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Latent learning in a radial arm maze following neonatal dopamine depletion

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ABSTRACT

Animals neonatally depleted of dopamine show decreases in exploratory behaviour. As latent learning may depend on exploratory behaviour the present study was undertaken to examine the effects of neonatal dopamine depletion on latent learning. In two experiments dopamine was depleted neonatally, using 6-hydroxydopamine injected intracisternally on day 1 after birth. In both experiments, exploratory behaviour, measured as rearing and head-dip responses in a modified openfield/ holeboard, was reduced in the dopamine depleted rats whereas ambulatory behaviour was elevated. In a modified radial arm maze also, rearing responses were decreased while ambulation was increased for the 6-hydroxydopamine treated rats. Latent learning was tested in each experiment following preexposure to the maze for either a single trial or four trials. 6-Hydroxydopamine treated rats demonstrated a comparable latent learning effect to vehicle treated rats after four maze exposures but showed a greatly attenuated latent learning effect following only a single exposure. It is suggested that the effects of neonatal dopamine upon maze and latent learning are secondary to the effects on hyperactivity, reduced exploration and/or increased neophobia shown by these rats.

Keywords Dopamine - 6-Hydroxydopamine - Ambulation - Rearing - Head-dips - Exploration - Radial arm maze - Latent learning - Rats

The latent learning phenomenon (Tolman, 1932) seems to provide conditions that allow for the direct assessment of exploratory behaviour upon later learning performance. Latent learning experiments (e.g. Blodgett, 1929; Tolman and Honzik, 1930; Thistlewaite, 1951) have demonstrated that rats can learn by exploring a novel maze in the absence of food reward. When reward was introduced later performance was superior relative to the condition wherein no opportunity for exploration had been presented.

The destruction of dopamine (DA) pathways in the central nervous system as a result of intracerebral neonatal microinjections of 6-hydroxydopamine (6-OHDA) causes alterations in the behaviour of both juvenile and adult rats (Shaywitz *et al.*, 1976*a,b*; Miller *et al.*, 1981; Heffner and Seiden, 1983; Smith *et al.*, 1985). We have recently found that DA depletions in neonates caused alterations in exploratory behaviour (Archer *et al.*, 1988; manuscript in preparation). Neonatal denervation after either intracerebroventricular or intracisternal administration of 6-OHDA produced increases in ambulatory behaviour throughout testing but decreases in rearing behaviour during the first 10-15 min of testing in an open-field. Since decreases in head-dip behaviour (File and Wardill, 1975) were also shown (manuscript in preparation) we hypothesized that exploratory behaviour would be disrupted by neonatal DA depletion. Thus, Tolman's latent learning paradigm appears ideally suited to investigating the possible consequences of changes in exploratory behaviour on later instrumental maze learning. The radial arm maze task, which is sensitive to deficits in learning performance, was selected because (a) this is a well-established procedure for studying instrumental maze learning, and (b) we have consistently obtained deficits in radial arm maze performance in rats with neonatally induced DA depletions.

We first measured spontaneous motor activity and exploration in 6-OHDA treated and vehicle

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treated rats; this was carried out in the modified openfield/holeboard test. Later, these rats were given either access (LL groups) or no access (NL groups) to the radial arm maze either during four 5-min periods (experiment 1) or during a single 5-min period (experiment 2). Learning performance, essentially a latent learning test, was measured 48h later.

METHODS

Subjects

Male Sprague-Dawley rats, weighing 310-340g (vehicle-treated) and 290-320 g (6-OHDA-treated) and aged 61-70 days at behavioural testing, were randomly assigned to the different neonatal treatments and test conditions. Following weaning (day 25 after birth), they were housed in groups of 3 or 4 under laboratory conditions involving a 12 h on/12 h off lighting schedule (lights on at 06.00 h) in a room thermostatically maintained at 21 ± 1°C for the whole of the period before and after testing until sacrifice at around 85 days of age. Food (Lab.Chem.R3, Ewos, Sodertalje, Sweden) was freely available throughout, except for the 48 h immediately prior to testing in the radial arm maze when food was removed. Water was freely available throughout.

Neonatal treatment

In both experiments 6-OHDA (HCl base) was administered intracisternally (i.c.) on day 1 after birth. Female rats (Sprague-Dawley, ALAB, Sollentuna, Sweden) were obtained on the day 14 of pregnancy and were housed individually under the laboratory conditions described above. Male rat pups were randomly assigned to the 6-OHDA and Vehicle treatment conditions. Six pups of each treatment condition were randomly assigned to each dam. All the pups were injected with the noradrenaline uptake inhibitor, desipramine HCl (DMI, 25 mg/kg, subcutaneously) 30 min before 6-OHDA was injected i.c. (75 μg in 10 μl vehicle, 0.05% ascorbic acid in physiological saline). After weaning, each group of rat pups received food pellets both in the usual location (cage cover) and on the floor of the cage.

Apparatus

Openfield/Holeboard The modified openfield (80 × 8 cm) was divided into 16 units (each 20 × 20 cm) each containing a centrally located 3 cm wide hole. Head dips were defined by the thrusting of the rat's head into a hole up to the level of the eyes. Ambulation was defined as the passage of a rat's body from one unit to another, and rearing was scored each time a rat raised itself onto its hindlegs.

Radial arm maze

The radial arm maze task was modified to measure both spontaneous motor activity and cognitive function (Archer *et al.*, 1988). Each of the 8 arms (54 cm long and 10 cm wide) was "marked" off (divided) into three units (each 18 cm long and 10 cm wide) which gave a total of 25 units (counting the central hub, 25 × 25 cm) within walls that were 25 cm high. The radial arm maze was always placed on the floor of the test room, and a video-camera positioned in the ceiling recorded the behaviour of each rat. Behaviour was monitored on a TV screen placed in an adjoining room. The food cups, on the floor of the maze at the extremity of each arm, were not accessible during motor activity testing due to the presence of an extra, removable back wall. For the learning test the false back walls were removed and each food cup was exposed. In the present study, the latent learning groups (LL, see Table I) were allowed to explore the whole maze with the false back hiding the food cups whereas the no latent learning groups (NL, see Table I) were confined to the central hub, area by a circular wiremesh cage which allowed them to observe the arms but not enter them. At testing for latent learning the wire mesh obstruction was removed. Two measures of maze learning performance were obtained: (1) Latency to acquire all 8 pellets from placement in the central hub with a cut-off time of 10 min; (2) Number of errors in acquiring all 8 pellets, i.e. the total number of arms visited minus 8.

Procedure

For experiment 1, following birth and neonatal treatment with either 6-OHDA or vehicle, each treatment group (n =16) of rats was weaned and assigned randomly to either the LL (n =8) or NL (n =8) conditions (see Table I). On day 61, all 32 rats (16 6-OHDA and 16 vehicle rats) were tested for spontaneous motor activity and exploratory behaviour in the openfield/holeboard test. Each rat's behaviour was monitored on the video TV apparatus placed in an adjoining room. Ambulation, rearing and head-dips were measured over 10 min periods on each test occasion. After each animal had been tested, the whole surface of the openfield was wiped carefully

with a sponge rinsed in water containing liquid soap. On days 64, 65, 66, and 67, 8 6-OHDA and 8 vehicle rats (the LL-groups) were placed in the central hub and allowed to explore the radial arm maze ("false" back walls in position) over a 5 min period. Once again, each rat's behaviour was monitored on video TV.

TABLE I. *Chronological details of treatment and behavioural testing.*

Experiment 1	
Day 1	Intracisternal administration of 6-OHDA (75 μg, 30 min after DMI, 25 mg/kg) or vehicle.
Day 61	10 min Holeboard/ Open-field test.
Day 64-67	Four 5 min exposures to radial arm maze (activity measured) =LL-Groups; Four 5 min exposures to central hub only =NL groups.
Day 70	Radial arm maze test for all four groups.
Experiment 2	
Day 1	Intracisternal administration of 6-OHDA (75 μg, 30 min after DMI, 25 mg/kg) or vehicle.
Day 66	10 min Holeboard/Open-field test.
Day 67	Single 5 min exposure to radial arm maze (activity measured) =LL groups; single 5 min exposure to central hub only = NL groups.
Day 70	Radial arm maze test for all four groups.

Ambulation and rearing were measured on each occasion and the whole surface of the maze was wiped carefully after each rat. On the same days, 8 6-OHDA and 8 vehicle were each placed in the central hub for 5 min but denied access to the 8 arms by a wiremesh obstruction.

An identical procedure was maintained for Experiment 2 except that only a single exposure to the radial arm maze was presented to the LL-groups and the NL-groups were also confirmed to the central hub on a single occasion (day 67). Following exposure to the maze on day 67, all the rats were deprived of food for 48 h. Radial arm maze performance was tested at 69 days of age. Two weeks later all the rats were sacrificed and brain regions were dissected out and analyzed for catecholamine concentrations.

Neurochemical analysis

The concentrations of noradrenaline (NA), dopamine (DA) and dihydroxyphenylacetic acid (DOPAC) were assayed by use of high performance liquid chromatography with electrochemical detection according to the method previously reported (Magnusson *et al.*, 1980). The frozen samples were weighed and homogenized in 0.1M perchloric acid containing 4×10^{-5} sodium bisulfite and epinine as an internal standard. The supernatants were injected directly onto a Nucleosil C18 (5 μg) column connected to an amperometric detector (Bioanalytical Systems, La Fayette, USA) with its TL-3 carbon paste electrode (CP-O) set to 0.7V versus the Ag/AgC1 electrode.

Statistical analysis

Ambulation, rearing and head-dips from the openfield/holeboard test were each subjected to two-way ANOVA based on factorial design (Kirk, 1968). Ambulation and rearing from the LL-group in the radial arm maze activity tests on days 64, 65, 66 and 67 were subjected to split-plot ANOVA. Latency to acquire all 8 pellets and number of errors made were each subjected to two-way ANOVA based on a factorial design. The 1% level of significance was maintained throughout unless otherwise stated.

RESULTS

Experiment 1: 4 training trials

In the openfield/holeboard test on day 61 after birth, the rats that had been treated neonatally with 6-OHDA showed more ambulation [$F(1,28) = 12.4$] but less rearing [$F(1,28) = 43.1$] and head-dips [$F(1,28) = 31.1$] than the vehicle treated rats. No significant differences were observed between the two 6-OHDA groups, i.e. LL and NL, or between the LL-vehicle and NL-vehicle groups (see Table II). 6-OHDA rats (LL-groups) also showed more ambulatory behaviour and less rearing than the vehicle rats (LL-groups) during the 5 min exposures to the radial arm maze on days 64, 65, 66, and 67. Split-plot ANOVA indicated significant Groups effects for both ambulations and rearing [$F(1,14) \geq 5.2$, $p<0.05$]. Table II indicates that both the 6-OHDA and vehicle groups decreased ambulation and rearing from day 64 to day 67; this was supported by significant effects of days in the ANOVA [$F(3,42) \geq 14.2$].

Two-way factorial ANOVA of radial maze performance indicated significant between-Groups effects for both the latency to all 8 pellets [$F(1,28) = 13.5$] and the number of errors made [$F(1,28) = 17.9$] in acquiring all 8 pellets. Figure.1 presents the latency and errors data from the latent learning test. Tukey HSD tests indicated

that the 6-OHDS-LL group showed shorter latencies and made fewer errors than the 6-OHDA-NL group; the vehicle-LL group similarly performed better than the Vehicle-NL group. Scheffé's test indicated that the combined means of the Vehicle-LL and -NL groups were significantly lower than the combined means of the 6-OHDA-LL and NL groups for both the latency and errors data. Thus, while the 6-OHDA treated rats evidenced latent learning to the same extent as the vehicle treated rats, DA depletion following neonatal 6-OHDA treatment resulted in an overall retarded learning performance in the radial arm maze.

TABLE II. *Ambulation, rearing and head-dips by neonatal 6-OHDA treated (75 μg, i.c. on day 1 after birth 30 min after DMI, 25 mg/kg) and vehicle (0.1% ascorbic acid dissolved in saline) treated rats from Experiments 1 and 2 in the holeboard/openfield and radial arm maze activity test (n =8 throughout).*

Holeboard/Openfield test (day 61): Experiment 1				
		Ambulation	*Rearing*	*Head-dips*
6-OHDA-LL		191 ± 13[1]	27.1 ± 2.0[1]	15.3 ±1.3[1]
6-OHDA-NL		218 ± 16[1]	29.3 ± 1.6[1]	18.2 ± 1.4[1]
Vehicle-LL		158 ± 7	41.6 ± 1.7	29.9 ± 1.3
Vehicle-NL		153 ± 7	40.0 ± 2.2	32.9 ± 3.7
Holeboard/Openfield test (day 66): Experiment 2				
		Ambulation	*Rearing*	*Head-dips*
6-OHDA-LL		200 ± 12[1]	26.3 ± 1.6[1]	17.7 ± 1.3[1]
6-OHDA-NL		210 ± 17[1]	29.7 ± 1.4[1]	15.9 ± 1.1[1]
Vehicle-LL		161 ± 6	42.3 ± 1.7	30.8 ± 3.5
Vehicle-NL		148 ± 7	40.4 ± 1.6	31.4 ± 1.9
Radial arm maze activity tests (days 64-67): Experiment 1				
Day 64	6-OHDA-LL	353 ± 26[2]	5.5 ± 4[2]	
	Vehicle-LL	305 ± 21	76.6 ± 5	
Day 65	6-OHDA-LL	321 ± 18[2]	53.9 ± 3[2]	
	Vehicle-LL	249 ± 20	61.7 ± 4	
Day 66	6-OHDA-LL	283 ± 12[2]	46.0 ± 4[2]	
	Vehicle-LL	246 ± 17	54.5 ± 4	
Day 67	6-OHDA-LL	261 ± 16[2]	47.0 ± 3[2]	
	Vehicle-LL	235 ± 13	54.1 ± 3	
Radial arm activity test (day 67): Experiment 2				
Day 67	6-OHDA-LL	302 ± 81	36.1 ± 3.1[1]	
Day 67	Vehicle-LL	254 ± 12	60.1 ± 2.2	

Values are expressed as means ± s.e.m.

[1]$p<0.01$; [2]$p<0.01$ over all 4 days (64-67), Tukey's HSD test compared to appropriate vehicle control.
LL= Latent learning group; NL=No latent learning group.

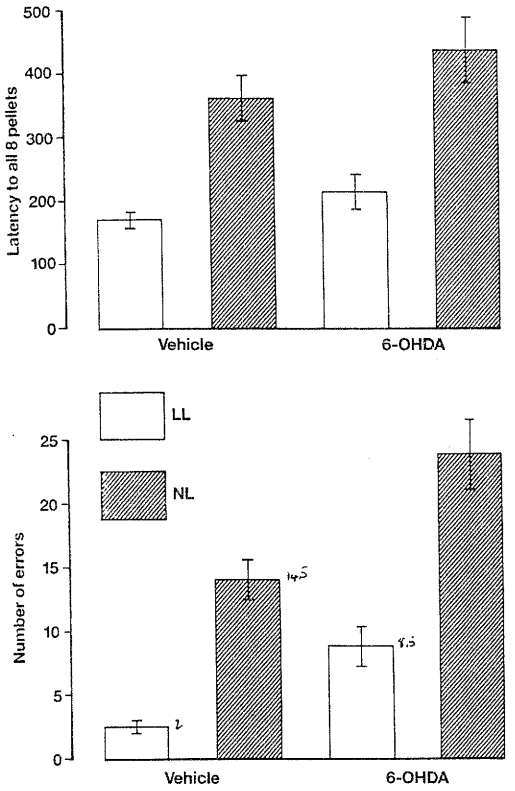

FIG.1. Latency to acquire all 8 pellets (one placed in each of the 8 arms) and the number of errors incurred in acquiring all 8 pellets, by neonatal 6-OHDA treated and vehicle treated rats in the LL (Latent Learning) and NL (No Latent Learning) conditions. Rats in the LL conditions were allowed to explore the maze during four 5-min, trials prior to the learning test (see text for details).

Experiment 2: Single training trial

As in experiment 1 rats that had been treated neonatally with 6-OHDA showed more ambulation [F(1,28) =14.6] but less rearing [F(128) =49.3] and head-dips [F(1,28) =31.2] than the vehicle reared rats in the openfield/holeboard test on day 66 after birth (see Table II). No differences were observed between the two 6-OHDA groups, i.e. LL and NL, or between the LL-vehicle and NL-vehicle groups. 6-OHDA rats (LL-group) also showed more ambulatory and less rearing behaviour than the vehicle rats (LL-group) during the 5 min exposure to the radial arm maze on day 67 (Table II). ANOVA indicated significant Between-Groups effects for both ambulation and rearing [F(1,14) $\geq$ 13.7].

Two-way factorial ANOVA of radial maze performance indicated significant Treatment $\times$ Exposure interaction for the latency to all 8 pellets [F(1,28) = 4.3, $p<0.05$], but only a Treatment effect [F(1,28) = 43.9] and an Exposure effect [F(1,28) = 9.9] for the number of errors made in acquiring all 8 pellets. Figure 2 presents the latency and errors data from the latent learning tests. Tukey HSD test indicated that the Vehicle-

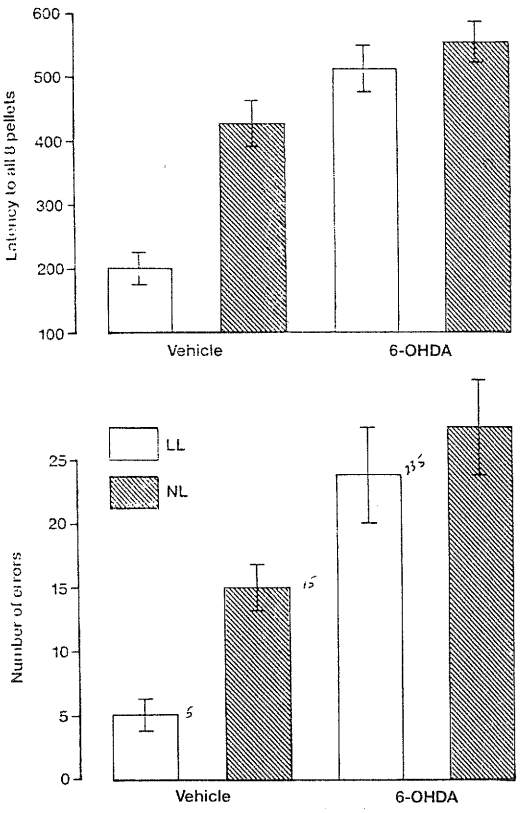

FIG 2. Latency to acquire all 8 pellets (1 placed in each of the 8 arms) and the number of errors incurred in acquiring all 8 pellets by neonatal 6-OHDA treated and vehicle treated rats in the LL (Latent Learning) and NL (No Latent Learning) conditions. Rats in the LL conditions were allowed to explore the maze during a single 5-min trial prior to the learning test (see text for details).

LL group showed shorter latencies and made fewer errors in attaining all 8 pellets than the Vehicle-NL group whereas no significant differences between the 6-OHDA-LL and -NL groups was obtained. As in experiment 1, Scheffe's test indicated that the combined means of the Vehicle-LL and -NL-groups were

significantly lower than the combined means of the 6-OHDA-LL and -NL groups for both the latency and errors data. Thus, it appears that the single 5 min exposure to the maze in this experiment was sufficient to result in a latent learning effect for the vehicle control groups but not for the DA depleted rats.

Neurochemical Analysis

Table III presents the concentrations of NA, DA and DOPAC in the nucleus accumbens and striatum of the rats tested in Experiment 2. Rats treated neonatally with 6-OHDA showed severe DA depletions in the striatum (4% and 8% of control values, respectively) but somewhat lesser depletions in the nucleus accumbens (25% of control values). NA was not significantly affected by neonatal treatment with 6-OHDA.

TABLE III. *Noradrenaline, dopamine and dopamine metabolite concentrations in the striatum and nucleus accumbens of adult rats treated neonatally with 6-OHDA (75 μg, intracisternally, 30 min after DMI, 25 mg/kg) on day 1 after birth.*

	Concentrations (pmol/mg wet weight) of		
	Noradrenaline	*Dopamine*	*DOPAC*
Striatum:			
Vehicle	0.82 ± 0.09	57.14 ± 2.33	14.91 ± 0.65
6-OHDA	0.92 ± 0.17	2.25 ± 0.081**	1.12 ± 0.46**
%	(112)	(4)	(8)
Nucleus Accumbens:			
Vehicle	11.98 ± 0.96	36.25 ± 1.81	5.81 ± 0.44
6-OHDA	10.51 ± 2.45	9.23 ± 3.78**	1.43 ± 0.49**
%	(88)	(25)	(25)

n =6, results are expressed as means ± s.e.m.
**$p < 0.001$, *student's t*-test
Values in parentheses are the means of the 6-OHDA animals expressed as a percentage of the corresponding vehicle controls.
Neurochemical assays were performed as described previously (Magnusson *et al.*, 1980).

DISCUSSION

The purpose of this study was to investigate whether or not dopaminergic pathways in the brain were involved in the latent learning phenomenon, by inflicting a DA lesion neonatally using 6-OHDA, with DMI pretreatment protecting NA pathways. Latent learning effects were assumed to have occurred when the LL groups, that received prior exposures to the maze (i.e. opportunity to explore the maze), showed significantly shorter latencies and fewer errors to acquire all 8 pellets, one from each of the 8 arms, than the NL groups that did not receive prior exposure to the maze. The main findings indicated that the DA depleted rats showed latent learning similar to that of the vehicle treated rats when four 5 min exposures to the radial arm maze were given (Experiment 1). However, when only a single 5 min exposure to the maze was allowed the 6-OHDA treated rats demonstrated an attenuated latent effect relative to the robust effect evidenced by the control rats. The ancillary findings pertain to the evidence from each experiment that 6-OHDA treated rats showed more ambulatory behaviour but less rearing and head-dipping behaviour in the holeboard/open-field during the 5 or 10 min testing intervals.

Further, motor activity testing of the groups exposed to the maze (LL groups) indicated once again that the 6-OHDA treated rats showed more ambulation but less rearing during the 5 min exposure period. Neurochemical analysis of the rats from experiment 2 confirmed severe depletion DA depletion in the striatum but less severe depletion in the nucleus accumbens.

Rats inflicted with neonatal DA depletions have been found to demonstrate reductions in exploratory behaviour, as indexed by rearing, head-dip and modified, complex openfield behaviour (Archer *et al.*, 1988; Experiments 1 and 2; unpublished data). Assuming that rearing may be a more selective measure of exploratory behaviour than locomotion (Russell, 1973) and the validity of head-dip behaviour as a measure of exploration (File and Wardill, 1975), it may be that the disruptions of exploratory behaviour following neonatal DA loss result from the increase in ambulatory/locomotor and total activity that are consistently observed (Miller *et al.*, 1981; Shaywitz *et al.*, 1976*a*). Tolman's latent learning phenomenon (e.g. 1932) appears to provide a particularly suitable circumstance of stimulus priming by the initial, exploratory exposures to the radial arm maze by which the rats "learned" in the absence of food reward. In Experiment 1, 6-OHDA treated rats showed effective latent learning when several exploration trials were presented. In experiment 2, the exploratory trials were limited to a single 5 min instance and unlike the controls the 6-OHDA treated rats failed to show effective latent learning. Thus, although DA appears, to some extent, to modulate latent learning the effect may be overcome by more prolonged exposure to the maze.

Although the radial arm maze deficit was reliably demonstrated here and in our previous

study (Archer *et al.*, 1988), Pearson *et al.* (1984) obtained an improved performance in the radial arm maze after neonatal DA depletions. Similarly, Hagan and co-workers (1983) testing rats treated with 6-OHDA as adults, suggested DA depletions did not lead to spatial learning deficits but rather a sensorimotor impairment. However, Whishaw and Dunnett (1985) indicated that severity of DA loss determined the extent of both the spatial navigation and sensimotor deficits. Most important, Whishaw *et al.* (1987) produced severe DA depletions of the caudate-putamen region following neonatal 6-OHDA treatment and found drastic impairments on several cognitive and motor tasks. DA depletion resulted in impairments of both place and cue navigation in a circular water maze (Morris-type) but not in sensorimotor orienting behaviour or in tests of catalepsy. Thus, these authors suggest that neonatal DA depletion caused disruptions in spatial navigation that were quanlitatively and qualitatively similar to those following adult 6-OHDA damage (Whishaw *et al.*, 1987).

Consideration of the latent learning procedure suggests at least two possible means by which the latent learning (or pre-exposure) trial(s) may affect later performance in the radial arm maze: (1) by decreasing neophobia to the novel environment, (2) through the implicit recognition of specific characteristics of the maze. From the point of view of the neophobia hypothesis, perhaps the higher frequency of repeat visits to arms (i.e. "search" behaviour) where the food already had been eaten, in the latent learning 6-OHDA pretreated animals in Experiment 2, reflected higher fear (neophobia) of the yet-to-be-visited arms. Similarly, the overall higher number of arm entries in the two lesion groups compared to the two non-lesion groups in both experiments might reflect neophobia. One problem for the neophobia hypothesis may be that the no latent learning (NL) groups consistently demonstrated an increased number of errors together with increases in the latency to acquire all eight pellets. The alternative hypothesis would be that DA denervated rats may have failed to learn the particular characteristics of the maze following a single exposure, since under these conditions performance was not improved by the latent learning trial. One explanation may by that under conditions of limited exposure the DA loss leads to a retardation of the development of higher-order associations, e.g. those between the positions of various extra-maze cues and the false back walls of each of the arms of the maze. A different explanation pertains to the conceptualization of radial arm learning, in general, by Staddon (1983). By this view, each rat has to use three types of learning in the radial arm maze: a place code, a short term working memory of which arms it has been in, and a response rule based on a win-shift strategy. Both explanations may indirectly implicate the hyperactive condition of the DA depleted rats: in the first case through some interference with the development of higher-order associations and in the second case as a consequence of some failure of the response rule, since DA receptor blockade has been suggested to interfere with response initiation (e.g. Fibiger *et al.*, 1974; Beninger *et al.*, 1980).

There is some evidence of dopaminergic involvement in the relationship between prior exploratory behaviour and later latent learning performance in a maze situation. Ahlenius *et al.* (1977) administered either a DA antagonist, haloperidol, or a DA agonist, apomorphine, to mice, 10 min and 5 min, respectively, before preexposure to a modified quadruple-T maze. In the control mice (untreated) successful latent learning was established, i.e. the mice preexposed to the maze showed a better learning performance to obtain food reward than the non-preexposed mice. Haloperidol treatment suppressed exploratory behaviour during the preexposure trial. During the subsequent latent learning test on the following day, haloperidol treated animals performed normally, but the groups administered apomorphine (1.6 or 3.2 mg/kg) failed to show latent learning. It was concluded that the over-activation of DA receptors during the pre-exposure phase disrupted latent learning. Apomorphine, at doses above 0.8 mg/kg, stimulates motor activity quite considerably, possibly through an activation of postsynaptic DA receptors (Strömbom, 1976; Thornburg and Moore, 1974). It is tempting to suggest that it may have been the hyperactive condition of the 1.6 and 3.2mg/kg apomorphine groups that disrupted latent learning. Similarly, in the present study it is likely that the DA denervation, produced in the rats treated neonatally with 6-OHDA, caused a postsynaptic DA supersensitivity (Seiden *et al.*, 1989). Although both these results suggest some hyperactivation of postsynaptic DA receptors as mediating the latent learning failure, Ahlenius *et al.* (1977) did not obtain any dose-related gradient in the apomorphine result. In summary, there is some plausible indication that an alteration of DA neurotransmission may interfere with latent

learning. This may be related to the consequences of reductions in normal exploratory behaviour and/or increased neophobia to the novel environment accompanied by increases in motor activity. It is possible that under conditions of limited maze preexposure latent learning is adversely affected by an overactivation of postsynaptic DA receptors.

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