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Effects of Hippocampal X-Irradiation-Produced Granule-Cell Agenesis on Instrumental Runway Performance in Rats

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BRUNNER, R. L., S. J. HAGGBLOOM AND R. A. GAZZARA. *Effects of hippocampal x-irradiation-produced granule-cell agenesis on instrumental runway performance in rats.* PHYSIOL. BEHAV. 13(4) 485–494, 1974. – Rats in which x-irradiation during early postnatal life had interfered with the acquisition of dentate granule cells ran faster than controls during extinction of a runway response acquired under a consistent food reward schedule. A training schedule of randomly rewarded and nonrewarded trials increased running speeds to an equal extent in x-irradiated and control groups during extinction. The second and third experiments showed that unlike a reported total inability of hippocampal lesioned rats to pattern their running responses appropriate to a single alternation schedule of reward and nonreward, x-irradiated rats, while impaired in acquiring response alternation, did pattern and had persistent deficits compared to controls only when the task was made very simple by reducing the number of daily trials to two. The results are discussed in terms of an hypothesized reduction in the aversiveness of nonreward and a consequent reduction in the growth of inhibition in x-irradiated rats.

Dentate granule-cell agenesis Runway performance

TWO previous studies have explored the behavior of rats in which neonatal acquisition of granule cells of the dentate gyrus had been almost totally prevented (termed "granule-cell agenesis") by exposure of that region of the brain to low-level x-irradiation between days two and fifteen of life [4,15]. The three experiments reported here sought to determine the effects of early hippocampal x-irradiation on appetitively motivated instrumental behavior in the straight runway. Although runway studies have traditionally been a rich source of information about reinforcement influences on acquisition performance and extinction, relatively few studies have been completed in hippocampal lesioned animals. Moreover, the possible importance of motivational changes in hippocampal lesioned rats was again advanced in a recent review [1].

EXPERIMENT 1

The retardation of extinction of an instrumental response by randomized partial reinforcement (PRF) rela-

tive to consistent reinforcement (CRF) during acquisition is known as the partial reinforcement extinction effect (PREE). Gray [12] and Gray, Araujo-Silva and Quintao [13] postulated that PREE is at least in part mediated by a system involving hippocampal theta rhythm. Gray, Quintao and Araujo-Silva [14] lesioned the septal region, usually causing a disruption or elimination of theta in the hippocampus. Septal lesions made before acquisition resulted in a small but significant reduction in the size of the PREE, as lesioned PRF animals extinguished more rapidly than nonlesioned PRF animals and lesioned CRF animals extinguished slower than nonlesioned CRF animals. Gray's hypothesis that interference with normal hippocampal theta activity produced the alteration in the PREE was not supported by Bloom and McFarlain [5] or by Franchina and Brown [9]. Bloom and McFarlain did not find a significant attenuation of the PREE in rats given hippocampal lesions prior to acquisition while Franchina and Brown did not obtain a difference in resistance to extinction between lesioned and nonlesioned PRF groups.

It may be that the hippocampal lesions made by Bloom and McFarlain [5] did not match septal lesions [14] or stimulation [12,13] in ability to disrupt a critical neural circuit. Alternatively, the PREE may be regulated by the medial septal nucleus rather than the hippocampus. That the hippocampus participates in the process underlying the PREE, however, has also been argued by Amsel, Glanzer, Lakay and McCuller [3]. Amsel *et al.* [3] showed that a novel stimulus presented during appetitive bar pressing for food increased resistance to extinction in operated controls but not in rats with lesions of the hippocampus. According to Amsel [2] the PREE may represent a specific instance of the counterconditioning of a general class of stimuli which otherwise interfered with an ongoing response. Possibly, hippocampal damage interferes with a rat's ability to process disruptive or emotional events.

The present experiment investigated the PREE in normal and hippocampal x-irradiated rats. There is some evidence that hippocampal x-irradiation, like hippocampal lesions, interferes with the rats' ability to process disruptive or emotional events [4,15]. Thus, it would be useful to know whether x-irradiation-produced interference with dentate gyrus granule cell acquisition disrupts behavior, e.g., the PREE, thought to be regulated largely by stimulus consequences of an aversive emotional reaction to nonreward [2,7].

Method

Animals. Male Wistar rats 80–120 days old at the time of testing were used. Ten rats were randomly selected from litters that had been x-irradiated according to a procedure described in an earlier study [4]. Ten rats of comparable age and weight were selected from control litters bred in the laboratory. All rats were housed singly.

Apparatus. The apparatus was an L-shaped runway-goal box unit 10 cm wide × 18 cm high. The runway section was 122 cm long and the goal box, which was mounted perpendicular to the end of the left side wall of the runway, was 30.4 cm in length. The runway had a 10 cm wide guillotine door at the goal box entry which could be lowered manually to prevent retracing. The runway and initial 15 cm of the goal box were painted medium grey and the remaining 15.5 cm of the goal box was painted white. Both the runway and goal box had hinged hardware cloth lids and wood floors. A wood cube painted white with a 3 cm × 1.5 cm depression served as a food cup.

The apparatus was divided into four segments. Placing the animal in the beginning of the alley interrupted a photo beam 10 cm from the forward wall and started the first 0.01 sec clock. Interruption of a photo beam 23 cm beyond the first beam stopped Clock 1 (start time) and activated Clock 2. When the animal interrupted a third photo beam 61 cm beyond the second photo beam Clock 2 stopped (run time) and Clock 3 started. Clock 3 stopped (goal −1 time) and Clock 4 was activated when a photo beam 15.5 cm past the third photo beam was interrupted. Interruption of a photo beam 5 cm inside the goal box stopped Clock 4 (goal −2 time).

Procedure. On Day 1 all animals were placed on a 12 g/day feeding cycle which was continued throughout the experiment. Water was available ad lib in the home cage. During acquisition the amount of food was adjusted by subtracting from it the amount of food received in the runway. Over Days 1–7 the animals were adjusted to the feeding schedule with food being delivered at approximately the same time each day. The animals were handled on Days 8–12 in groups of 4 for 90 sec/group. On Days 11 and 12 each animal was given ten 0.045 g Noyes pellets in a small dish placed in the home cage. Each then received three rewarded runway trials, one per day, on Days 13, 14 and 15. On Day 16 the animals were assigned to one of four experimental groups defined by a 2 × 2 factorial combination of irradiation treatment (irradiation vs. control) and reinforcement schedule (partial, PRF, vs. consistent, CRF, reward) and acquisition training began. The 10 CRF rats received five rewarded trials per day for eight days. The 10 PRF rats received 5 trials per day on one of the following four reinforcement schedules where R identifies reward and N identifies nonreward: RNRNR, NRNNR, RRNNR, RNNNR. The schedules were used in the above order on Days 16–19 and repeated in the same order for Days 20–23. On rewarded trials the animals received ten 0.045 g Noyes pellets while on nonrewarded trials in both acquisition and extinction they were confined to the goal box for 20 sec.

The animals were run in squads of four, composed of one animal from each group. Each animal in a squad received its first trial before any animal in that squad received its second trial, and so on, resulting in an intertrial interval of 3–4 min. The squad order was constant across days but the order of running animals within each squad was randomized daily. Extinction began on Day 24 with each rat receiving 5 trials per day for four days. The running procedures were the same as in acquisition except that all trials were nonreinforced. During extinction a maximum criterion time of 30 sec was allowed in each section of the apparatus. If an animal exceeded the criterion time in any one section, this additional time was subtracted from the criterion time allowed in the next section forward and added to the latency score of that section. When an animal refused to approach the food cup within the criterion time, it was placed in the goal box and confined for the usual 20 sec.

Histology. All x-irradiated rats and five randomly selected control rats were perfused with 10% buffered Formalin. The brains were removed and post-fixed in Bouin's solution for 24 hr after which they were returned to Formalin which was changed several times during a period of from 1–2 weeks before further processing. Most

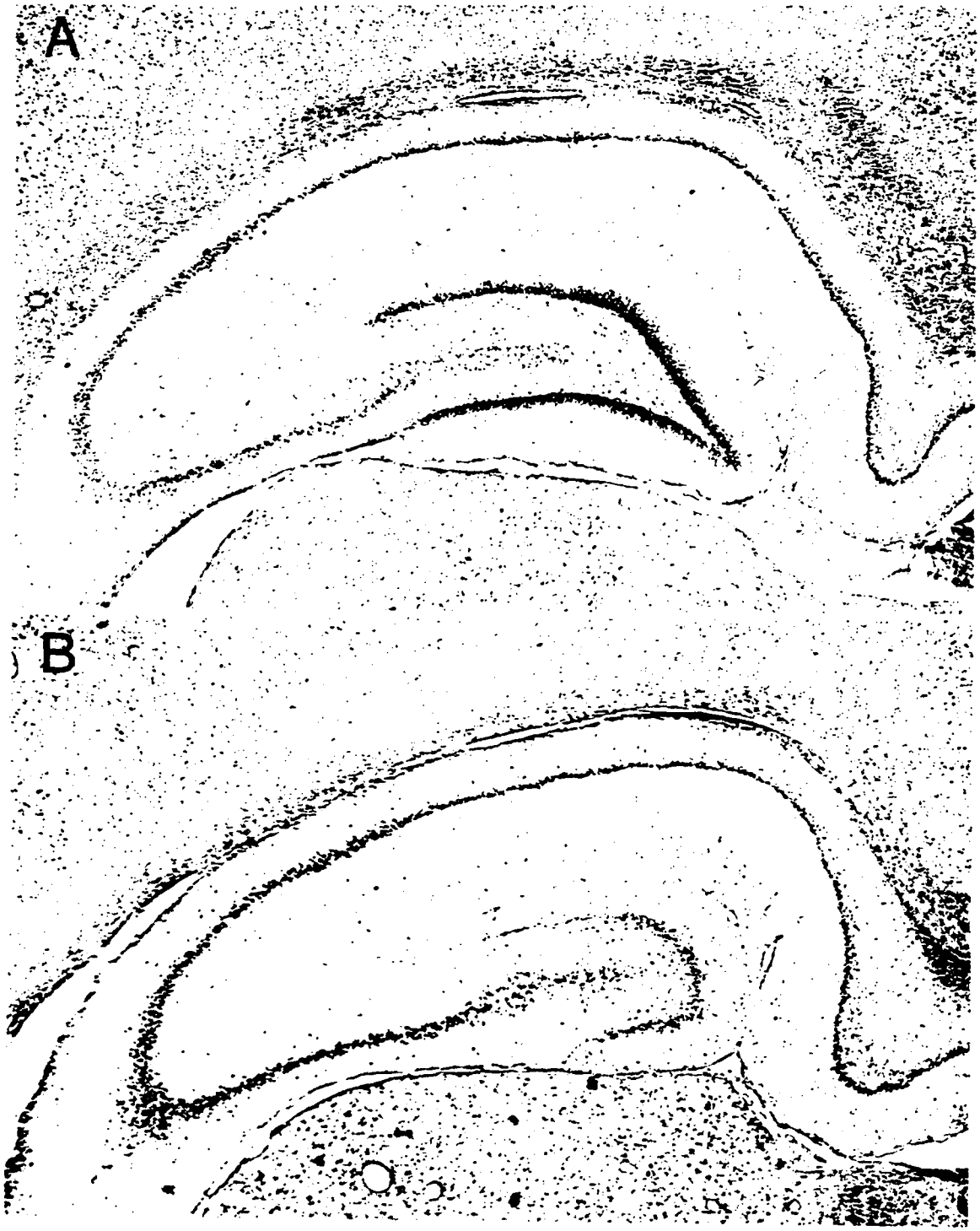

FIG. 1. Photomicrographs of representative coronal brain sections showing the dorsal hippocampus in a non-irradiated subject (A) and the reduction in the granule cell population of the dentate gyrus produced by x-irradiation (B). Magnification 28.5X, H&E.

brains were sectioned sagittally, mounted and stained for examination to verify a reduction in dentate granule cells as previously reported [4,15]. Photomicrographs of typical brain sections appear in Fig. 1. The brains of five irradiated and two controls were sectioned at 6 μm throughout the frontal extent of the hippocampus and stained with hematoxylin and eosin. Anatomically matched sections were selected and all granule cells counted at a magnifi-

TABLE 1

GRANULE CELL NUMBERS IN SINGLE ANATOMICALLY MATCHED CORONAL BRAIN SECTIONS OF ANIMALS SELECTED FROM THE PRESENT STUDY

	Animal	Cell Count
Control		
PTE-SA	C-2	1918.0
PTC-SA	C-9	1995.0
Irradiated		
PTC-SA	XL 4-3	348.0
PTC-SA	XL 3-5	267.0
PTC-SA	XL 3-3	311.0
PTE-SA	XL 3-1	278.0
PTE-SA	XL 4-4	323.0

cation of 312.5X with the aid of a microscope fitted with an ocular grid. Dentate granular-cell counts appear in Table 1.

Results

The times from each runway section were converted to speeds by reciprocation (1/sec). As results were essentially the same in each alley section, only run speeds are reported. Histology revealed that one animal in group H-PRF had not been irradiated, therefore, this animal's data were omitted from all analyses.

Figure 2 shows the mean speed of each of the four experimental groups on each day of acquisition. As can be seen, differences due to reward schedule were small. However, differences due to irradiation treatment were apparent throughout acquisition with irradiated animals running slower than controls regardless of reward schedule. A 2 × 2 × 8 × 5 analysis of variance (unweighted means solution for unequal n, 23) which included irradiation treatment (Treatment) and reinforcement schedule (Schedule) as between-animals factors and Trials and Days as within-animals factors was applied to run speeds over the entire acquisition period. The analysis of variance showed that differences due to Treatment were significant ($F = 6.91$, $df = 1/15$, $p<0.01$) while differences due to Schedule and the interaction of Treatment and Schedule ($F<1$) were not. The Days factor was the only other significant source

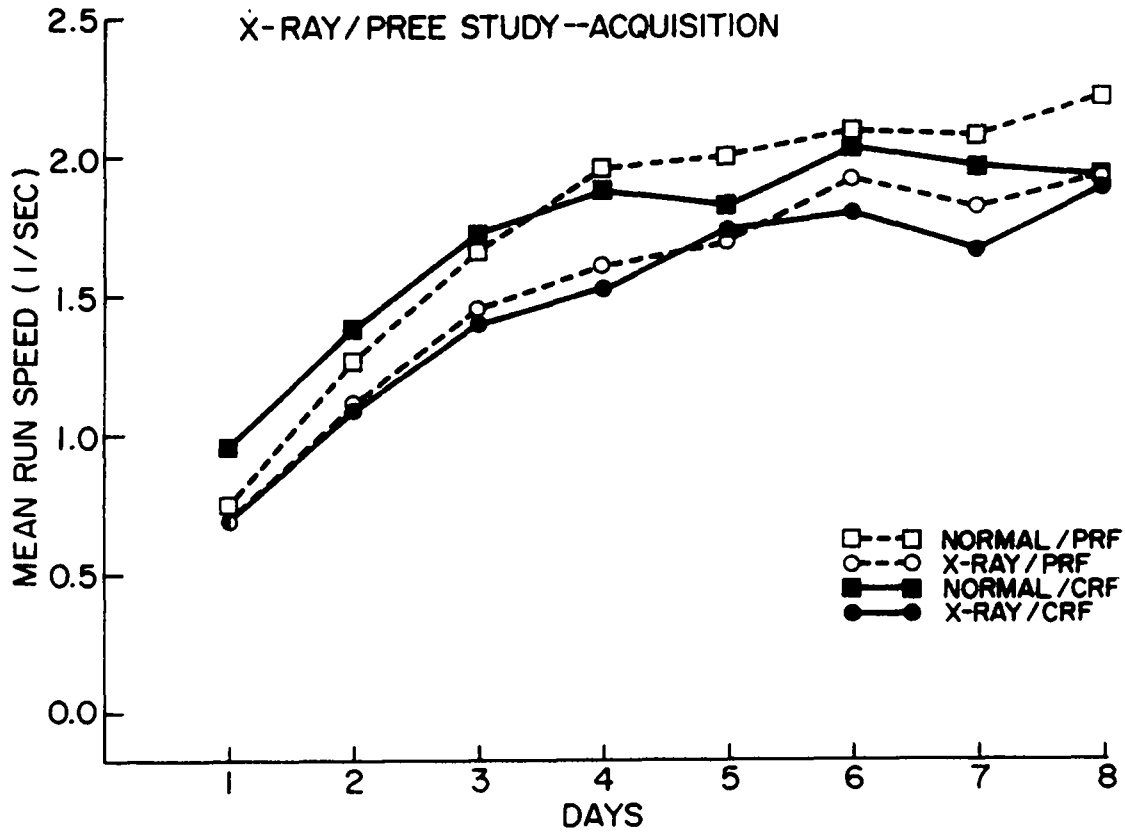

FIG. 2. Speed of running for each of the four groups on each day of acquisition in the run section.

of variance. Newman-Keuls tests, employing the appropriate pooled error term from the overall analysis of variance [23] showed that the irradiated-PRF animals were still running slower than the control-PRF by the last day of acquisition ($p<0.01$) while no other differences among groups were significant.

Figure 3 shows the speed of running on each of the 20 extinction trials for all four groups. Discontinuations in the curves for each group occur between the last trial of one extinction day and the first trial of the following day. As can be seen, both irradiated and control PRF groups appear to be more resistant to extinction than their respective CRF control groups. However, the PREE was larger for control than for irradiated animals as irradiated PRF animals were less resistant than control PRF animals and irradiated CRF animals were more resistant than control CRF animals. It should be noted, however, that differences between the CRF groups developed during extinction, and became larger over trials and days. Differences between the two PRF groups remained constant throughout extinction and appeared to reflect a continuation of the trend toward slower running observed in irradiated rats during acquisition. These observations were corroborated by a 2 (Treatment) x 2 (Schedule) x 4 (Days) x 5 (Trials) between-within analysis of variance on extinction speeds. The greater resistance to extinction of PRF animals over CRF animals was supported by a significant effect of Schedule ($F = 136.67$, $df = 1/15$, $p<0.001$) while the difference in the size of the PREE contributed to a significant Schedule x Treatment interaction ($F = 42.86$, $df = 1/15$, $p<0.001$). Partitioning this interaction into simple effects [23] of Schedule at each Treatment showed that the PREE was significant for both control ($F = 176.7$, $df = 1/15$, $p<0.001$) and irradiated ($F = 12.5$, $df = 1/15$, $p<0.01$) animals. In addition, simple effects of Treatment at each Schedule showed that hippocampal x-irradiation increased resistance to extinction after CRF training ($F = 25.97$, $df = 1/15$, $p<0.001$) but that the irradiated PRF animals were less resistant than the control PRF animals ($F = 17.59$, $df = 1/15$, $p<0.001$). However, the observation that these differences developed during extinction for CRF animals, but reflected a continuation of acquisition differences for PRF animals, was supported by a Treatment x Schedule x Trials interaction ($F = 2.55$, $df = 4/60$, $p<0.05$). Simple interactions of Treatment x Trials at each Schedule showed that the two PRF groups did not differ in rate of extinction over trials ($F<1$) while the control-CRF group extinguished faster than the irradiated-CRF group ($F = 11.34$, $df = 4/60$, $p<0.001$). It has been suggested that differential resistance to extinction between groups performing differently in acquisition cannot be unambiguously attributed to effects of acquisition treatment per se on resistance and extinction unless those groups extinguish at different rates (e.g., [6]).

Discussion

Hippocampal x-irradiated rats were found to extinguish

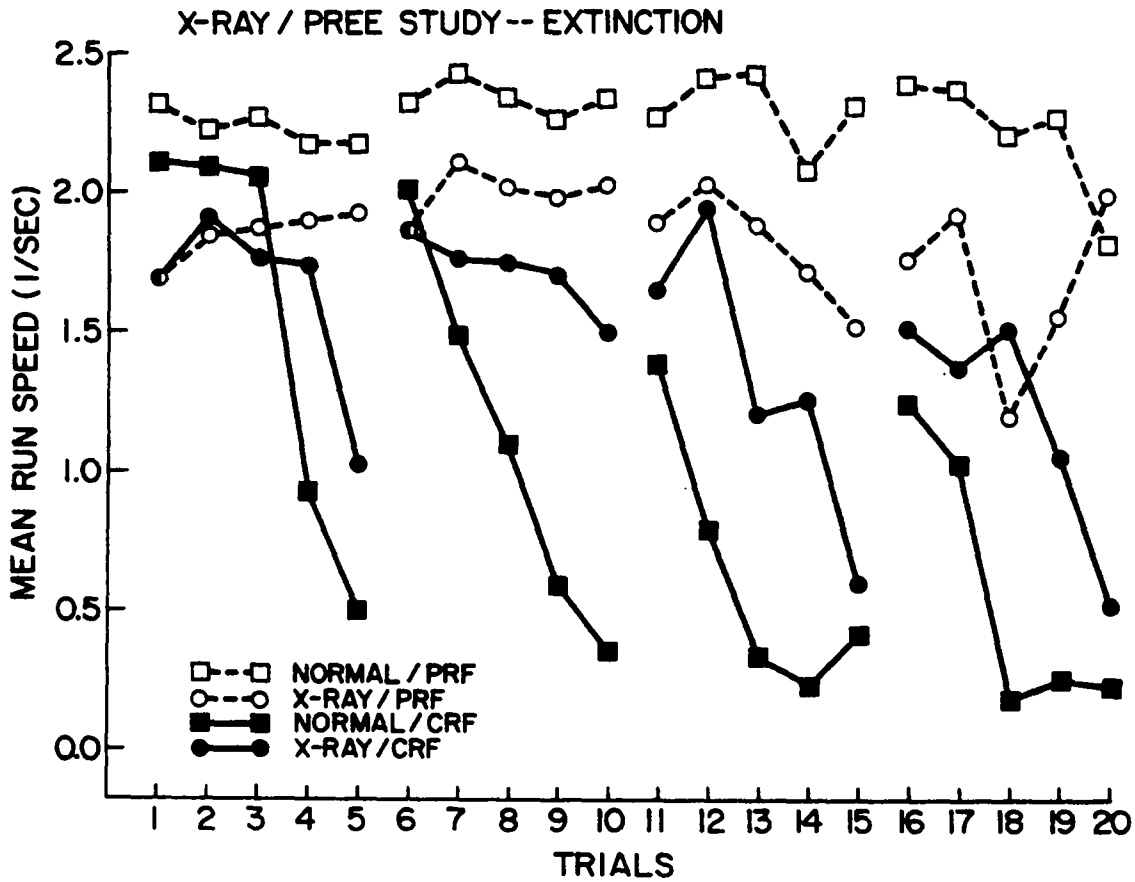

FIG. 3. Speed of running for each of the four groups in each trial of extinction in the run section. Group curves are interrupted between the last trial of one extinction day and the first trial of the subsequent day.

a runway response acquired on a CRF schedule more slowly than controls. This same result has been reported for animals that had conventional lesions of the hippocampal complex [18,20]. In the current experiment, hippocampal x-irradiated rats responded like both hippocampal lesioned rats and control rats [5] in running faster during extinction after PRF training than after CRF training. The relative magnitude of the PREE was smaller in x-irradiated rats than in controls due in part to faster running of irradiated CRF rats but also in part to the continuation during extinction of the slow overall pace of irradiated PRF rats observed during acquisition. While slower running in hippocampally damaged animals has been reported [5,22] it has not been a consistent finding ([10], Experiments 2 and 3 of the present study), and the cause of these differences has not been determined.

It would appear that the PREE is not entirely dependent on the integrity of the hippocampus. The fact that x-irradiated rats in the present experiment and lesioned rats in another experiment [5] showed a PREE suggests that hippocampal rats are in some way responsive to nonreward. Hence, their heightened responding during extinction after CRF acquisition cannot be attributed to a failure to notice changing reinforcement contingencies. It might, however, be due to a failure of irradiated rats to respond to some portion of the stimulus complex produced by nonrewarded extinction trials. For example, the present results are similar to those obtained with rats trained and extinguished under sodium amobarbital, a drug which seems to interfere with the aversive or frustrative reaction to nonreward and with theta activity in the hippocampus [11]. Capaldi and Sparling [7] suggested that extinction performance after partial reinforcement can be regulated in large part by neutral stimuli produced by nonreward. This conclusion was based on the ability of partial reinforcement to increase resistance to extinction even under amobarbital or training procedures which reduce anticipatory frustration or other aversive emotional reactions to nonreward. Thus, it would be argued that an attenuation of such aversive consequences of nonreward in hippocampal lesioned or x-irradiated rats would not necessarily reduce resistance to extinction following partial reward training but would be expected to increase resistance to extinction following continuous reinforcement.

EXPERIMENT 2

When reward and nonreward occur on alternate trials in the straight runway, rats eventually learn to pattern their responses appropriately, i.e., to respond fast on rewarded and slow on nonrewarded trials. Single alternation behavior in the runway, where external stimuli remain relatively constant from trial to trial, appears to be extensively regulated by internal stimulus consequences of reward and nonreward occasioned on the immediately preceding trial [6] as stimuli produced by reward (S^R) are always followed by nonreward and stimuli produced by nonreward (S^N) are always followed by reward.

Franchina and Brown [9] reported that hippocampally lesioned rats failed to acquire an appropriate single alternation pattern of responding after as many as nearly 100 trials although normal and neocortically damaged rats had solved the discrimination problem much earlier.

Single alternation learning was assessed in the present experiment as a continuation of a program of testing hippocampal x-irradiated rats in behavioral paradigms which have been shown to be sensitive to the effects of hippocampal lesions.

Method

Animals. Fourteen male Wistar rats, seven controls and seven irradiated of the same description as those used in Experiment 1 were used in this experiment.

Apparatus. The apparatus consisted of a straight runway 136 cm long × 9 cm high and wide constructed of wood with a hinged hardware cloth lid. The runway had a 25 cm long × 5 cm wide start box, with the final 8.5 cm of each side wall tapered to accomplish the increase in width from start box to alley. The start box and runway were painted black. The runway was divided into three sections over which start, run, and goal times were recorded. Lowering the solenoid-operated guillotine door through a hole in the floor permitted the animal access to the runway and activated the start (0.01 sec) clock. Interruption of a photo beam 55 cm into the runway stopped the start clock and started the run clock. Interruption of a second photo beam 96 cm into the runway stopped the run clock and started the goal clock which was stopped when the animal broke a third photo beam 126 cm into the runway and 3.5 cm in front of the goal cup. A manually operated guillotine door was lowered to confine the animal within the final 30 cm of the runway which constituted the goal box.

Procedure. The subjects were placed on a 12 g/day feeding schedule on Day 1, adjusted during training for the amount of food received as reinforcement. The animals were handled on Days 6–10 and were fed fifteen 0.045 g Noyes pellets in their home cage out of a glass dish on Days 11 and 12.

Single alternation training began on Day 13 with each animal receiving four trials followed by six trials on Day 14 and fourteen trials per day thereafter for twelve days. All odd numbered trials were nonrewarded and the animal was confined to the goal box for 30 sec, while all even numbered trials were rewarded with fifteen 0.045 g Noyes pellets.

The animals were run in squads of two, one animal from each group per squad, with an intertrial interval of approximately 1 min.

Results

All times were converted to speeds (1/sec) prior to analysis of variance. One animal in the control group died during the experiment and its data were discarded and the unweighted means solution for unequal n was employed in all analyses [23]. Because of apparatus failure, start times were lost and so only run and goal speeds are reported.

Figure 4 shows the mean run and goal speeds of irradiated and control subjects on both rewarded and nonrewarded trials for each of the 12 days of training. As can be seen, both groups eventually ran slower on nonreward trials than on rewarded trials, although alternation behavior appeared to develop earlier for controls and, at least in the run section, the irradiated animals appeared to show a somewhat smaller degree of alternation than controls throughout training. In the goal section, on the other hand, the irradiated animals were clearly alternating as well as the controls by the end of training. Alternation for both groups ran consistently faster on both rewarded and nonrewarded trials than the control group on its comparable trials in the run section, but not in goal section,

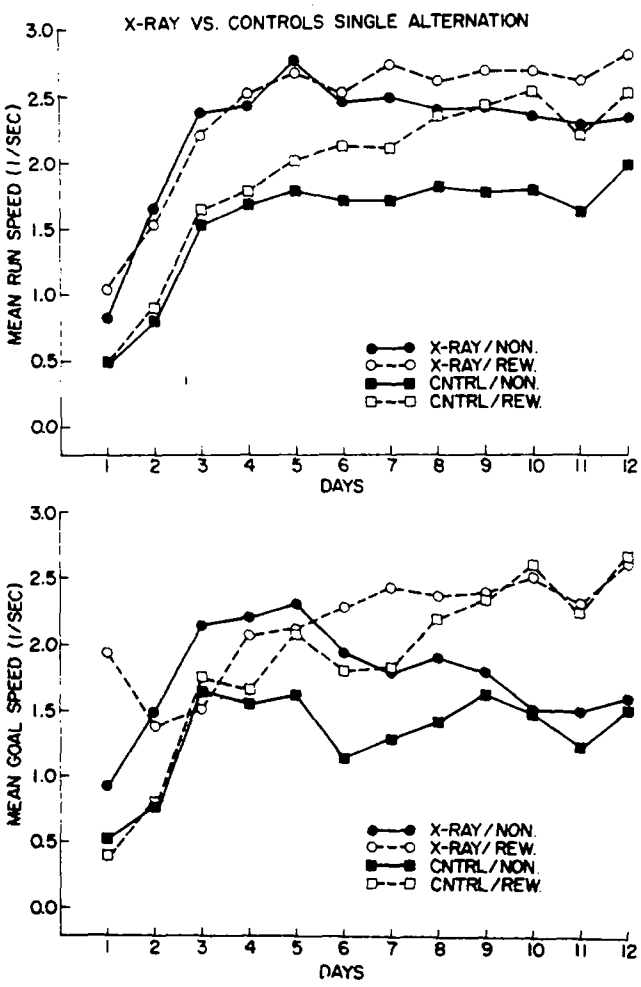

FIG. 4. Speed of running on rewarded and nonrewarded trials for both groups on each day of single alternation training in the run and goal sections in Experiment 2.

where their level of performance on the alternation task eventually equalled that of the control group.

Performance on the single alternation task was evaluated over the last three days of training, when performance appeared to be relatively stable for both groups, by a 2 x 2 x 5 x 3 analysis of variance applied separately to run and goal speeds. The analysis of variance included irradiation treatment and reinforcement outcome as between-animals factors and Trials and Days as within-animals factors. The observation of pattern responding in the run section was not supported statistically. Neither reinforcement ($F = 3.31$, $df = 1/22$, $0.05>p<0.10$) nor interactions with reinforcement (all $ps>0.10$) attained a conventional level of significance. Treatment also had no effect on performance over the last three days of training in the run section ($F = 2.15$, $df = 1/22$). A similar analysis of variance over the entire training period also failed to yield a significant reinforcement effect ($F = 1.35$, $df = 1/22$) but suggested the observation that irradiated animals tended to run faster than controls ($F = 6.27$, $df = 1/22$, $p<0.05$ for treatment). Planned comparisons showed that the treatment effect was due largely to slower running by controls compared to irradiated on nonrewarded trials ($F = 4.39$, $df = 1/22$, $p<0.05$) as the two groups did not differ significantly on rewarded trials ($F = 2.09$, $df = 1/22$). In the goal section, on the other hand, there was a highly reliable reinforcement effect ($F = 8.90$, $df = 1/22$, $p<0.01$). Planned comparison between speeds on rewarded vs. nonrewarded trials showed that speeds on nonrewarded trials were slower in both control ($F = 5.97$, $df = 1/22$, $p<0.05$) and irradiated rats ($F = 5.10$, $df = 1/22$, $p<0.05$) indicating significant patterning in both groups. The groups did not differ on either rewarded or nonrewarded trials in the goal section ($Fs<1$).

Discussion

The two main results obtained in this experiment were unexpected in terms of Experiment 1 and of reports in the literature. First, whereas in Experiment 1 irradiated rats ran more slowly than controls, in Experiment 2 they tended to run as fast or faster than controls. Second, although alternation behavior appeared to develop more slowly in x-irradiated rats, x-irradiated and control rats eventually showed comparable alternation behavior in the goal section. Previous experiments have shown a close behavioral correspondence between x-irradiated and lesioned rats on a variety of tasks [4,15] and it was expected that the failure of lesioned rats to establish significant patterning [9] would be replicated in x-irradiated rats. A possible explanation for the discrepancy presented itself in a procedural difference between the present experiment and the one by Franchina and Brown [9]. In their experiment rats received several days of CRF prior to the introduction of single alternation training while rats in the present study had no prior CRF experience. It has been reported that hippocampal lesioned rats show no impairment of DRL responding [21] or heightened response rates on a VI schedule [17] if not previously trained on a CRF schedule. Winocur and Mills [24] found that hippocampal lesions impaired performance only on a task which provided a pretraining period followed by a shift in experimental conditions. Therefore, Experiment 3 of the present investigation tested irradiated rats in a single alternation learning task either with or without prior CRF conditioning.

EXPERIMENT 3

Method

Animals. Twenty-four adult Wistar rats, twelve controls, and twelve x-irradiated as in previous experiments were used.

Apparatus. The runway described in Experiment 2 was used in the present experiment.

Procedure. The animals were placed on a 12-g/day feeding schedule on Day 1 adjusted during training for the amount of food received as reinforcement. The animals were handled and then fed fifteen 0.045 g Noyes pellets in their home cages on Days 11 and 12. The CRF pretraining phase began on Day 13 for six irradiated and six control animals. Each rat was given two trials per day for 10 days and received fifteen 0.045 g Noyes pellets per trial. The remaining nonpretrained rats were brought to the testing room, and removed from and immediately returned to their cages on two occasions daily which intervened between trials for the pretrained animals, and received thirty Noyes pellets in their home cage. On Day 24 single alternation training was initiated for all rats, the first trial of each day being rewarded and the second trial nonrewarded. In the

present single alternation situation, then, reward preceded nonreward by a short intertrial interval (about 60 sec) and nonreward preceded reward by a long (24 hr) interval, and the reinforcement sequence over the entire training period was a single alternation pattern. This task differs from conventional alternation in the runway only in that a different intertrial interval separated rewarded from unrewarded trials than occurred between nonrewarded and rewarded trials.

Results

All times were converted to speeds (1/sec). An analysis of variance applied to speeds during pretraining (not shown) showed that there were no significant differences between x-irradiated and control animals in any alley section although irradiated rats ran slightly faster than controls throughout the pretraining phase. Single alternation performance was evaluated by a 2 x 2 x 2 x 3 analysis of variance, having irradiation treatment (treatment), reinforcement outcome (reinforcement) and pretraining as between-animals factors and Days as the within-animals factor, applied to speeds in each alley section over the last three days of training. The analysis of variance showed that pretraining was not a significant source of variance in Start ($F<1$), Run ($F = 2.39$, $df = 1/40$), or Goal ($F<1$) nor did it differentially effect the development of single alternation in irradiated or control groups (all $Fs<1$). Therefore, the pretraining variable will not be mentioned further and single alternation performance is presented in Fig. 5 for irradiated and control animals collapsed across the pretraining variable but with rewarded and nonrewarded trials plotted separately.

As can be seen in Fig. 5, both groups were responding faster on rewarded than on nonrewarded trials, but alternation was markedly impaired by x-irradiation in all alley sections relative to control animals. As in Experiment 2, irradiated animals ran faster than controls on rewarded and nonrewarded trials alike. Although reinforcement was a significant source of variance in each alley segment ($F = 19.53$, $F = 26.35$, and $F = 27.37$, $df = 1/40$, all p's<0.001, in start, run and goal, respectively), the reinforcement x treatment interaction was also significant in each section ($F = 6.80$, $F = 5.05$, and $F = 5.93$, $df = 1/40$ all p's<0.05, in start, run and goal respectively). In order to evaluate single alternation behavior within each treatment condition, the reinforcement x treatment interaction was partitioned into simple effects of reinforcement within both treatment levels. These comparisons (all $df = 1/40$) showed that control animals ran significantly faster on rewarded than on nonrewarded trials in start ($F = 24.77$, $p<0.001$), run ($F = 27.24$, $p<0.001$) and goal ($F = 29.39$, $p<0.001$), while irradiated animals showed reliable alternation only in the run section ($F = 4.16$, $p<0.05$) but not in start ($F = 1.66$) or goal ($F = 3.91$). Simple effects also showed that irradiated animals ran faster than controls on nonrewarded trials in all alley sections ($F = 23.55$, $F = 116.04$, and $F = 19.07$, all p's<0.001, in start, run, and goal, respectively) and were faster than controls on rewarded trials in the run section ($F = 4.47$, $p<0.05$) but not in start ($F = 1.35$) or goal ($F<1$).

Discussion

Prior continuous reward experience had no apparent effect on the subsequent acquisition of single alternation performance in either hippocampal x-irradiated or control rats. This would appear to be at variance with the reported deficit in hippocampal rats on a DRL task only following prior experience on a CRF schedule [21].

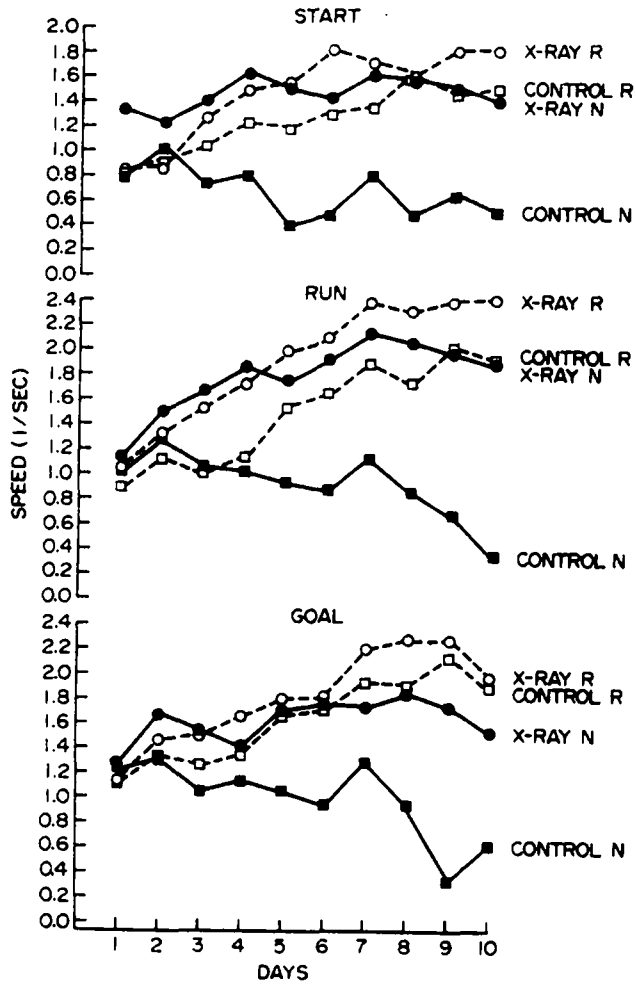

FIG. 5. Speed of running on the single daily rewarded and nonrewarded trials for both groups in the start, run, and goal sections of the alley in Experiment 3.

The present experiment is interesting in that hippocampal x-irradiated rats showed more marked and persistent impairment of single alternation performance than in Experiment 2. This impaired patterning, however, is a smaller loss than the complete absence of patterning found by Franchina and Brown [9] in hippocampal lesioned rats.

The procedure used in the current experiment gave two trials per day whereas Experiment 2 allowed ten trials in each daily session. It was found here, as previously [16], that control rats learn to alternate very rapidly in a two trial per day reward-nonreward sequence. Indeed, the control animals in Experiment 3 were patterning after only ten trials compared with fifty or more in Experiment 2. Although the reasons for these differences have not been explored experimentally it seems reasonable that one nonrewarded trial each day would be a more salient event than five nonrewarded trials interspersed with rewarded

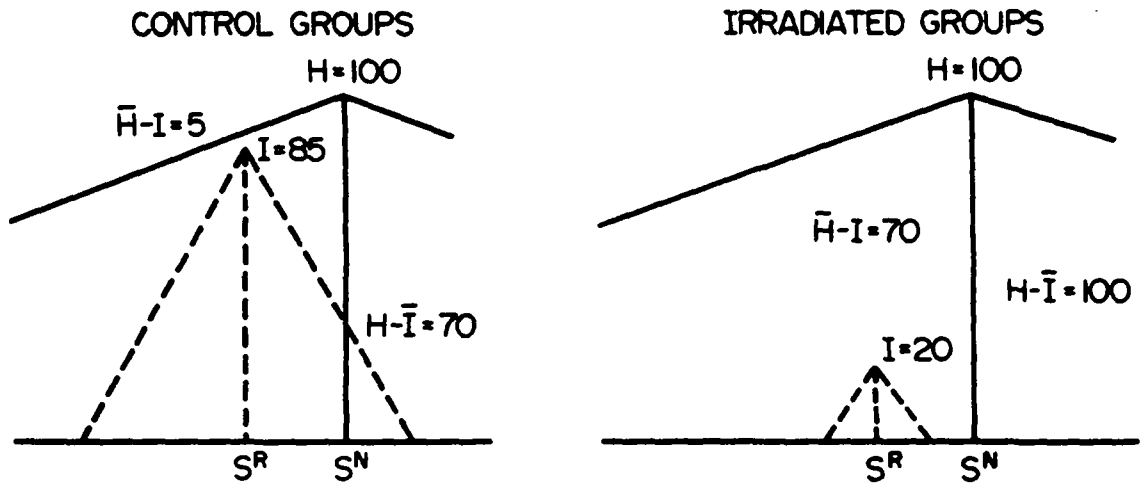

FIG. 6. Theoretical curves for control groups and x-irradiated groups. The left panel shows units of habit strength (solid vertical lines) conditioned to S^N and units of inhibition (broken vertical lines) conditioned to S^R and, respectively, generalization of habit to S^R and inhibition to S^N following single alternation training for control groups. The right panel shows units of habit and inhibition and their respective generalization gradients following single alternation training for x-irradiated groups.

trials in a span of approximately ten minutes. In any case, a deficit appeared in hippocampal irradiated rats only in what would appear to be an easier alternation task where the cues controlling behavior were presumably highly distinctive. While it is not proposed that task complexity is the relevant continuum along which hippocampal damaged rats differ from normals, it is noteworthy that whatever cues facilitated patterning in normal rats in Experiment 3 did not similarly aid alternation learning in irradiated rats.

One way to understand the single alternation deficit in irradiated rats obtained in Experiment 3 would be to assume, consistent with assumptions entertained to account for the results of Experiment 1, that hippocampal lesions or irradiation interfere to some extent with the aversiveness of frustrative nonreward. This is similar to Douglas' [8] account of the hippocampus as a stimulus gating mechanism which acts to inhibit stimuli which have been associated with nonreinforcement.

It has been suggested that inhibitory response tendencies established by nonreward are an increasing function of the aversiveness of nonreward [19]. If x-irradiation of the hippocampus leads to a reduction in the aversiveness of nonreward and a consequent reduction in the growth of inhibition, faster overall running speeds in irradiated rats and impaired alternation might be predicted from the generalization of excitatory and inhibitory response tendencies conditioned to cues associated with reward or nonreward. Figure 6 shows the theoretical picture for control animals (left panel) and irradiated animals (right panel) following single alternation training. The abscissa represents a continuum of stimulus similarity along which the stimuli occasioned by reward (S^R) and nonreward (S^N), regulating alternation behavior, may be ordered. Arbitrary units (actual numbers are illustrative) of habit (H) and inhibition (I) are represented by the height of the solid and dotted lines, respectively. The figure shows S^N, which was always followed 24-hr later by reward, having acquired 100 units of H for both control and irradiated groups while the control group would acquire greater I, e.g., 85 units versus 20 units than the irradiated group on the assumption that I is related to the aversiveness of nonreward and that nonreward was less aversive in the irradiated group.

Consider first the faster overall running shown by the irradiated group during single alternation. Speed on rewarded trials would be determined by the amount of H acquired to S^N minus the generalized inhibition ($\bar{I}$) present at S^N. Clearly, $H-\bar{I}$ is greater for irradiated ($H-\bar{I} = 100$) than control ($H-\bar{I} = 70$) groups on rewarded trials. Similarly, on nonrewarded trials running speed would be determined by the difference between the amount of I established to S^R and the amount of generalized Habit ($\bar{H}$) from S^N ($\bar{H}-I$). Again effective associative strength would be greater for irradiated ($\bar{H}-I = 70$) than for control ($\bar{H}-I = 5$) groups and thus the irradiated group would also run faster on nonrewarded trials. Indeed, with the values chosen, the control group would run at approximately the same speed on rewarded trials ($H-\bar{I} = 70$) as the irradiated group on nonrewarded trials ($\bar{H}-I = 70$), a result also obtained in the present investigation.

Presumably the degree of alternation would be determined by the size of the difference between effective habit strength present at S^R and S^N. Clearly, this difference would be larger for controls ($70-5 = 65$) than for irradiated groups ($100-70 = 30$) and, hence, alternation should be smaller in the irradiated group, a result also obtained here.

In applying the above model to the results of Experiment 2, it is important to note that it does not predict that control groups will always alternate better than irradiated groups. Hippocampal x-irradiation has only been assumed to retard the growth of inhibition. not necessarily to prevent it. Presumably, when a large number of trials is used, as in Experiment 2, I eventually becomes asymptotic for both groups. In that event, both control and irradiated groups would be expected to show good alternation, and further, there should be no difference between the two groups on either rewarded or nonrewarded trials, as was the

case in the goal section in Experiment 2. However, if I was acquired only in the goal section for the irradiated groups but had reached a high level in the run section for the control groups, (inhibition is assumed to develop first in the goal and only later during training in preceding sections [6]) because of the more rapid development of I in control groups, the theoretical picture would be similar to that in Fig. 6. Irradiated groups would show poorer alternation and would be faster on both rewarded and nonrewarded trials than the control group on comparable trials. While neither group showed reliable alternation behavior in the run section in Experiment 2, the results appear to favor better alternation by control animals and control animals were slower than irradiated animals on both rewarded and nonrewarded trials.

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