Pretraining effects on the DRL performance of rats with septal lesions*

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Normal rats and rats with septal lesions were run on a DRL 20 schedule following 0, 1, or 10 days of CRF pretraining. Regardless of amount of pretraining, operated animals emitted more responses and obtained fewer reinforcements than did normals. Additionally, the extent of pretraining did not influence the final level of DRL performance. These results were contrasted with findings obtained previously with hippocampal lesions, and the differences in the nature of the dysfunction following septal and hippocampal lesions were explicated.

Perhaps few phenomena in the neuropsychological literature have been as well documented as the overresponding shown by animals with septal and hippocampal lesions on a DRL or differential reinforcement of low rates operant schedule (Agnew & Meyer, 1969; Burkett & Bunnell, 1966; Caplan & Stamm, 1967; Caplan, 1970; Carey, 1967a, b; Clark & Isaacson, 1965; Ellen & Aitken, 1970, 1971; Ellen, Aitken, & Walker, 1973; Ellen & Butter, 1969; Ellen, Wilson, & Powell, 1964; Haddad & Rabe, 1967; MacDougall, Van Hoesen, & Mitchell, 1969a, b; Schmaltz & Isaacson, 1966a, b, 1968). Typically, such animals emit high rates of response and persist in doing so despite extended training on the DRL schedule. As a consequence, relatively few reinforcements are obtained by the operated animals.

In view of the phenotypic similarity between the behavioral effects of septal and hippocampal lesions on DRL schedules, some investigators have been tempted to attribute systemic significance to the phenomenon (e.g., MacDougall, Van Hoesen, & Mitchell, 1969a). Indeed, this hypothesis becomes particularly compelling in view of the intimate anatomical connections between septum and hippocampus (e.g., Nauta, 1956, 1958; Powell, 1963, 1964b, 1966; Raisman, Cowan, & Powell, 1966; Russell, 1961). For example, in a study of the anatomical organization of septal projections in the maintenance of DRL behavior in rats, MacDougall, Van Hoesen, and Mitchell (1969a) found that the "greatest deficits" in DRL 20 performance were "associated with damage to the entire fornical-fimbrial bundle, which would interrupt virtually all afferent and efferent septal-hippocampal and hippocampal-septal fibers [p. 574]." More recently, Fried (1972), in referring to the inability of animals with septal lesions to alter behavior in those situations in which only response-produced feedback is available as a cue, suggests that because septal, fornix, and hippocampal damage all lead to similar alterations in operant (and

other) behaviors, and since septum has both afferent and efferent connections with hippocampus via fornix-fimbria fibers, then "it is likely that this aspect of septal dysfunction is mediated via the septal-hippocampal system [p. 304]."

However, anatomic connectivity and a similarity in the behavioral patterns exhibited following septal and hippocampal lesions are not a sufficient basis for assuming a common dysfunction. Rather, similar appearing behavior patterns may actually be quite different in terms of the mechanisms underlying such behavior (Ellen, 1966). To the extent that this can be demonstrated, it would argue strongly against the hypothesis of a common function being implicated by different lesions or that a single function is being mediated over the particular pathways. The present study will demonstrate that the influence of CRF pretraining in animals with septal lesions is not comparable to that found when this factor was previously investigated in animals with hippocampal lesions (Ellen et al, 1973), and hence the overresponding by animals with septal lesions on this schedule would seem to represent a qualitatively different impairment than that obtained with damage to the hippocampus.

METHOD

Subjects

Thirty male Long-Evans hooded rats, averaging 377 g in weight at the beginning of the experiment, served as Ss in this study. Fifteen rats received electrolytic septal lesions and 15 served as unoperated control animals. Each normal and operated group was further subdivided according to the CRF (continuous reinforcement) pretraining conditions of 10, 1, and no days of CRF, making a total of six groups of 5 rats each. Each rat was individually housed with water available ad lib for the duration of the experiment. All animals were maintained at 80% of ad lib body weight throughout the experiment through a post-run feeding of an appropriate amount of a wet mash of ground Purina Lab Chow, available for 1 h. Thus, the animals were also 22 h deprived at the beginning of each daily session.

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Fig. 1. Changes in responding (A) and frequency of obtained reinforcement (B) on DRL as a function of amount of CRF pretraining (septal, open figures; normal, closed figures).

Apparatus and Behavioral Procedures

Pretraining

Four of the six groups (two with septal lesions and two normal) were given either 1 or 10 days of CRF pretraining prior to being placed on the DRL schedule. These animals were placed in the operant chamber until they received 150 reinforcements on the CRF schedule. This constituted the only day of CRF pretraining for the 1-day CRF pretrained group and the first day of pretraining for the 10-day groups. Additionally, the operated 10-day pretraining group was run for 5 consecutive days on CRF, operated upon the following day, and exposed to 5 more consecutive days of CRF beginning the day following surgery. The control animals in the 10-day condition received 10 consecutive days of CRF pretraining. The operated and normal groups in the 1-day pretraining condition received their pretraining on the day following the surgery of the operated group. These groups were placed on the DRL schedule on the day following completion of the CRF pretraining. The remaining two groups (no-CRF pretraining condition) were placed in the operant chambers on the DRL schedule with no prior bar training whatsoever on the day following the surgery of the operated group. These latter groups acquired the barpressing habit under the DRL schedule and then were allowed an additional 50 min of training as their first DRL day.

DRL Training

All animals were run 50 min daily on the DRL 20 schedule for 15 days. On this schedule, only those responses which were separated by 20 or more sec were reinforced by a 45-mg food pellet (Noyes). The five animals in a particular lesion-pretraining condition were run at the same time in five Scientific Prototype

single-bar operant chambers. The operant chambers were linked to the IBM 1800 Data Acquisition and Control System described previously (Ellen & Aitken, 1971), which programmed the runs and reinforcement schedules and recorded interresponse times for each animal.

Surgery and Histology

The operated groups received bilateral anodal electrolytic septal lesions (2.0 mA for 15 sec on both sides) placed bilaterally to the midline, 7.8 mm anterior to and 6.5 mm above the interaural line. The electrode consisted of a stainless steel sewing needle insulated except for 0.50-0.75 mm at the tip with acrylic plastic spray. Lesion coordinates were taken from the rat brain atlas of Pellegrino and Cushman (1967) and localized with the aid of a Baltimore Instrument Company stereotaxic instrument. All operated animals received sodium pentobarbital (Nembutal) anesthesia (40 mg/kg body weight, IP) supplemented with 0.5 cc (0.2 mg) atropine sulfate to reduce respiratory distress. In addition, local infiltration of lidocaine hydrochloride (2%) with epinephrine (Xylocaine) was used locally to supplement the Nembutal anesthesia and to reduce any bleeding. Following anesthetization, the head was shaved and a longitudinal incision was made to expose the skull. Holes were drilled in the skull at the appropriate coordinates with a dental drill, the electrode was lowered to the lesion coordinate, and the lesion made. Then the electrode was withdrawn, the scalp sutured, and the rat was given a 0.2-cc IM injection of procaine penicillin G (60,000 units, Duracillin). At the completion of the experiment, the brains of the operated animals were removed and fixed in Formalin, frozen, and serially sliced, with sections photographed as wet slides in order to verify the localization of the lesion (Powell, 1964a).

RESULTS

Anatomical Findings

Septal lesions were nearly total and typically uniform, extending from the level of the medial parolfactory area (or about 9.0 mm anterior to the interaural line) and terminating at the level of the hippocampal commissure where fimbria forms the body of the fornix, approximately 5.5 mm anterior to the interaural line. Additionally, two animals in each of the pretraining groups suffered very slight damage to corpus callosum and overlying neocortex at this point.

Immediately following surgery, all animals showed some degree of "septal rage," which, in most cases, disappeared within 6-10 days postoperatively. In no instance was there any obvious evidence of a relationship between this behavior and the DRL performance of the various operated groups.

Behavioral Findings

Figure 1 presents the changes in responses emitted and reinforcements obtained over the 15 days of DRL 20 training by the various groups of normal and operated animals. For each of the response and reinforcement measures, a separate three-factor analysis of variance was performed (Lesions by Days of CRF Pretraining by Days of DRL Training, with repeated measures on days of DRL). Amount of CRF pretraining

had no significant effect on either the number of responses emitted ($F = 0.13$, $p > .10$) over the 15 days of DRL training or the number of reinforcements obtained ($F = 0.01$, $p > .10$). However, as can be noted in Fig. 1A, animals with septal lesions responded more than did normals, irrespective of pretraining conditions, over the entire course of DRL training ($F = 4.26$, $p < .05$), and both normals and operated animals showed a general decline in responding over the course of DRL training ($F = 4.88$, $p < .01$). The Pretraining by Days interaction effect was also significant ($F = 1.82$, $p < .01$), reflecting the fact that the changes in responding over days of DRL training were different depending on the type of pretraining received. That is, responding of normal and operated animals receiving 10 days of CRF pretraining declined from the first to the last day of DRL 20 training, while that of the operated groups receiving little or no pretraining and normals receiving no pretraining started at a lower point and increased early in training up to the levels of the other groups, and then all groups declined together for the remainder of DRL training with pretraining making no further differences.

Turning next to reinforcements (Fig. 1B), once again only lesion effects, days of DRL training effects, and the Pretraining by Days of DRL interaction effects were significant. Operated animals received fewer reinforcements than did normals ($F = 17.23$, $p < .01$), and reinforcement levels tended to increase over the course of DRL training ($F = 3.25$, $p < .01$), in both cases irrespective of pretraining conditions. Thus, the higher response levels of the operated animals was accompanied by lower reinforcement levels. The significant Pretraining by Days of DRL interaction ($F = 1.96$, $p < .01$) reflects the fact that the level of reinforcement on only the first day of DRL training varied somewhat as a function of pretraining, the groups receiving no pretraining obtaining somewhat more reinforcement than the other pretraining groups.

Responses emitted and reinforcements obtained in each succeeding 5-min interval of the 50-min session on Days 1, 4, 8, and 12 were determined for all animals. Then, response and reinforcement measures were subjected to separate four-factor analyses of variance (Lesions by Days of Pretraining by DRL Days by Intervals, with repeated measures on DRL days and intervals). Once again, operated animals responded more overall ($F = 52.24$, $p < .01$) and received fewer reinforcements overall ($F = 23.58$, $p < .01$) than did normals. However, even though pretraining had no significant overall effects on responding ($F = 1.82$, $p > .10$) or reinforcements obtained ($F = 0.24$, $p > .10$), the within-session changes in both responses and reinforcements were found to depend on the amount of pretraining as well as on the lesion. Figure 2A shows the within-session responding, collapsed over days. Here it can be seen that the within-session responding of normals tended to decline, while that of animals with

Fig. 2. Changes in response output (A) and reinforcements obtained (B) in successive 5-min intervals of the 50-min DRL session as a function of amount of CRF pretraining. Data in these figures are collapsed over days of DRL training (septal, open figures; normal, closed figures).

septal lesions tended to increase (Interval by Lesion, $F = 20.34$, $p < .01$). Moreover, the magnitude of the changes within the session depends on the amount of pretraining ($F = 10.74$, $p < .01$). That is, the within-session decline in responding of normals was *greatest* with the longest pretraining, while the within-session increase in responding of the operated animals was *least* with the most pretraining. In addition, within-session changes in reinforcement can be noted in Fig. 2B, again collapsed over days. Here, reinforcement levels increase early in the session only for normals receiving 1 day of CRF, while reinforcement levels of only those operated animals receiving no pretraining decrease early in the session. Hence, once again both of the interactions of intervals with pretraining ($F = 9.58$, $p < .01$) and lesions ($F = 4.49$, $p < .01$) are significant.

Finally, Figs. 3A and 3B show the day-to-day within-session changes in responses and reinforcements, collapsed over pretraining conditions. It will be noted that again the within-session change depends both on the lesion and the particular day of DRL training (Intervals by Lesion by Days of DRL, $F = 5.59$, $p < .01$). That is, while normal animals show a decline in responding within a session which is present regardless of whether it is the first day of DRL or the 12th day of DRL, operated animals show an increase in responding within a session with the increase being greatest early in the course of DRL training. However, by the 12th day of

Fig. 3. Changes in response output (A) and reinforcements obtained (B) in successive 5-min intervals of the 50-min DRL session as a function of days of DRL training. Data in these figures are collapsed over pretraining conditions (septal, open figures; normal, closed figures).

DRL the operated animals show no within-session changes in responding.

In Fig. 3B the within-session changes in reinforcement similarly depend upon the lesion and the stage of DRL training (Intervals by Lesions by Days of DRL Training, $F = 1.63$, $p < .05$). That is, normal rats obtain approximately the same number of reinforcements in each succeeding 5-min interval of the session, and this does not vary as a function of whether it is the first or the last day of DRL training. In contrast, the operated animals obtain more reinforcements in the early 5-min segments of a session and less in the later 5-min segments. Moreover, this effect becomes less pronounced as training on the DRL schedule progresses, i.e., from Day 1 to Day 12.

DISCUSSION

The present data clearly demonstrate that duration of CRF pretraining does not affect the asymptotic response output of animals with septal lesions on DRL 20. Accordingly, it would be difficult to characterize the overresponding by the operated animals as a perseverative deficit, i.e., a failure to give up a previously established pattern of behavior.

The absence of a pretraining effect in rats with septal lesions on DRL performance stands in marked contrast

to what has been found by ourselves and others with respect to hippocampal lesions (Ellen et al, 1973; Schmaltz & Isaacson, 1966a). In the case of hippocampal lesions, the overresponding symptom occurs only when *both* a large lesion and prolonged CRF pretraining are present. In the absence of prolonged CRF pretraining, hippocampal lesions do not result in overresponding. Thus, the overresponding of animals with hippocampal lesions, when it occurs, would seem to result from a failure to give up or shift from a previously acquired pattern of responding.

The differences between operated animals and normals with respect to the sequential changes in responding within a session are of particular interest in clarifying the role of the septum in behavior. It will be recalled that normal animals showed a within-session decrease in responding that varied directly with the amount of CRF pretraining, i.e., the more pretraining, the greater the decline in responding. This effect, however, did not depend on the stage of DRL training, i.e., Day 1 vs Day 12. In the case of the animals with septal lesions, there was an increase in responding within the session that varied inversely with the amount of CRF pretraining, i.e., the less CRF pretraining, the greater the increase. Moreover, whether or not there was a within-session increase in responding depended on the stage of DRL training. That is, late in the course of DRL training (Day 12), little or no within-session changes are apparent as compared to early in training. Correlated with this was a progressive decrease in the reinforcements obtained by animals with septal lesions within the session, while normals obtained reinforcement at a relatively constant rate. However, it is of great importance to note that regardless of CRF pretraining or stage of DRL training, normal-septal differences are not uniform within a session. That is, the differences in responses and reinforcements emerge only after 5-10 min within the session. It would appear that the relatively few reinforcements obtained by the operated animals had an activating effect not seen in the normals. This activation generates a higher response rate, which in turn leads to less reinforcement, with the final level of responding probably being determined by the density of reinforcement delivered. After continued training on the DRL schedule, this activation resulting from reinforcement tends to habituate. In short, these data would suggest that animals with septal lesions are hyperreactive to reinforcing events, and this hyperreactivity to reinforcement has maladaptive consequences since it generates a persistent overresponding.

It would seem from the results of the present study and our previous one concerning hippocampal lesions (Ellen et al, 1973) that there are a number of limbic response mechanisms having anatomic specificity. The data from the present study suggest that the septal lesion produces a deficit in a response modulating or attenuating mechanism that is reflected by a

hyperreactivity to external stimuli (Schwartzbaum, Green, Beatty, & Thompson, 1967) such as reinforcement, while the data from our study of hippocampal lesions would point to an impairment in a response flexibility mechanism, i.e., a mechanism which allows animals to shift from one response to another. Either of these dysfunctions apparently leads to the same behavioral outcome, namely, an overresponding on DRL. Thus, it is evident that a common behavioral symptom resulting from different lesions is not sufficient evidence in and of itself of a common dysfunction in anatomically related structures.

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