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Time Course of Certain Behavioral Changes After Hippocampal Damage and Their Alteration by Dopaminergic Intervention into Nucleus Accumbens[1]

DANIEL K. REINSTEIN,[2] JOHN H. HANNIGAN, JR. AND ROBERT L. ISAACSON[3]

Department of Psychology and Center for Neurobehavioral Sciences
State University of New York at Binghamton, Binghamton, NY 13901

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REINSTEIN, D. K., J. H. HANNIGAN, JR. AND R. L. ISAACSON. *Time course of certain behavioral changes after hippocampal damage and their alteration by dopaminergic intervention into nucleus accumbens.* PHARMAC. BIOCHEM. BEHAV. 17(2) 193–202, 1982.—Independent groups of rats with hippocampal, neocortical, or sham lesions were observed 7, 14, or 28 days after surgery in an open field-hole board apparatus and in a smaller circular apparatus. In the circular apparatus, animals were observed after unilateral injection of the dopamine agonist, 3,4-dihydroxyphenylamino-2-imidazoline (DPI) or saline into nucleus accumbens. Behavioral changes in locomotion, exploration and grooming measured in the open field were consistent with those found previously after hippocampal damage, with each behavioral anomaly demonstrating a specific pattern of change after surgery. In general, the injection of DPI into nucleus accumbens produced greater behavioral change in animals with hippocampal damage than in animals with either neocortical or sham lesions. The drug-induced changes in the hippocampally lesioned rats made their behavior more like that of control animals. These results suggest that destruction of the hippocampus may induce alterations in dopaminergic mechanisms in nucleus accumbens which can be modified by appropriate pharmacologic intervention.

Hippocampal lesion Nucleus accumbens Recovery Dopamine systems

DAMAGE to a specific portion of the brain often produces a syndrome of behavioral changes, although these changes may not be due directly to the tissue destroyed. Every form of brain damage produces not only a loss of viable tissue but, in addition, transient or permanent alterations in cellular activities, physiology, and metabolism, in regions with which it has direct, and even indirect, connections [1, 14, 16, 33]. The effects of these secondary changes can be mistaken for the direct consequences of the primary tissue destruction. The behavioral alterations due to secondary changes may be distinguished in part on the basis of whether changes in behavior vary over post-operative time and whether they can be altered by suitable interventions.

Established behavioral changes of animals with bilateral hippocampal lesions have been found in locomotion, spontaneous alternation, spatial or time-restricted tasks, active and passive avoidance, various types of operant schedules, and discrimination problems (see [13,30]). Some limited amount of work has been done with changes occurring at different times after surgery with some of these behaviors [19, 24, 25].

The number of regions whose activity or structure could be altered by hippocampal formation lesions is considerable, but there are compelling reasons for believing that alterations in the nucleus accumbens would have behavioral significance. Anatomically, there are monosynaptic connections from ventral subiculum to n. accumbens [36, 39, 40]. Alterations of the dopaminergic mesolimbic projection system to n. accumbens produce behavioral reactions similar to those found after hippocampal damage, particularly increased locomotion, deficits in passive avoidance, and changes in attention and exploration [10, 22, 37, 38]. Also, the hyperactivity and hyperresponsiveness found after hippocampal damage can be reduced by acute administration of neuroleptics [14]. However, interpretation of pharmacologic manipulations of the basal ganglia is difficult because of the existence of multiple dopamine (DA) receptors in both caudate and n. accumbens (e.g., [7, 20, 21, 28]). The functional roles played in the multiple receptors are not resolved, but one theory proposes antagonistic excitatory (DAe) and inhibitory (DAi) receptors which have selective distributions in caudate nucleus and n. accumbens [4,5]. The behavior of the animal

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[2]Now at the Laboratory of Neuroendocrine Regulation, Massachusetts Institute of Technology, Cambridge, MA 02139.
[3]To whom requests for reprints should be addressed.

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is thought to be based in part on the relative balance of activity between the DAe and DAi systems [3]. Other data supporting a "compensatory" model of DA system interactions have been reported [6, 18, 31].

If the destruction of the hippocampus results in behaviorally significant changes in dopaminergic systems in n. accumbens then it might be possible to modulate the behavioral sequelae of the lesion by readjusting the balance between the DAe and the DAi systems. Assuming increased locomotor activity to be a consequence of exaggerated DAe activity, the approach in this study was to "restore" the balance through stimulation of the DAi system thought to be predominant in n. accumbens [3] and considered to act antagonistically to the DAe system.

We undertook to do this by injecting the DA agonist 3,4 dihydroxyphenyl-amino- 2-imidazoline (DPI) into n. accumbens of animals with either bilateral hippocampal and neocortical damage, damage restricted to the neocortex, or "sham" operations. This drug is thought to be a relatively selective agonist of the DAi system [5]. In a recent study we found that it affects dopamine metabolism in the n. accumbens but not the caudate after systemic administration [35]. If, as anticipated, hippocampal destruction produces relatively enhanced activity in the DAe systems, treatment with the DAi agonist DPI could restore more normal behavior in the lesioned animals.

In this study we investigated the effects of unilateral injection of DPI into n. accumbens. We reasoned that unilateral injections might be effective in restoring normal behavioral patterns since unilateral hippocampal lesions are without behavioral consequences in our testing situations. Since the hippocampal formation-n. accumbens projections are predominantly—if not exclusively—unilateral [34], this suggested that the presence of one intact n. accumbens region might be adequate to support essentially normal behavior. If this were the case then unilateral restoration of a nearly normal hippocampal-accumbens axis ought to be sufficient to restore normal behavior.

All animals were tested in two situations: Once in an open field/hole board apparatus (see [18]) without pharmacologic intervention, and shortly afterwards in a circular apparatus following intra-accumbens administration of saline or DPI. These procedures were repeated at three different postoperative times in independent groups in order to assess changes in responsiveness to dopaminergic intervention after surgery as well as the time course of behavioral change without intervention.

METHOD

Experiment 1

Approximately 200 male, Long-Evans hooded rats weighing between 250–350 g at the time of surgery were used. Animals were individually housed on arrival which was at least one week prior to surgery. The colony room was on a 15/9 light-dark cycle with lights on at 0700 hours. Food and water were provided ad lib.

At the time of surgery, animals were anesthetized with a mixture of chloral hydrate, Nembutal, atropine, and saline. Animals were randomly assigned to receive either sham, cortical (Cort), or hippocampal (Hpc) lesions. The cortical and hippocampal lesions were performed using aspiration as described by Isaacson and Woodruff [17]. Animals receiving sham lesions were anesthetized, their scalps opened, bone drilled, and scalp sutured. After their respective lesions, each animal was implanted bilaterally with stainless steel cannulae (0.022 in. o.d.) with the bevelled tips ending just above n. accumbens at coordinates—A 9.0 mm, L 1.4 mm, and 4.0 mm ventral to dura, according to König and Klippel [26]. Cannulae were cemented into place with dental cement anchored to skull by two stainless steel machine screws. A stainless steel wire stylet was placed inside each cannula with the tip extending down to one-half of the distance of the bevel. After surgery, the animals were returned to their home cages in the colony room. After one of three postoperative recovery periods (7, 14, or 28 days), animals were chosen from each lesion group and tested in an open field. On the assigned testing day, animals were taken from the colony room and transported in their home cages to a holding room in the testing suite. All testing took place between 1300 and 1600 hrs. The animals were placed in an open field apparatus located in an adjacent, quiet and dimly illuminated (red light) observation room. Observations were made for 10 min via a closed circuit video system by trained observers located in a third room. The observers were uninformed as to the experimental conditions being studied. The open field was white Plexiglas and measured 71×71×46 cm high. Sixteen holes (3.2 cm diameter) were placed 14 cm apart (center to center) on the floor, forming a 4×4 matrix. The open field was cleaned between animals with a dilute Lysol solution. The measures employed over the 10-min session were the following:

Peripheral locomotion: Movement of greater than 50% of the animal's head and body into one of the 12 squares bordering the four walls of the apparatus.

Central locomotion: Movement of greater than 50% of the animal's head and body into one of 4 central squares.

Rearing: A lifting of both forepaws off the ground with a vertical extension of the body. Rears against the wall were included in this measure.

Peripheral hole poke: Placement of the animal's nose into one of the holes in the 12 squares bordering the apparatus walls.

Central hole poke: Placement of the animal's nose into one of the 4 centrally located holes.

Grooming: This measure included face washing, paw, body, and genital licking, and body scratching.

In addition to measuring the frequency of occurrence of each behavior, the durations of individual hole poke, grooming, and rearing episodes were measured. All behaviors scored by the observers were encoded into audio signals using telephone touch-tone pads. The signals were recorded and subsequently decoded for digital analysis by a microcomputer which approximated a continuous behavior measurement by a 0.1-sec time sampling interval. From this it was possible to derive measures of frequency, duration, and occurrence over time.

Experiment 2

All animals had been used in Experiment 1. Following the observation period, each animal was removed from the open field and placed in its home cage which had been transported to a nearby holding room. Two hours after the open field observation period each animal was restrained, its guide wire removed from one of the cannula, and the injection cannula inserted. The side injected was chosen randomly. The inner cannula extended 1 mm below the bevelled tip of the outer sleeve to allow direct injection into the n. accumbens area. Unilateral injections of either 10 μg of DPI in 0.5 μl of saline

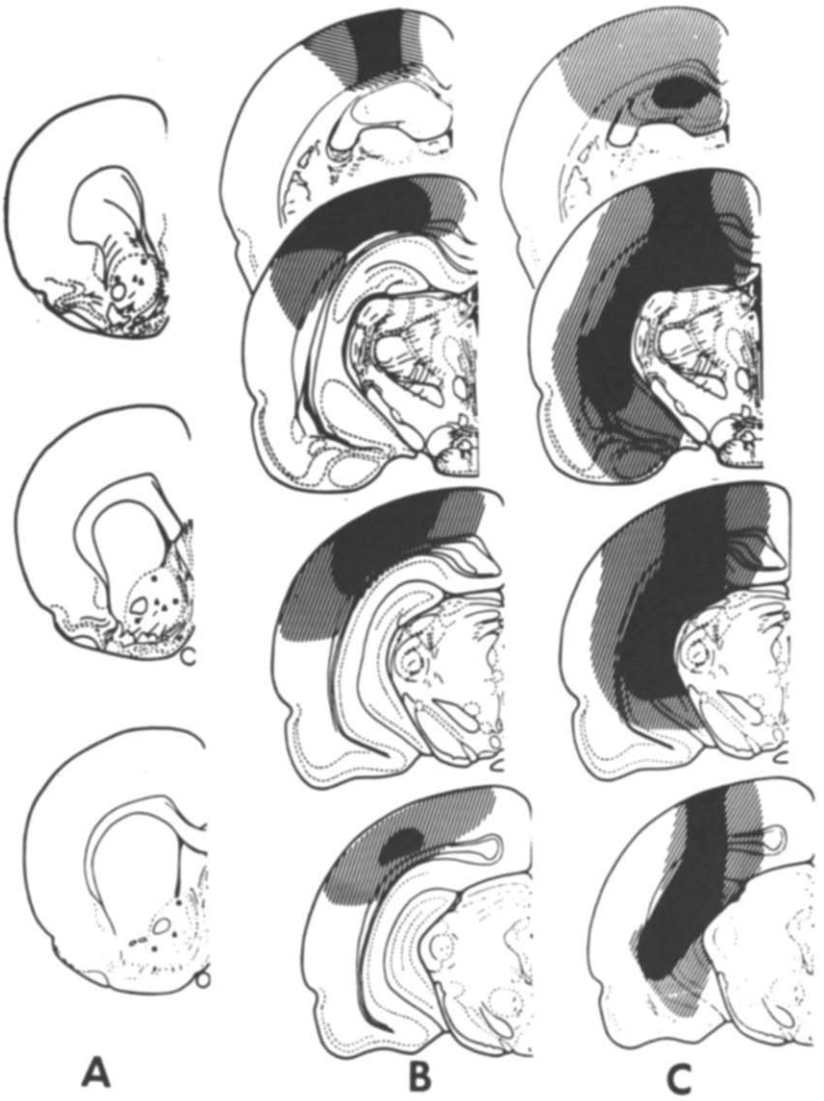

FIG. 1. Column A. Representative cannula tip placements in the nucleus accumbens. The most commonly found central loci (▲; 60% of placements) and those placements near the borders of the nucleus accumbens and either caudate nucleus (10%) or nucleus of the diagonal band (30%) which were still within accumbens (■) are shown. Column B shows the minimum (solid area) and maximum (striped) extent of cortical and (Column C) hippocampal lesions.

(pH 6.0) or 0.5 μl of saline were infused over 45 sec [3]. The inner cannula remained in place for 30 sec after injection. Then it was removed and the stylet replaced. The animal was then returned to its cage for 10 min. Each animal was then placed in the circular apparatus. This was made from a standard circular metal waste paper basket with a floor diameter of 25 cm and a height of 33 cm. The sides of the basket had gently sloping walls resulting in a diameter of 33 cm at the top. The floor of the apparatus was delineated into 4 equal quadrants. Grooming, rearing, and locomotion were measured using the same procedure as Experiment 1 over a 15 min interval.

In this apparatus movements of greater than 50% of the animal's head and body into adjacent quadrants in either direction were counted. Grooming and rearing were measured as in Experiment 1.

After each animal completed Experiment 2, it was returned to its cage in the holding room. After all the animals had been run on a particular day, they were all returned to the colony room. Shortly thereafter, all animals were sacrificed by decapitation, their brains removed and placed in a gluteraldehyde-formaldehyde solution. After fixing, the brains were frozen and sectioned at 80 μ, saving every section cut through the cannula tracks and every 5th throughout the lesion. Sections were stained with cresyl violet, and cannula tip location and the extent of each lesion were verified.

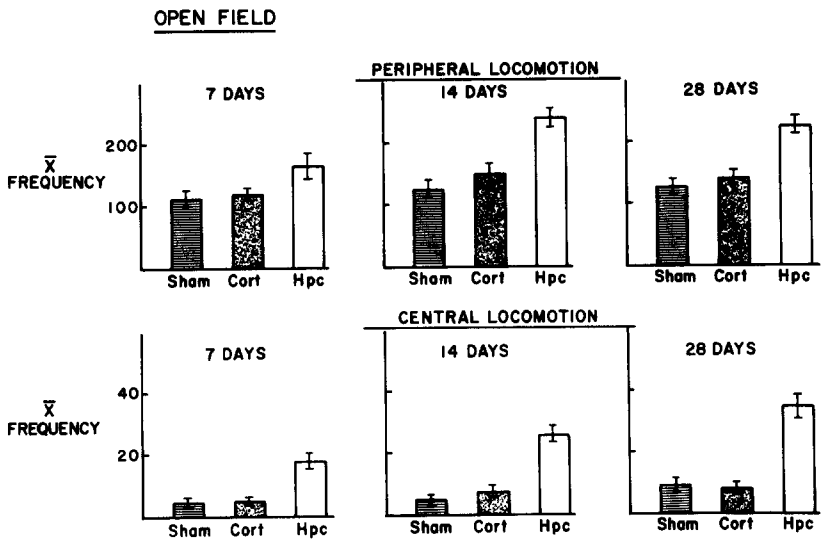

FIG. 2. Frequency of peripheral and central locomotion in the open field as measured by matrix crossings. Three post-operative periods designated 7, 14, and 28 days. Day 7—Sham (n=19), Cort (n=19), Hpc (n=17); Day 14—Sham (n=22), Cort (n=17), Hpc (n=21); Day 28—Sham (n=19), Cort (n=19), Hpc (n=21). Values are means±S.E.M.

RESULTS

Histology

A total of 180 brains were stained and analyzed histologically. Of these, six were discarded due to problems with the lesion (e.g., damage to hippocampus in the Cort group or to thalamus in the Hpc group). The remaining 174 animals were included in the first experiment. Figure 1 shows the minimum and maximum damage incurred in each of the lesion groups.

Of the 174 animals, 25 animals were rejected for analysis in Experiment 2 because of an inability to determine cannula tip location or because the tip of the cannula was outside of n. accumbens. Cannula tip placement was acceptable if it was within the extent of n. accumbens. Figure 1 illustrates representative placements, including those near the borders of n. accumbens which were rated acceptable. Analysis of cannula placement for the drug and saline groups across all lesions and postoperative recovery periods revealed no significant differences between placements in the body of n. accumbens and those on the edge of n. accumbens and the diagonal band or the caudate.

Behavior

Since no more correlations among the various behavioral measures were found statistically significant than would be expected by chance alone, the individually scored behaviors were considered as independent measures within each experiment.

Analyses of variance were performed on each behavior followed by Duncan's Multiple Range Tests for differences between means. In light of the large amount of data and because the comparisons considered were planned, the results of the Duncan's test alone will usually be reported. Where interactions of interest were found, the F ratios derived from the ANOVAs will also be reported. The level for statistical significance for all comparisons made with the Duncan's test was set at $\alpha<0.05$.

Locomotion

There were no differences in locomotion for sham or cortically lesioned groups tested at different times. After hippocampal destruction, peripheral locomotion in the open field was elevated at all recovery periods (Fig. 2). Within the hippocampal groups there was greater peripheral locomotion exhibited by the group tested at day 14 than day 7, but the difference between groups tested on days 14 and 28 was not significant.

As with peripheral locomotion, central locomotion was greater at longer recovery periods for the hippocampal group (Fig. 2). A statistically significant difference was found between animals tested on days 14 and 28. The cortical lesion groups were not different from one another on any test day, but the sham group had a higher level of activity on day 28 than on day 14.

There was hippocampal lesion-induced hyperactivity in the circular apparatus which paralleled that in the open field (Fig. 3). ANOVAs showed a significant effect of brain damage, $F(2,123)=10.57, p<0.001$, which was due to the changes in the hippocampal groups at all recovery periods. Activity was greater on day 28 than on day 7 but not different from that on day 14.

Intra-accumbens injection of the dopamine agonist DPI produced a significant drug-by-lesion interaction $F(2,112)=3.20$, $p<0.05$, in that DPI significantly reduced activity in hippocampally lesioned rats tested at 7 or 28 days after surgery (Fig. 3). There were no significant changes following DPI in either control group at any postoperative period.

Sham lesioned rats showed the ipsilateral bias to unilat-

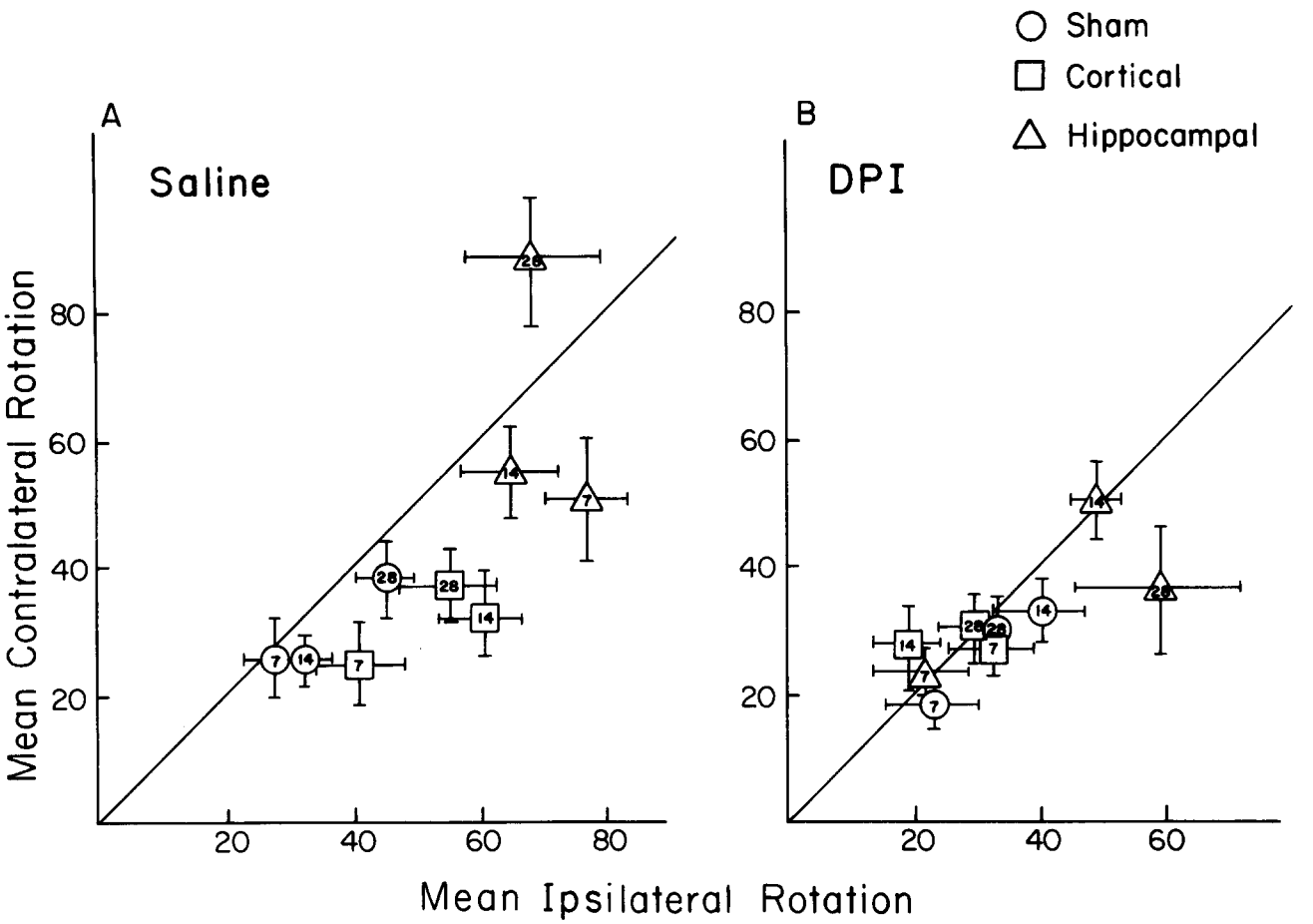

FIG. 3. Frequency of matrix crossings in the rotation apparatus after either (A) saline, or (B) DPI. Data is plotted as mean rotation (±S.E.M.) toward the injected side (ipsilateral) vs mean (±S.E.M.) away from injected side (contralateral). Numbers inside figures (○=Sham, □=Cort, △=Hippocampal) represent days recovery. The numbers of subjects in each group receiving intra-accumbens saline (Sn) or DPI are: Day 7—Sham (Sn=6, Dn=7), Cort (Sn=9, Dn=8), Hpc (Sn=6, Dn=10); Day 14—Sham (Sn=9, Dn=8), Cort (Sn=7, Dn=9), Hpc (Sn=9, Dn=6); Day 28—Sham (Sn=7, Dn=6), Cort (Sn=9, Dn=8), Hpc (Sn=8, Dn=9).

eral saline injections on all test days (Sign tests: $p<0.05$), whereas the lesion groups showed the bias only at 7 days after surgery (Sign test: $p<0.05$; see Fig. 3). Ipsilateral turning predominated in all groups with the exception of the hippocampal lesion group that was tested 28 days after surgery. This turning effect was not seen after DPI injections. There was no differential response between the cortical and hippocampal lesion groups at any postoperative time after DPI treatment.

Hole Poking

Hippocampal damage significantly increased the frequency of peripheral hole pokes 28 days after surgery (Fig. 4A). Hippocampally lesioned animals were not different from the sham or cortical groups tested 7 or 14 days after surgery. While there was a trend to increase the frequency of hole pokes for all lesion groups across testing days, this increase was only significant for the hippocampal groups on days 7 or 28, and for the sham groups tested on days 14 or 28.

Animals with hippocampal lesions tested 14 or 28 days postoperatively did not hole poke as long as control animals. There was a progressive trend toward decreased average hole poke durations for the hippocampal groups tested longer after surgery.

At all recovery periods the hippocampal lesion groups exhibited more central hole pokes than the comparable sham or cortical lesion groups which did not differ from each other (see Fig. 4B). This is likely related to the increased tendency for the animals to move into the center of the open field. Within lesion groups there were progressive increases in the frequency of central hole pokes for the sham and hippocampal groups which paralleled increases in central locomotion over time. Both groups had significantly higher frequencies on days 28 relative to day 14. There were no differences in mean central hole poke duration between lesion groups at any test period and no changes in duration across days for any lesion group.

Rearing

Figure 5 illustrates the relative differences of the hippocampal animals from the controls on the frequency and duration of rearing behavior. The control groups did not differ from each other on either measure at any recovery period. Hippocampally lesioned rats reared less frequently in

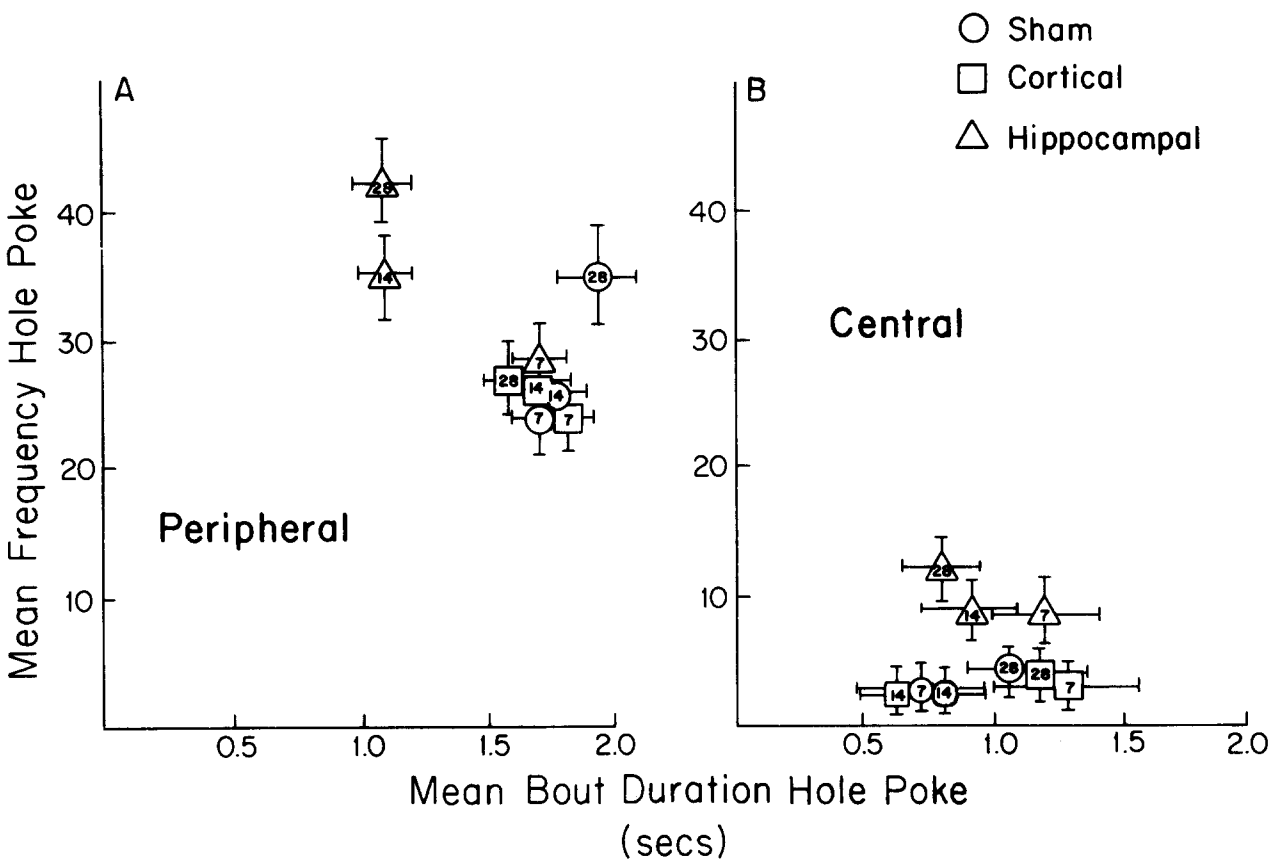

FIG. 4. Hole poking behavior in the open field periphery (A) or central area (B), plotted as mean (±S.E.M.) bout duration vs mean (±S.E.M.) frequency of bout occurrence. See Fig. 2 for key.

the open field than control rats tested 7 or 28 days after surgery, although not on day 14. Rearing scores of the hippocampal lesion group tested 14 days after surgery were different from the scores of animals with similar lesions measured at either 7 or 28 days after surgery. In the open field the means for rearing duration in hippocampal lesion groups were shorter than in the sham groups at 7 or 14 days and shorter than both the sham and cortical lesion groups measured at postoperative day 28.

As in the open field, animals with hippocampal lesions showed decreased durations of rearing bouts in the circular apparatus, $F(2,140)=18.25$, $p<0.001$. This is shown in Figs. 5 and 6A. However, in contrast to testing in the open field the animals with hippocampal damage reared more than controls. In other tests (unpublished observations) the difference in frequencies of rearing in the open field (decrease) and circular apparatus (increase) were found to be a result of the apparatuses themselves, and not to whether they were tested in one of the other apparatus first.

Rearing frequency was unaffected by DPI in any control group at any recovery period (Fig. 6B) except for an increase for the sham operates that were tested 28 days after surgery. DPI reduced the elevated frequency of rearing found in animals with hippocampal damage tested 7 days after surgery. In contrast to its effect on frequency, DPI did not alter rearing durations at any postoperative test period in the animals with hippocampal lesions.

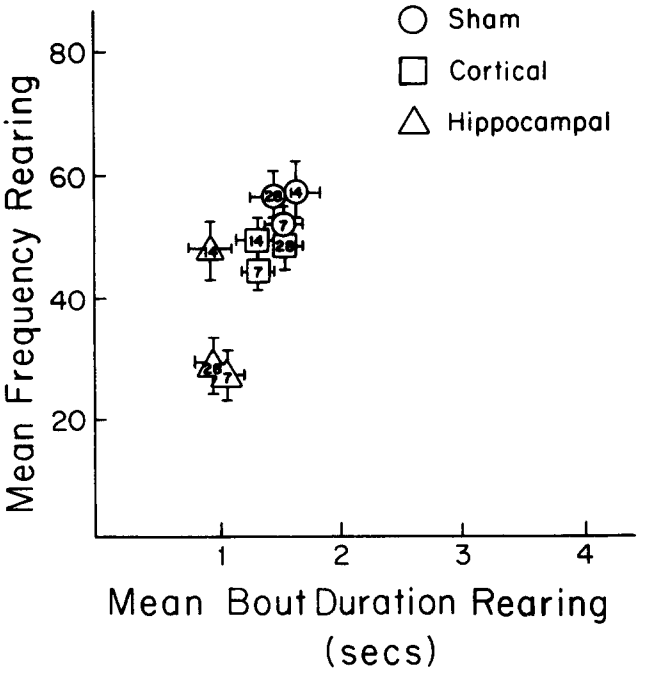

FIG. 5. Mean (±S.E.M.) frequency of rearing behavior in the open field/hole poke apparatus vs mean (±S.E.M.) bout duration. See Fig. 2 for key.

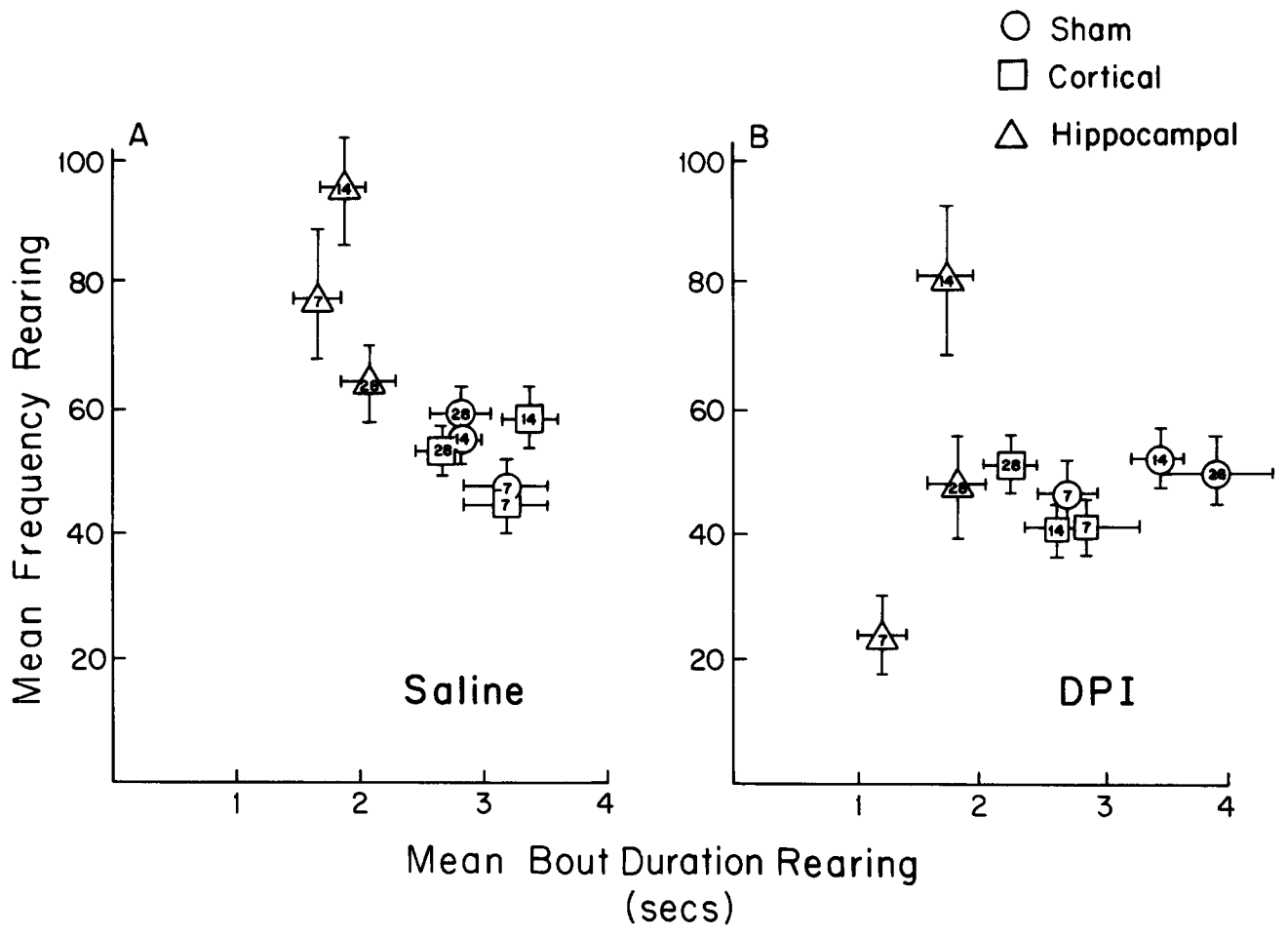

FIG. 6. Mean (±S.E.M.) frequency vs bout duration for rearing behavior in the rotation apparatus after (A) saline, and (B) DPI injection into n. accumbens. See Fig. 3 for key.

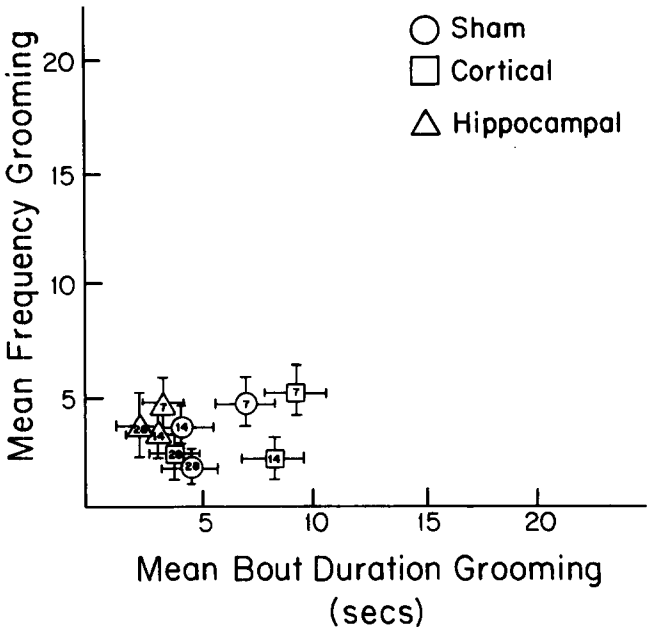

FIG. 7. Mean (±S.E.M.) frequency vs bout duration of grooming in the open field/hole poke apparatus. See Fig. 2 for key.

Grooming

There were no differences in the frequencies of grooming bouts in the open field as a function of brain lesion (Fig. 7). The only change between groups tested at different postoperative times was within the sham groups which showed fewer grooming bouts when tested at longer recovery periods: The number of grooming bouts exhibited on day 28 was significantly less than that on day 7.

Mean bout durations of grooming were less in the hippocampal groups than control groups but statistically different from the cortical groups only at 7 and 14 days after surgery. Only the cortical lesion groups showed a recovery period effect. The grooming durations of the group tested at 28 days were significantly less than those of animals tested on day 7.

In the circular apparatus, the only significant difference in grooming frequency among the saline injected groups was found on postoperative day 14 when the hippocampally lesioned animals groomed less than the sham operate group (Fig. 8A). The shams tested on postoperative day 14 groomed more often than the shams tested on day 28. The sham and cortical lesion groups had equivalent grooming bout durations at all test periods. The hippocampally lesioned animals groomed for shorter durations per grooming bout than did controls at the shortest postoperative period.

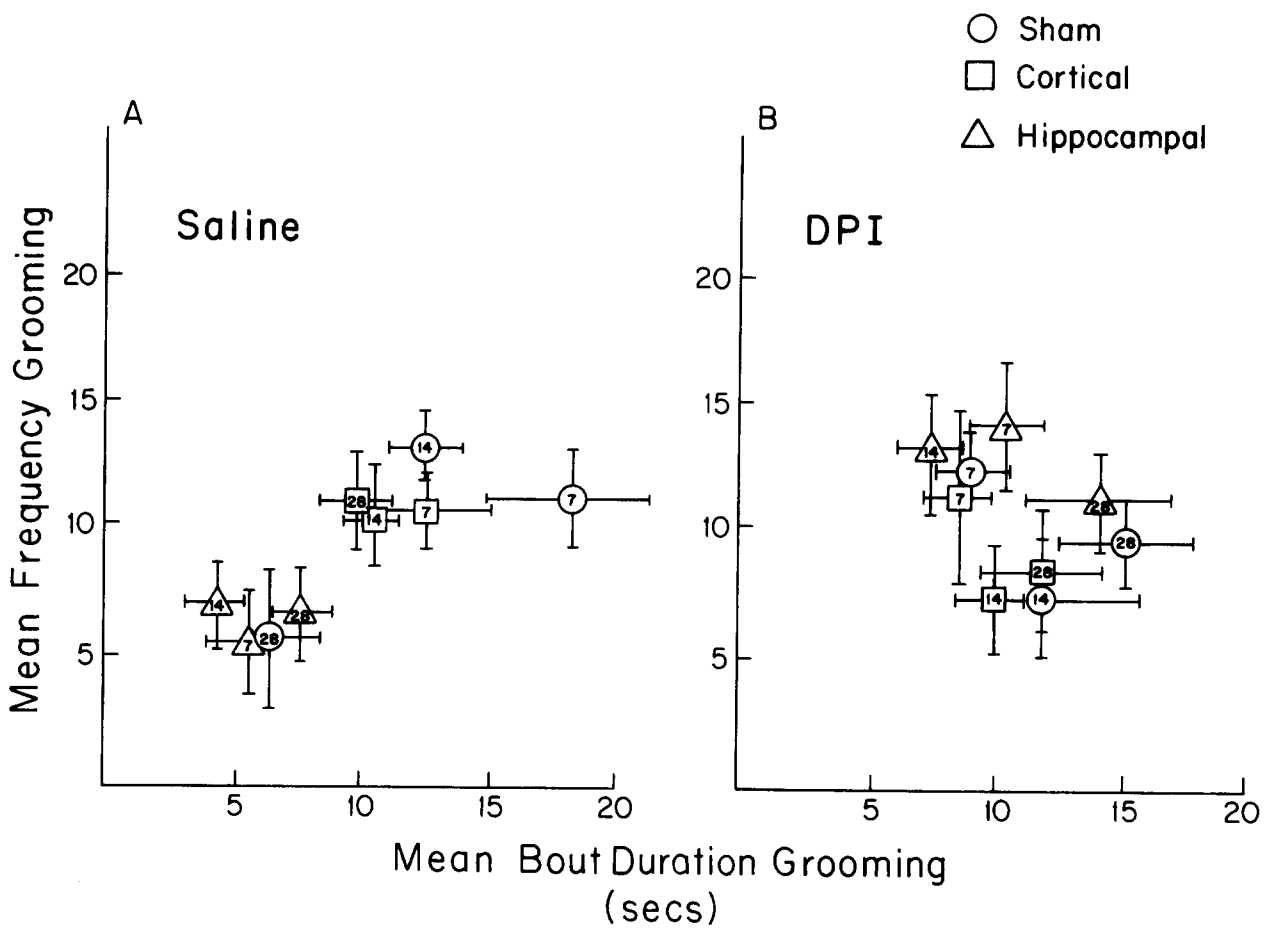

FIG. 8. Mean (±S.E.M.) frequency vs bout duration of grooming in the rotation apparatus after (A) saline, and (B) DPI injection into n. accumbens. See Fig. 3 for key.

When DPI was injected (Fig. 8B), there were no main effects for lesion or recovery period on grooming frequency, but there was a lesion-by-drug interaction, $F(2,123)=3.94$, $p<0.05$. While the simple main effects of DPI in the hippocampal lesion groups were not significant, DPI consistently increased grooming frequency at all recovery periods and eliminated the differences between the hippocampal lesion and control groups found after saline injection (cf. Fig. 8).

After DPI, there were no differences between the sham and cortical lesion groups at different postoperative periods on grooming bout duration. No effect was found across days within either control lesion group except for a decrease in grooming bout duration at 7 days in the sham operated groups (Fig. 8A). The scores of hippocampally lesioned animals given DPI did not differ from those of the control groups given DPI at any recovery period.

DISCUSSION

The two indications that behavioral changes arise from secondary reactions after selective brain damage sought in this study were both found: time-dependent alterations in behavior and the "restoration" of normal behavior after direct pharmacological intervention. In both the open field and the circular apparatus, animals with hippocampal lesions were more active than controls to different degrees at the three recovery periods. Increased locomotor activity was decreased by DPI administration even though control animals were unaffected at the dose used.

The fact that the DA agonist DPI produced effects in the hippocampally damaged animals but not the controls demonstrates an enhanced sensitivity to DAi manipulations in n. accumbens after hippocampal damage. Other work in our laboratory (in preparation) showed that similar dopaminergic stimulation of the caudate nucleus following hippocampectomy may not produce similar behavioral changes after the lesions, indicating that the present effects are probably not due to the spread of the drug up the cannula tract to the caudate. This possibility is also unlikely since there were no significant differences in the effects of DPI injected into regionally distinct parts of nucleus accumbens, including placements near the border of the caudate.

The effect of DPI injections into n. accumbens is greatest at 7 days after surgery, minimal at 14 days, and greater again at 28 days after surgery for several behaviors. This indicates that behaviorally potent dopaminergic changes in the basal ganglia after hippocampectomy change in a complex way after surgery.

Unilateral saline injections induced ipsilateral turning in animals with sham or cortical lesions. After hippocampal lesions, animals observed at 7 or 14 days also exhibited ip-

silateral turning bias after saline. By 28 days after hippocampal lesion, however, the bias was in the opposite direction. When DPI instead of saline was injected into n. accumbens, there was no bias produced in the control groups or in the 7 or 14 day hippocampal lesion groups. The drug injection also eliminated the contralateral turning in the group of animals with hippocampal lesions tested 28 days after surgery.

These results suggest that the saline injections caused a functional alteration of the n. accumbens which potentiated movement toward the injected side. The fact that the dopamine agonist counteracts this response bias indicates both the behavioral effectiveness of the agonist and the importance of dopaminergic activities in producing the bias. The differences found in animals with hippocampal lesions 28 days after surgery following saline injection indicates that the nature of the DA system may have been changed. For example, if the receptor population had changed from predominantly excitatory to predominantly inhibitory 28 days after hippocampal damage, then disruption of the system by saline would produce contralateral rather than ipsilateral turning. Indeed, preliminary work in our lab with [^{3}H]-haloperidol binding suggests that hippocampectomy may differentially affect populations of DA receptors in n. accumbens and caudate.

While previous reports purported to describe changes in exploratory behavior after hippocampal damage in the rat, the measured changes were usually alterations in locomotor activity [32] or perseveration of choices in maze arms [27]. Contrary to some theoretical predictions [30], we found animals with hippocampal lesions explore just as much or more than control animals when measured in an apparatus which allows assessment of locomotion and exploration as separate behavioral components [9].

The hippocampally damaged animals' tendency to exhibit shorter duration grooming bouts supports previous observations [30]. Animals with such damage initiate grooming bouts as frequently as control animals but only exhibit bouts of short durations [11]. Recently, Elstein, Hannigan and Isaacson [8] found that animals with hippocampal damage have a reduced sensitivity to intraventricular ACTH which induces excessively long bouts of grooming in non-lesioned rats. Since grooming bout duration was increased by DPI injections in hippocampal lesioned rats, but not controls, it is possible that the altered sensitivity to ACTH-induced grooming involves dopaminergic changes in basal ganglia regions (see also [6]).

Animals with hippocampal damage were found to rear less often in the open field, as was found previously [29]. It is surprising, however, that these same animals demonstrate a significantly greater number of rearing bouts relative to controls in the circular apparatus. Control animals respond to the circular apparatus with an approximately twofold increase in total frequency and bout length of rearing relative to that found in the open field. Animals with hippocampal lesions demonstrate a threefold increase in frequency of rearing with a twofold increase in bout length. This difference in rearing behavior between the two apparatuses suggests a certain contribution of environmental features in the elicitation of the rearing response.

From these results it is clear that numerous behavioral changes occur after hippocampal damage and that each may have a different temporal sequence. These differences may reflect a complex series of secondary changes. Furthermore, the hippocampus may modulate different dimensions (e.g., initiation and maintenance) of several behaviors via separate neural mechanisms. The return of some behaviors to within "normal" limits produced by injections of DPI into n. accumbens suggests that some of the neural mechanisms responsible involve the dopaminergic (DAi) systems in n. accumbens. These dopaminergic changes have a dynamic character since the injection of DPI is not effective at all postoperative times for all of the behaviors which can be modified by the drug. Further, since DPI has no discernible effect in "normal" or intact animals, or in animals with neocortical damage, hippocampal destruction may produce a supersensitive state in the DAi system.

We believe that it is valuable to consider behavioral changes after hippocampal damage along dimensions of response initiation and duration. The reduced durations of acts found after hippocampal damage may have adverse effects on some adaptive acts. For example, in a study by Glickman *et al.* [12], nest building in gerbils was inefficient and the nests poorly formed because the individual acts required in the complete action were too short in duration. Comparable results were reported in the rat by Kim [23]. The altered attentional abilities of animals with hippocampal lesions could be due to a reduction in the duration of attentional acts to below some optimal level [2,15]. A useful question is whether or not injections of DPI into n. accumbens would lengthen the duration of such acts and thus restore attentional capacities.

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