INTERHEMISPHERIC TRANSFER OF LEVER PRESSING AS STIMULUS GENERALIZATION OF THE EFFECTS OF SPREADING DEPRESSION¹

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Rats trained to lever-press with spreading depression in one cerebral hemisphere showed weak responding when tested with depression shifted to the trained hemisphere. The rats were then divided into two groups: one group (normal) was permitted a single reinforced response with neither hemisphere depressed, the other group (depressed) was permitted a single reinforced response with the trained hemisphere depressed; both groups were then tested with the trained hemisphere depressed. Responding during this second test increased for both groups, but the magnitude of the increase tended to be greater for the depressed than for the normal group. Since memory transfer could not have occurred with the trained hemisphere depressed, the results were taken to indicate that the single reinforced response strengthened stimulus generalization between train-test conditions.

Potassium chloride (KCl) applied topically to a cerebral hemisphere produces a temporary depression of electrocortical activity which spreads over the stimulated hemisphere but does not spread interhemispherically (Bures and Buresova, 1960). This phenomenon, known as spreading cortical depression, has recently been used to study the functional relations between the cerebral hemispheres. Russell and Ochs (1963), for example, trained rats to press a lever for food while one hemisphere (nontrained) was depressed and the other hemisphere (trained) was functional. They then tested the rats under extinction, with depression shifted to the trained hemisphere, and found that responding during the extinction test was weak. They then permitted the same rats one reinforced lever press with neither hemisphere depressed (interextinction period), again tested the rats under extinction with depression shifted to the initially trained hemisphere, and found that responding during the extinction test was strong. They concluded, on the basis of the weak responding during the first test, that a memory trace was confined to the trained hemisphere. On the basis of the strong responding during the sec-

ond test, they concluded that the memory trace was provoked to transfer to the non-trained hemisphere during the one interextinction training trial. They further noted, in a second group of rats, that if the response was not reinforced during interextinction training, interhemispheric transfer did not occur.

While the evidence is clear that interextinction training produces interhemispheric transfer, it does not demand an explanation in terms of transfer of memory traces. Rather, it seems equally plausible to hypothesize that interextinction training may produce interhemispheric transfer by a process similar to one which is seen in other cases of transfer, namely the process of stimulus generalization.

If the response conditioned during spreading depression is under the control of the stimuli available to the animal during depression, and if these stimuli are different for the two states of unilateral depression, then processes which are related to stimulus control in general, such as generalization decrement and stimulus generalization, should be relevant here. Specifically, when a response is conditioned in the presence of one set of stimuli, and is tested in the presence of another set, the response strength lost during the test is attributed to the difference between stimuli (generalization decrement), while the remaining response strength is attributed to the similarity between stimuli (stimulus generalization). These stimulus control factors have recently been shown to bear some relationship

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to behavior under spreading depression. Observations of shuttle-avoidance behavior have indicated that weakening of the conditioned response, following a shift from one state of depression to another, may be determined to a large part by generalization decrement (Schneider, 1966) and that strengthening of the conditioned response following interextinction training may be due to stimulus generalization (Schneider and Hamburg, 1966).

Two related assumptions are required to fit the Russell and Ochs study within the stimulus control framework. First, it must be assumed that the few responses emitted during the first extinction test session before the one reinforced lever-press were not made adventitiously, as claimed by Russell and Ochs, but rather were conditioned responses, weakened by the generalization decrement which was produced by the shift in depression. It should be noted that Russell and Ochs' conclusion can be questioned on empirical grounds. Russell and Ochs (1963) assumed that test responses were due to chance factors, since they showed no change in frequency from operant-level responses observed before initial conditioning. However, test responses were observed under unilateral depression, whereas operant-level responses were observed under normal cortical conditions. Since depression lowers the rate of lever pressing (Moelis, 1963), it is inappropriate to employ operant-level responding observed under normal cortical conditions as a baseline for assessing the strength of test responding observed under depression. Secondly, it must be assumed that the one reinforced lever-press during the interextinction period increased responding in the subsequent extinction test by strengthening the weak generalized response, rather than by promoting memory transfer. On the basis of these assumptions we can predict that responding after the single reinforced response will be greater if the trained hemisphere is depressed during both the interextinction and test periods, since stimulus conditions with respect to depression are similar, than if neither hemisphere is depressed during the interextinction period and the trained hemisphere is depressed during the test period, since stimulus conditions are different. Moreover, increased responding following the one reinforced lever-press with the trained hemisphere depressed cannot be accounted for by

the memory transfer hypothesis: it is based on both hemispheres functioning during the interextinction period with one hemisphere emitting and the other receiving the memory trace.

METHOD

Subjects and Surgery

Sprague-Dawley male albino rats, each weighing approximately 250 g, were prepared for spreading depression. A hole, 6 mm long and 3 mm wide, was drilled in the skull over the *parieto-occipital* area of each hemisphere and the incised scalp was retracted and sutured to a rubber grommet which was centered over the holes and plugged with saline-soaked cotton. The surgical preparation is described in detail elsewhere (Schneider and Behar, 1964). To produce spreading depression, a small cotton pledget soaked with 22% KCl solution was placed on the dura of the exposed cortex. In order to determine whether the rats were unilaterally depressed, a behavioral index, directly correlated with spreading depression (Bures, 1959), was employed: the rats were tested for a placing reflex 10 min after KCl was applied. If the paw opposite the depressed hemisphere was lifted, the animal was redepressed. Fourteen animals were discarded because of brain damage and convulsions, and 22 animals were not trainable under spreading depression.

The debilitating effect of repeated spreading depression, and the temporary nature of the surgical preparation, placed the following limitations on the procedure: (1) Skull regrowth and infection appear with increasing frequency after five days, limiting the length of the experiment. Because of this limitation, the training phase consisted of double sessions on each of the first two days. (2) The FR 5 value (every fifth response reinforced) for the training schedule was chosen to ensure a moderate response rate under unilateral depression. Preliminary work indicated that responding could not be reliably sustained with higher ratio values.

Procedure

The animals were placed on a daily 23.5-hr water deprivation regimen six days before surgery and were trained to lever press with one hemisphere depressed the day after sur-

gery. During the next three days, each animal was trained for four sessions with one hemisphere depressed and was tested under extinction with the other hemisphere depressed. The training consisted of lever pressing in a standard Lehigh Valley rat chamber for water delivered on a continuous reinforcement schedule during the first session; for the next three sessions, every fifth response was reinforced (FR 5). Each session lasted 1 hr; two training sessions were given daily for the first two days with approximately 8 hr between each daily session. The first extinction test (Ext 1), with only the nontrained hemisphere functional, lasted 1 hr and was given 23 hr after the fourth training session. Water was given for 30 min after the fourth training session and after Ext 1.

The animals were divided, 23 hr later, into two groups and were permitted one reinforced lever press (interextinction training). In one group ($N = 8$, Normal) the reinforced response occurred with both hemispheres functional; in the other group ($N = 8$, Depressed) the reinforced response occurred with only the nontrained hemisphere functional. In all 16 cases, the response occurred within 30 min. Thirty minutes later, each group was given a 1-hr test (Ext 2) with only the nontrained hemisphere functional.

RESULTS AND DISCUSSION

The acquisition behavior was similar for both groups: the median number of responses emitted during the final training session by the normal group was 857 and by the depressed group, 884. There was no indication of the characteristic fixed-ratio pattern of responding in either group. Figure 1 presents the median responses made by each group during the two extinction sessions. Under two different types of interextinction training a common result was obtained: with neither hemisphere depressed, or with the trained hemisphere depressed, a single reinforced response produced an increase in responding. The effect with neither hemisphere depressed was identical to that obtained by Russell and Ochs; however, the effect with the trained hemisphere depressed was at variance with their memory transfer position.

It may be argued, however, that the increased responding that followed the single

reinforcement under depression can be accounted for by the memory transfer hypothesis if an additional assumption is made: that the single reinforced response during depression can provoke a memory trace to transfer from the depressed to the functional hemisphere. This line of reasoning may account for the observed increase in responding that followed the single reinforced response with one hemisphere depressed, but it offers no basis for the finding that the magnitude of the increase tends to be greater for the unilaterally depressed than for the normal group. This difference between the groups is not surprising, however, when evaluated in terms of the stimulus generalization hypothesis. Specifically, generalization between interextinction training and Ext 2 would be expected to be somewhat greater in the unilaterally depressed group, where depression conditions did not change, than in the normal group, where depression was maintained only during extinction.

A second argument against the stimulus generalization hypothesis is that the increased responding during Ext 2, following the single reinforced response under depression, was produced by reinforcement of a chance response rather than reinforcement of a weak conditioned response. This notion was rejected for two reasons: first, operant-level responding was so low under unilateral depres-

Fig. 1. Median number of lever presses for each group before (Ext 1) and after (Ext 2) the single reinforced response. Solid bars represent the group that was permitted the single reinforced response with neither hemisphere depressed, striped bars represent the group that was permitted the single reinforced response with the trained hemisphere depressed.

sion that animals were difficult to condition initially; 22 animals were not trainable; second, trainable animals required a large number of reinforcements during initial training to condition and to sustain the lever-press under unilateral depression. It seems likely, therefore, that the high rate of responding after the single reinforced response under depression was due to the reconditioning of a conditioned response weakened by generalization decrement, rather than the original conditioning of a chance response.

The stimulus control hypothesis has important implications for the one other study that has demonstrated single-trial interhemispheric transfer under spreading depression (Ray and Emley, 1964). Following initial unilateral training in a T-maze, Ray and Emley failed to obtain interhemispheric transfer of a successive light-dark discrimination if the trained hemisphere was depressed 15 sec (immediate group) after one interextinction trial; transfer was obtained if the trained hemisphere was depressed 10 min (delayed group) after the interextinction trial. These results were taken to indicate that immediate depression interfered with the memory trace produced by interextinction training, that delayed depression did not interfere with the memory trace, and thus did not interfere with the subsequent transfer.

Although this explanation is plausible, it may be subject to question on the basis of the striking results obtained by Ray and Emley during the extinction tests, in which the animals were supposed to behave naively (choose both sides of the maze equally). Specifically, out of the 24 trials with the trained hemisphere depressed before and after (immediate depression) interextinction training, only two correct responses were made. These results indicate that some of the effects of prior learning were retained, in that the animals actively avoided making the correct choice. Ray and Emley conjectured that "the original learning may have been an inhibition of the incorrect response and the release of this inhibition, following depression of the trained hemisphere, made the incorrect response highly probable." In a later study, however, Bivens and Ray (1965) reported that with a simultaneous light-dark discrimination in a T-maze, chance responding occurred with the trained hemisphere depressed during the

same "naive" conditions mentioned above. Thus, the basic problem raised for Ray and Emley is precisely how to explain that "release of inhibition" makes the incorrect response highly probable in the successive but not in the simultaneous discrimination.

If, on the other hand, the training during unilateral depression is visualized within a stimulus control framework, the difference between simultaneous and successive discrimination is not surprising. Consider an animal depressed in the right hemisphere and trained on a successive discrimination to respond to the right side of the maze with light-on and to the left side with light-off. If depression in the right hemisphere produces unique sensory or motor feedback (*e.g.*, paralysis in left limbs) then conditioning may come under partial control of depression-produced cues; with light-on, responding away from the impaired limb is reinforced; with light-off, responding toward the impaired limb is reinforced. With depression then shifted to the left hemisphere during extinction (paralysis in right limbs), responding should be reversed in a manner noted by Ray and Emley. In contrast, in a simultaneous discrimination, responding to depression-produced cues is randomly reinforced, and therefore depression should not acquire differential control of left and right responding. Therefore, when depression is shifted to the trained hemisphere, responding should not be reversed, but rather should be generally disoriented as noted by Bivens and Ray.

This interpretation does not account for the differential effects on transfer of immediate and delayed depression. The immediate group, however, was depressed almost twice as long as the delayed group at the onset of the retention test, which was given 30 min after the interextinction trial. It is possible, therefore, that the two groups were under different stimulus conditions during the test, so that depression-produced cues operated for the immediate group but not for the delayed group.

Thus, the present findings, together with Ray and Emley's, support the notion that responding during depression is, at least in part, under control of depression-produced stimuli, and that transfer following interextinction training is a stimulus generalization phenomenon.

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