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EFFECTS OF CENTRALLY ACTING DRUGS ON EXPLORATORY BEHAVIOUR IN RATS

BY

A. S. MARRIOTT AND P. S. J. SPENCER

From the Research Division, Allen & Hanburys Ltd., Ware, Herts.

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Steinberg and her colleagues have investigated the effects of amphetamine, amylobarbitone and of mixtures of these two drugs on the exploratory activity of rats placed into a symmetrical Y-shaped box. They found that some of the drug mixtures produced great increases in exploratory activity, although alone each substance produced little or no increase. When a mixture of amphetamine and amylobarbitone was given to rats which had had repeated, or even a single exposure to the Y-box beforehand, there was no increase in exploration (Steinberg, Rushton & Tinson, 1961; Rushton & Steinberg, 1963; Rushton, Steinberg & Tinson, 1963). A possible interpretation of these results is that some mixtures of amphetamine and amylobarbitone may lead to increased exploratory activity by reducing the susceptibility of rats to environmental stimuli; this would not be inconsistent with the clinical use of such drug combinations in anxiety states. It was decided that the Y-box offered an interesting approach to the study of centrally acting drugs. In the present investigation the actions of several such drugs on the exploratory activity of rats placed into this environment have been investigated.

The action of each drug was investigated at several dose-levels; in some experiments, drug actions were studied in rats which had had previous experience of the environment in which exploratory behaviour was tested. Some experiments were also carried out at different times after injection in order to determine when peak effects occurred. Part of this work has already been communicated to the British Pharmacological Society, July 1964.

METHODS

Animals

Male Wistar rats (A. Tuck & Sons) were purchased at 10 weeks old, weighing 85 to 100 g. The animals were kept for 6 to 9 days, housed ten per cage in home cages 50 cm long × 25 cm wide × 18 cm high. The home cages were kept in a room in which the effect of outside noise was substantially reduced and which was artificially illuminated during working hours. Apart from once-daily replenishment of food (No. 41 B Cube diet, E. Dixon & Sons) and water, the rats were left undisturbed before use. Housing and laboratory temperatures were maintained at 18 to 22° C.

dministration of drugs

All drugs were injected subcutaneously in the loose fold of skin at the back of the neck in a volume of 0.2 ml./100 g body weight, either dissolved in 0.9% w/v saline or suspended in 5% gum acacia solution. All doses in the text refer to the free acid or base. The following drugs were used: amphetamine sulphate,

amylobarbitone sodium, chlordiazepoxide hydrochloride, chlorpromazine hydrochloride, haloperidol, imipramine hydrochloride, meprobamate, methylpentynol, perphenazine hydrochloride, phenelzine dihydrogen sulphate and tranylcypromine hydrogen sulphate.

Apparatus

The apparatus consisted of a wooden, symmetrical Y-shaped box similar to that described by Steinberg *et al.* (1961). Each arm of the box was 38 cm long, 13 cm wide and had walls 33 cm high. The box had a wooden floor but no roof. All surfaces of the apparatus were coated with hard copal varnish to assist cleaning. The Y-box was situated in a darkened room and was illuminated by means of a 100-W lamp placed above the centre of the apparatus and 70 cm from its floor.

Experimental procedure: measurement of exploratory behaviour and defaecation

All doses of drugs or vehicles were administered randomly to dose-groups of at least eight rats. The rats were taken randomly from their home cages, given drug or vehicle and placed singly in metal cages 36 cm long, 15 cm wide and 11 cm high. After 35 min, unless otherwise stated, each rat was transferred to one arm of the Y-box and observed continuously for 5 min. The number of complete entries with all four feet into the arms of the box and also the number of faecal boli deposited during this period were recorded. All faecal matter and urine were removed from the apparatus between trials.

Repeated experience experiments

In each experiment twenty rats were given previous experience by means of five 5-min trials in the Y-box over a period of 2 weeks, whilst another twenty (inexperienced or naive rats) were given precisely the same amount of handling but were not introduced into the Y-box on any of the five occasions. At each handling, or at each trial during the experiencing procedure, all rats received 0.9% saline (0.2 ml./100 g body weight, subcutaneously) and were housed singly for 35 min before being either handled or placed in the Y-box. Between trials the animals were housed in their home cages. Two days after the fifth trial the effects of drugs were investigated and compared with saline controls in both the experienced and inexperienced (handled) groups of animals, using the procedure already outlined.

Single experience experiments

In these experiments the effects of drugs on the acquisition of experience in the Y-box were studied as well as the effect of a single previous experience on the subsequent activity of drugs. Each experiment consisted of two distinct trials separated by three complete days. In each experiment six groups of eight rats were used. At the first trial two groups received saline and were introduced into the Y-box for 5 min as described previously (" experienced " rats); two groups received a drug and were introduced into the Y-box as before (" experienced " under the influence of the drug); one group received saline but was handled only (" inexperienced " rats); and a final group received drug and was handled only (" inexperienced " rats). At the second trial the effect of the drug was investigated and compared with saline on each of the three groups: experienced rats, rats experienced under the influence of the drug and inexperienced rats. The procedure is summarized in Table 1.

TABLE 1

GENERAL PLAN OF THE INVESTIGATION

Forty-eight rats were divided into six groups of eight animals. With the exception of groups 5 and 6 each group was given two trials 3 days apart in a Y-shaped box after the administration of either saline or drug. Groups 5 and 6 were subjected to an equivalent handling procedure at the first trial but were not introduced into the Y-box until the second trial

Group	Trial 1	Trial 2
1. Experienced	Saline	Saline
2. Experienced	Saline	Drug
3. Experienced with drug	Drug	Saline
4. Experienced with drug	Drug	Drug
5. Inexperienced	Saline (handled only)	Saline
6. Inexperienced	Drug (handled only)	Drug

Analysis of results

Throughout this investigation, differences between mean exploratory activities or mean defaecation scores for different experimental groups were always assessed for significance by applying Student's *t*-test. The values of *P* for significant differences are quoted wherever comparisons are made.

RESULTS

Effect of several centrally acting drugs on exploration and defaecation by naive rats

Table 2 summarizes the effects of several major tranquillizers, minor tranquillizers, antidepressants and amphetamine and amylobarbitone mixtures on the exploratory activity of experimentally naive (inexperienced) rats in the Y-box. The effects on defaecation are also shown.

TABLE 2

EFFECT OF DRUGS ON THE EXPLORATORY BEHAVIOUR OF RATS PLACED IN A Y-BOX

All doses were administered subcutaneously to naive rats 35 min before placing the rats into the Y-box. Values are the mean entries into the arms of the box and the mean number of faeces recorded during a 5-min observation period. Standard errors and the values of *P* for significant changes are shown. NS = $P>0{\cdot}05$

		Exploration			Defaecation		
Drug	Dose (mg/kg)	Mean entries	*P*	Effect	Mean faeces	*P*	Effect
Major tranquillizers							
Chlorpromazine	0·25	4·6 ±1·53	NS		3·9 ±0·85	NS	
	0·5	3·9 ±1·19	NS		4·0 ±0·84	NS	
	1·0	1·9 ±1·06	<0·05	Reduced	2·0 ±0·65	<0·01	Reduced
	4·0	1·1 ±0·16	<0·02		0·5 ±0·37	<0·001	
	8·0	0·1 ±0·13	<0·001		0·5 ±0·5	<0·001	
	Saline	5·9 ±1·29	—		6·0 ±0·84	—	
Haloperidol	0·01	8·3 ±1·9	NS		2·8 ±0·81	NS	
	0·1	4·6 ±1·27	<0·05		3·6 ±0·54	NS	
	1·0	0·25±0·16	<0·001	Reduced	1·8 ±0·55	NS	No effect
	4·0	0·4 ±0·18	<0·001		2·3 ±0·79	NS	
	8·0	1·1 ±0·71	<0·001		4·0 ±0·87	NS	
	5% Acacia	8·9 ±1·55	—		2·3 ±0·79	—	
Perphenazine	0·1	5·0 ±1·15	NS		2·5 ±1·1	NS	
	1·0	1·5 ±0·5	<0·01		1·9 ±0·35	<0·05	
	4·0	0·25±0·5	<0·01	Reduced	1·4 ±0·63	<0·001	Reduced
	8·0	0·25±0·5	<0·01		0·6 ±0·63	<0·001	
	Saline	9·1 ±2·2	—		4·4 ±0·92	—	
Minor tranquillizers							
Chlordiazepoxide	3·1	5·8 ±1·7	NS		3·6 ±0·46	NS	
	6·3	13·7 ±2·2	<0·01		4·6 ±0·35	NS	
	12·5	15·5 ±2·2	<0·001		4·5 ±0·55	NS	
	25·0	16·9 ±2·8	<0·001	Increased	4·5 ±0·37	NS	No effect
	50·0	13·9 ±4·1	<0·01		3·4 ±0·25	NS	
	100·0	8·1 ±1·8	NS		2·4 ±0·62	NS	
	200·0	3·9 ±0·5	NS		2·5 ±0·47	NS	
	Saline	5·7 ±1·2	—		4·0 ±0·76	—	
Meprobamate	12·5	8·9 ±1·8	NS		4·8 ±0·95	NS	
	25·0	8·9 ±1·5	NS		3·7 ±0·78	NS	
	50·0	8·3 ±1·5	NS		4·2 ±0·53	NS	
	100·0	11·8 ±2·4	NS	Increased	3·8 ±0·59	NS	No effect
	200·0	14·5 ±1·9	<0·01		2·5 ±0·22	NS	
	400·0	18·9 ±3·8	<0·01		2·0 ±1·0	NS	
	800·0	13·8 ±2·45	<0·02		1·6 ±0·61	NS	
	5% Acacia	6·5 ±1·38	—		3·2 ±0·59	—	

TABLE 2—(CONTINUED)—

Drug	Dose (mg/kg)	Exploration: Mean entries	*P*	Effect	Defaecation: Mean faeces	*P*	Effect
Methylpentynol	5·0	12·0 ±2·7	NS		1·5 ±0·63	NS	
	10·0	9·5 ±2·1	NS		3·5 ±0·84	NS	
	20·0	12·8 ±2·5	NS	Increased	3·4 ±0·68	NS	No effect
	40·0	17·6 ±3·0	<0·01		2·8 ±0·77	NS	
	80·0	16·7 ±2·0	<0·001		4·5 ±0·63	NS	
	160·0	14·9 ±3·2	<0·05		4·9 ±0·44	NS	
	320·0	7·4 ±2·6	NS		2·6 ±0·89	NS	
	5% Acacia	7·6 ±1·4	—		3·8 ±1·3	—	
Antidepressants							
Imipramine	2·5	8·0 ±2·4	NS		4·3 ±0·81	NS	
	5·0	4·9 ±1·7	<0·02		4·8 ±0·67	NS	
	10·0	9·4 ±2·3	NS	Little	4·3 ±0·69	NS	Little
	20·0	9·1 ±2·4	NS	effect	2·8 ±0·67	<0·02	effect
	40·0	9·0 ±3·0	NS		4·0 ±0·73	NS	
	Saline	10·6 ±1·1	—		5·3 ±0·64	—	
Phenelzine	1·0	5·9 ±1·4	NS		4·4 ±1·16	NS	
	5·0	2·1 ±0·9	<0·001		3·9 ±0·48	NS	
	10·0	2·4 ±0·7	<0·001	Slightly	2·3 ±0·48	<0·05	Reduced
	20·0	4·3 ±1·8	NS	reduced	2·0 ±0·68	<0·05	
	40·0	6·6 ±2·6	NS		0·25±0·58	<0·001	
	Saline	7·6 ±1·0	—		4·4 ±0·71	—	
Tranylcypromine	0·1	10·0 ±2·8	NS		3·8 ±0·92	NS	
	1·0	7·1 ±2·4	NS		1·5 ±0·71	NS	
	4·0	2·4 ±0·6	<0·05	Slightly	0·4 ±0·27	NS	Reduced
	8·0	4·0 ±1·7	NS	reduced	0·4 ±0·18	<0·05	
	Saline	7·5 ±1·9	—		1·8 ±0·58	—	
Drug mixture							
Amphetamine-amylobarbitone	0·25/ 5·0	14·4 ±2·8	NS		1·75±0·75	NS	
	0·75/15	18·4 ±5·4	NS		1·75±0·45	NS	
	1·0 /20	26·0 ±3·3	<0·01	Increased	1·38±0·37	NS	Reduced
	2·0 /40	28·1 ±3·2	<0·01		1·75±0·62	NS	
	4·0 /80	1·25±0·98	<0·001		0·5 ±0·27	<0·02	
	Saline	13·25±1·8	—		3·1 ±0·94	—	

Chlorpromazine, perphenazine and haloperidol all reduced exploration. Chlorpromazine- and perphenazine-treated rats showed signs of sedation such as ptosis, lowered body tone, splaying of limbs and passivity. Unlike the other two drugs, haloperidol did not significantly reduce defaecation, and rats given this agent, although showing catatonia and slight ptosis, squeaked and showed other signs of fear when touched. The antidepressants phenelzine and tranylcypromine reduced defaecation; these drugs also reduced exploration but only at the intermediate dose levels. Imipramine had little effect on either index of activity at the single interval between administration and testing investigated.

Meprobamate, methylpentynol and particularly chlordiazepoxide caused marked increases in exploratory activity, although none of these drugs significantly affected defaecation. These results are compared with those obtained with various doses of a fixed-ratio (1 : 20) mixture of amphetamine and amylobarbitone. As with the mixture of amphetamine and amylobarbitone, the dose/response relationship for each drug was biphasic; there was a rise to maximal activity, but as the dose increased further the effect declined. This decline was most marked with the amphetamine and amylobarbitone

mixture. Chlordiazepoxide increased exploratory activity, but there were no signs of ataxia except at 100 and 200 mg/kg. On the other hand, the amphetamine and amylobarbitone mixture produced ataxia at all dose levels. At the highest dose of the mixture there was considerable central nervous depression characterized by ataxia, ptosis, lowered body tone and reduced general activity. Virtually no exploratory activity occurred in these rats. Only the drug mixture reduced defaecation at doses which increased exploration, but the maximal reduction in defaecation did not coincide with the maximal increase in exploration.

On injection, chlordiazepoxide solutions caused some local, transient irritation. The effect of similar irritation upon subsequent exploration was investigated by determining the exploratory activity of rats 35 min after they had received 0.2 ml. of 0.03 N-hydrochloric acid subcutaneously. In these rats exploration was reduced, not increased.

In Table 2 it can be seen that the mean levels of exploration and defaecation in control groups show definite variations between experiments. These variations are to be expected since the investigations described were made over a period of several months. However, control levels were remarkably constant over periods of 2 to 3 weeks and the mean control scores shown for individual experiments give fairly reliable estimates of the normal levels of exploration or defaecation on the day of the test and with the particular animals used.

Comparative effects of chlordiazepoxide and the amphetamine and amylobarbitone mixture

Chlordiazepoxide was the most potent of the three minor tranquillizers in that it caused significant increases in exploratory activity at much lower dose-levels than either meprobamate or methylpentynol. Chlordiazepoxide was therefore investigated more closely to determine how far its actions resembled those of the amphetamine and amylobarbitone mixture.

First, the effect of various intervals between administration of drug and testing response was studied. Chlordiazepoxide (25 mg/kg) or the mixture of amphetamine (0.75 mg/kg) and amylobarbitone (15 mg/kg) was administered at various time intervals up to a maximum of 120 min before placing the animals in the Y-box (Fig. 1). With chlordiazepoxide, a peak or plateau effect on exploratory activity occurred between 35 and 60 min. No significant changes in defaecation were observed. On the other hand, the rise to maximal effect on exploration was more rapid with the mixture and the peak effect was of shorter duration. In this instance, the effects were accompanied by reduced defaecation but, as observed previously, the lowest level of defaecation did not coincide with the highest level of exploratory activity.

In the work reported so far, inexperienced or naive rats have been used throughout. Steinberg *et al.* (1961) showed that rats given a number of previous trials or experiences in the Y-box (without drug treatment) no longer responded to the mixture of amphetamine and amylobarbitone with an increase in exploration. Fig. 2,A shows that this is also true of chlordiazepoxide. In rats which had had five previous trials in the Y-box, chlordiazepoxide (25 mg/kg) failed to increase the level of exploratory activity, whereas it was effective in inexperienced rats ($P<0.01$). The activity of the experienced saline control group was significantly lower than the inexperienced saline control group ($P<0.01$). The results of

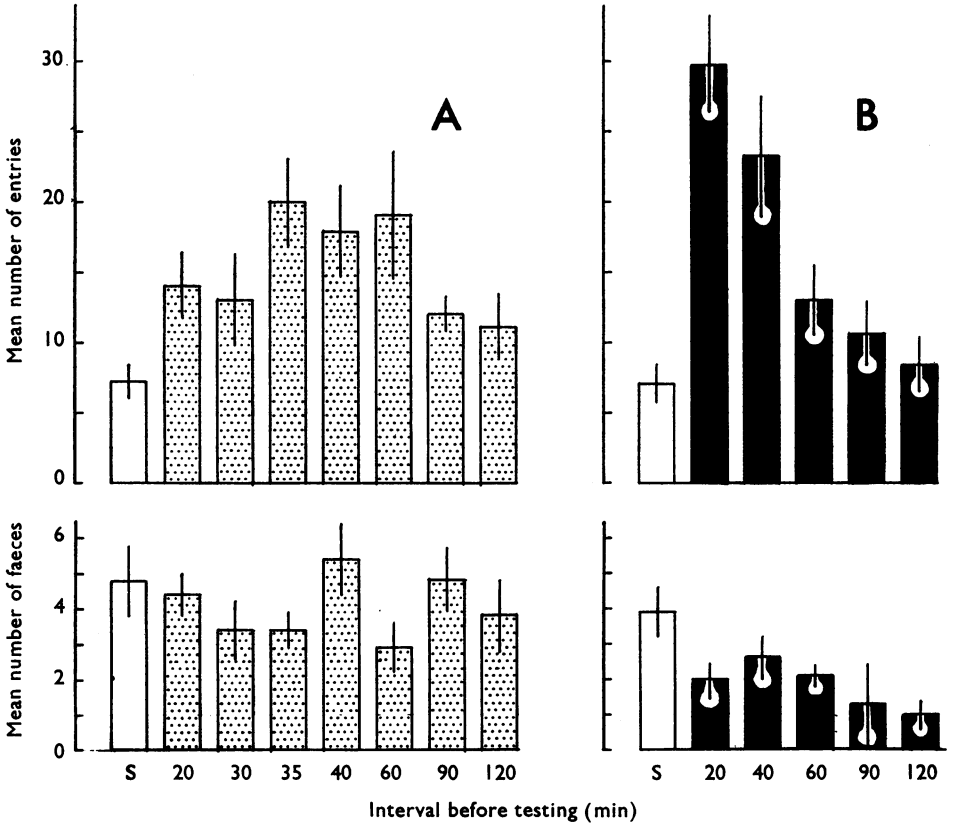

Fig. 1. Effect of varying the interval between drug and testing reactions to drugs. In **A**, chlordiazepoxide (25 mg/kg) was administered subcutaneously to groups of ten naive rats. At different times after drug administration the mean exploration and defaecation scores for each group were determined (dotted columns). Rats were placed individually into a Y-shaped box and the number of entries into the arms of the box and the number of faeces deposited during 5 min were recorded. One or two rats treated with saline (S) were investigated at each time interval, the mean activities of ten such rats serving as control scores (open columns). The vertical lines indicate standard errors. In **B**, the results of a similar experiment using an amphetamine and amylobarbitone mixture (0.75 and 15 mg/kg) are shown.

an identical experiment with the amphetamine and amylobarbitone mixture are illustrated in Fig. 2,**B**. Repeated previous experience (five trials) in the Y-box inhibited the subsequent action of the drug mixture, in the same way as it had inhibited the actions of chlordiazepoxide.

Rushton *et al.* (1963) showed that even a single previous experience in the Y-box is sufficient to inhibit the subsequent action of the amphetamine and amylobarbitone mixture, although a single previous experience under the influence of the drug mixture had no effect on the action of the drug mixture at a second trial. Fig. 3,**A** shows the results of an experiment in which the effect of a single previous experience on the subsequent activity of

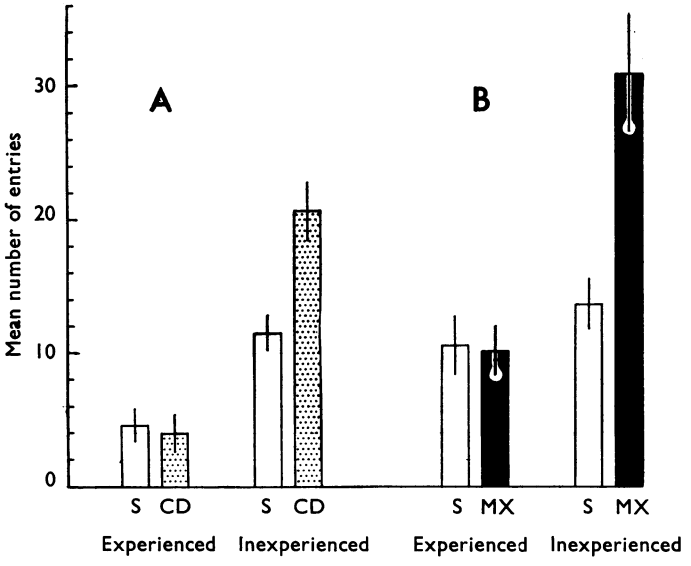

Fig. 2. Comparison between the effects of chlordiazepoxide and an amphetamine and amylobarbitone mixture on the exploratory activity of experienced and inexperienced rats. The experienced rats had been placed into the Y-box on five previous occasions. The inexperienced rats had been given an equivalent handling procedure, but had not been introduced into the Y-box on any of the five occasions. The mean numbers of entries into the arms of the Y-box during 5 min are shown for groups of ten rats. The vertical lines represent the standard errors of the mean. In **A**, rats treated with chlordiazepoxide (CD), 25 mg/kg, are compared with saline-treated rats (S). In all experiments drug or saline was administered subcutaneously 35 min before testing. In **B**, the results of an identical experiment using an amphetamine (0.75 mg/kg) and amylobarbitone (15 mg/kg) mixture (MX) are shown.

chlordiazepoxide, and the effect of this drug on the acquisition of experience, were studied. For comparative purposes, an identical experiment was carried out using the amphetamine and amylobarbitone mixture (Fig. 3,**B**). In the experiment shown in Fig. 3,**A** chlordiazepoxide did not cause significant increases in the exploratory activity of rats which had been given a single previous experience in the Y-box under the influences of either saline (*a*) or chlordiazepoxide (*b*). With inexperienced rats, however, an increase did occur (*c*), and this was highly significant ($P<0.01$). The control level of activity in rats experienced with saline (*a*) was very much lower than in inexperienced rats (*c*) ($P<0.05$), whereas the control level of activity in chlordiazepoxide-experienced rats (*b*) was not significantly lower than the control level in inexperienced rats (*c*). The results illustrated in Fig. 3,**B** show that the mixture of amphetamine and amylobarbitone caused increased exploration in both saline-experienced rats (*d*) ($P<0.01$) and mixture-experienced rats (*e*) ($P<0.1$), as well as in inexperienced animals (*f*) ($P<0.01$). Nevertheless, in rats previously experienced with saline (*d*) the levels of activity were very much lower than they were in inexperienced rats (*f*), the corresponding means both being significantly lower ($P<0.001$). There was also a reduction in activity with animals experienced with the mixture (*e*), but this reduction was slightly less than with the saline-experienced animals (*d*), the differences between the corresponding means of (*d*) and (*e*) being significant only at the 10% level ($P<0.1$).

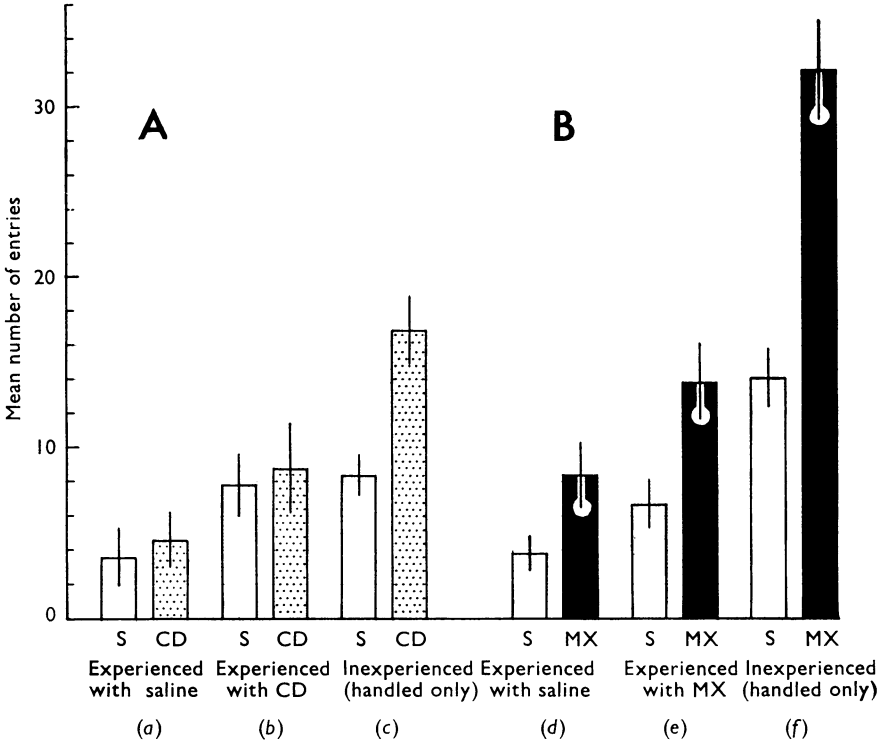

Fig. 3. The effects of a single previous experience upon subsequent actions of drugs and the effects of drugs on the acquisition of experience. In **A**, the effect of chlordiazepoxide (CD), 25 mg/kg, is compared with the effect of saline (S) on the exploratory activity of rats which had (*a*) been given a single 5-min trial in the Y-box 3 days previously following injection of saline, (*b*) been given a single 5-min trial in the Y-box 3 days previously following injection of chlordiazepoxide, or (*c*) received saline and equivalent handling to (*a*) and (*b*) 3 days previously, but had not been introduced into the Y-box before. In all experiments drug or saline was administered 35 min before testing. In **B**, the results of an identical experiment using an amphetamine, 0.75 mg/kg, and amylobarbitone, 15 mg/kg, mixture (MX) instead of chlordiazepoxide are shown.

DISCUSSION

The most striking observation in this work was a considerable and consistent increase in exploratory behaviour in inexperienced animals treated with the minor tranquillizers, chlordiazepoxide, meprobamate and methylpentynol. This finding is of particular interest because, although differing from each other in a number of ways, these drugs have the common clinical property of allaying fear and anxiety (Steinberg *et al.*, 1961; Berger, 1963; Baxter, 1964; Holmberg & William-Olsson, 1964). In each instance, the dose-response relationship proved to be biphasic, a decline in activity at the highest dose levels being well correlated with central nervous depression and ataxia. The increased exploration induced by chlordiazepoxide, meprobamate and methylpentynol was not accompanied by a decrease in defaecation. Although the amphetamine and amylobarbitone mixture reduced defaecation, this effect was not well correlated with exploration, and maximal effects on these two

indices of rat activity occurred at different dose levels (Table 2) and at different intervals between drug and testing (Fig. 1). Amylobarbitone alone had no effect upon defaecation in the Y-box and the effect produced by the mixture was probably due to the amphetamine content. The possibility that the three minor tranquillizers have a purgative effect in rats was considered, but none caused a significant increase in defaecation, and chlordiazepoxide had no effect on intestinal motility when examined by the charcoal meal method of Brittain & Collier (1958).

Like the 1 : 20 amphetamine and amylobarbitone mixture, chlordiazepoxide did not increase exploration in rats given five previous trials in the Y-box. Further comparison between chlordiazepoxide and the mixture of amphetamine and amylobarbitone showed that, whilst a single previous experience inhibited the subsequent effect of chlordiazepoxide, this degree of familiarization with the Y-box was not sufficient to inhibit completely the action of the mixture at the second trial; after five previous trials, however, the effect of the amphetamine and amylobarbitone mixture was completely blocked. When the rats were given experience under the influence of chlordiazepoxide, the subsequent action of the drug was still inhibited, indicating that the chlordiazepoxide was not blocking the acquisition of experience. On the other hand, the reduction in exploratory activity which usually occurs in untreated animals at a second exposure to the Y-box (Rushton *et al.*, 1963) was not observed if the rats received their first trial under the influence of chlordiazepoxide (Fig. 3,A). It is concluded that chlordiazepoxide only marginally inhibits the acquisition of experience in the Y-box.

In contrast, Rushton *et al.* (1963) found that an amphetamine and amylobarbitone mixture completely inhibited the experiencing process; animals experienced with the mixture behaved at their second trial in the Y-box as naive rats. However, our experiments with an amphetamine and amylobarbitone mixture have produced somewhat different findings to those reported by Rushton *et al.* (1963). We found that a single experience, whilst greatly reducing the exploratory activity levels, did not prevent the drug mixture from causing some increase in exploration when compared with experienced controls (Fig. 3). Moreover, when administered at the first trial, the amphetamine and amylobarbitone mixture had only a slight inhibitory effect on the experiencing process. The differences between our findings with the amphetamine and amylobarbitone mixture and those of Rushton *et al.* (1963) may be due to differences in experimental conditions, particularly the sex, strain and age of rat used in the two investigations; in addition, there is some difference in the ratio of doses used, since these workers expressed the doses as actual weights of substances used and not in terms of free acid or base. It is considered, from the experiments performed in this investigation, that there are slight differences between the effects of chlordiazepoxide and the 1 : 20 mixture of amphetamine and amylobarbitone. Although both these agents increased exploration in naive rats and were ineffective in repeatedly experienced rats, only the effect of chlordiazepoxide was completely inhibited by a single previous experience. In addition, the amphetamine and amylobarbitone mixture produced obvious ataxia at all dose levels investigated, whereas chlordiazepoxide caused ataxia only at the higher doses. Although it is evident that these drugs increase exploratory activity in the rat by modifying the reactions of the rat to external stimuli, the precise mechanisms involved are unknown. The drugs could, for example, impair memory, perception or brain mechanisms which normally inhibit organized motor output.

Chlorpromazine and perphenazine each reduced exploratory activity at dose levels which also reduced defaecation, but were without effect on either of these variables at lower dose levels. Haloperidol reduced exploration but did not affect defaecation. These findings agree with those of Janssen, Niemegeers, Schellekens, Verbruggen & Van Nueten (1963) who compared the actions of chlorpromazine and haloperidol on the behaviour of rats using an " open field " test similar to that first described by Hall (1934).

The significance of the results obtained with phenelzine, tranylcypromine and imipramine is not apparent. It is possible that the antidepressant actions of these drugs are mediated through changes in the metabolism of centrally acting catechol amines and may therefore increase the susceptibility of rats to environmental stimuli. Further investigation into the effects of these drugs on exploratory activity using longer intervals between administration of drug and testing is indicated.

SUMMARY

1. The effects of several major tranquillizers, minor tranquillizers and antidepressants on the exploratory behaviour of rats in a simple Y-box environment have been investigated.

2. The minor tranquillizers differed from the other drugs tested in causing considerable increases in exploration in naive rats; in all cases the dose/exploration curves were biphasic, resembling that of an amphetamine and amylobarbitone mixture.

3. In comparative studies on experienced and inexperienced rats, differences were found between the effects of chlordiazepoxide and of the amphetamine and amylobarbitone mixture. Chlordiazepoxide increased exploration without producing ataxia and its effects on exploration were completely inhibited by a single previous exposure to the Y-box.

4. No correlation was found between increased exploration and defaecation.

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