum, thalamus, and amygdala[2,7,21,23], result in perseveration of behavior and resistance to extinction. On the other hand, if extinction is considered to require an active learning process, then its relative absence in this preparation can be attributed to the absence of normal sources of reinforcement.

In conclusion, the data indicate that a mechanism for reinforcement is localized subcortically in the mesencephalon–hypothalamus–thalamus region. Although cortical and limbic structures undoubtedly serve important functions in the control of complex behaviors[5,6,15,24], the present results suggest that the search for primary electrophysiological, chemical or structural changes concomitant with simple operant learning should concentrate in the mesodiencephalic areas left intact in this preparation.

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1 ASDOURIAN, D., STUTZ, R. M., AND ROCKLIN, K. W., The effects of thalamic and limbic system lesions on self-stimulation, *J. comp. physiol. Psychol.*, 61 (1966) 468–472.
2 BÄTTIG, K., ROSVOLD, H. E., AND MISHKIN, M., Comparison of the effects of frontal and caudate lesions on delayed response and alternation in monkeys, *J. comp. physiol. Psychol.*, 53 (1960) 400–404.
3 BERDASHKEVICH, A. P., AND SHIK, M. L., Hypothalamic self-stimulation and frontal poles of the cerebral hemispheres in rats, *Bull. exp. Biol. Med.*, 6 (1971) 12–16.
4 BOYD, E. S., AND GARDNER, L. C., Effect of some brain lesions on intracranial self-stimulation in the rat, *Amer. J. Physiol.*, 213 (1967) 1044–1052.
5 BUREŠ, J., Reversible decortication and behavior. In M. A. B. BRAZIER (Ed.), *The Central Nervous System and Behavior, Trans. 2nd Conf.*, Josiah Macy Jr. Found., New York, 1959, pp. 207–248.
6 BUREŠ, J., BUREŠOVÁ, O., AND ZÁHOROVÁ, A., Conditioned reflexes and Leao's spreading cortical depression, *J. comp. physiol. Psychol.*, 51 (1958) 263–268.
7 CAZALA, P., ET CARDO, B., Rôle du noyau thalamique réticulaire dans l'acquisition de différents apprentissages chez le Rat, *Physiol. Behav.*, 6 (1971) 641–647.
8 DOUGLAS, R. J., The hippocampus and behavior, *Psychol. Bull.*, 67 (1967) 416–442.
9 ELLEN, P., AND POWELL, E. W., Effects of septal lesions on behavior generated by positive reinforcement, *Exp. Neurol.*, 6 (1962) 1–11.
10 GALLISTEL, C. R., The incentive of brain-stimulation reward, *J. comp. physiol. Psychol.*, 69 (1969) 713–721.
11 HOEBEL, B. G., AND TEITELBAUM, P., Hypothalamic control of feeding and self-stimulation, *Science* 135 (1962) 375–377.
12 HUSTON, J. P., Relationship between motivating and rewarding stimulation of the lateral hypothalamus, *Physiol. Behav.*, 6 (1971) 711–716.
13 HUSTON, J. P., Inhibition of hypothalamically motivated eating by rewarding stimulation through the same electrode, *Physiol. Behav.*, 8 (1972) 1121–1125.
14 KIMBLE, D. P., The hippocampus and internal inhibition, *Psychol. Bull.*, 70 (1968) 285–295.
15 LASHLEY, K. S., In search of the engram, *Symp. Soc. exp. Biol.*, 4 (1950) 454–482.
16 LORENS, S. A., Effect of lesions in the CNS on lateral hypothalamic self-stimulation in the rat, *J. comp. physiol. Psychol.*, 62 (1966) 256–262.
17 MARGULES, D. L., AND OLDS, J., Identical 'feeding' and 'rewarding' systems in the lateral hypothalamus of rats, *Science*, 135 (1962) 374–375.
18 MCCLEARY, R. A., Response-modulating functions of the limbic system and suppression. In E. STELLAR AND J. M. SPRAGUE (Eds.), *Progress in Physiological Psychology, Vol. I*, Academic Press, New York, 1966, pp. 209–272.
19 MOGENSON, G. J., AND MORGAN, C. W., Effects of induced drinking and self-stimulation of the lateral hypothalamus, *Exp. Brain Res.*, 3 (1967) 111–116.
20 OLDS, M. E., AND OLDS, J., Effects of lesions in medial forebrain bundle on self-stimulation behavior, *Amer. J. Physiol.*, 217 (1969) 1253–1264.
21 PELLEGRINO, L. J., AND CLAPP, D. F., Limbic lesions and externally cued DRL performance, *Physiol. Behav.*, 7 (1971) 863–868.
22 PELLEGRINO, L. J., AND CUSHMAN, A. J., *A Stereotaxic Atlas of the Rat Brain*, Appleton-Century-Crofts, New York, 1967.
23 ROSVOLD, H. E., AND SZWARCBART, M. K., Neural structures involved in delayed-response performance. In J. M. WARREN AND K. AKERT (Eds.), *The Frontal Granular Cortex and Behavior*, McGraw Hill, New York, 1964, pp. 1–15.
24 RUSSELL, I. S., Neurological basis of complex learning, *Brit. med. Bull.*, 27 (1971) 278–285.
25 SCHWARTZBAUM, J. S., KELLICUT, M. H., SPIETH, T. M., AND THOMPSON, J. B., Effects of septal lesions in rats on response inhibition associated with food reinforced behavior, *J. comp. physiol. Psychol.*, 58 (1964) 217–224.

26 SWANSON, A. M., AND ISAACSON, R. L., Hippocampal ablation and performance during withdrawal of reinforcement, *J. comp. physiol. Psychol.*, 64 (1967) 30–35.
27 VALENSTEIN, E. S., The anatomical locus of reinforcement. In E. STELLAR AND J. M. SPRAGUE (Eds.), *Progress in Physiological Psychology, Vol. I*, Academic Press, New York, 1966, pp. 149–190.
28 WARD, H. P., Basal tegmental self-stimulation after septal ablation in rats, *Arch. Neurol. (Chic.)*, 3 (1960) 158–162.