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Responses to Novelty in Rats with Lesions of the Dorsal Noradrenergic Bundle[1]

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Local injection of 6-hydroxydopamine was used to destroy selectively the dorsal ascending noradrenergic bundle in rats, producing more than 90% depletion of hippocampal noradrenaline. This lesion abolished spontaneous alternation in the T-maze (Experiment 1); abolished the approach response to an arm of changed brightness in the T-maze (Experiment 2); and reduced rearing (but did not change ambulation or defecation) in an unstressed open-field test (Experiment 3). In a stressed open field test (Experiment 4) the lesion increased habituation of ambulation but did not affect rearing or defecation — comparison with an anxiolytic drug, sodium amylobarbitone, suggested only a partial overlap of effects in this test. These findings are similar to the reported effects of administration of anti-anxiety drugs and lesions to the septo-hippocampal system. The results are in general consistent with the hypothesis that the dorsal ascending noradrenergic bundle mediates *some* of the behavioural effects of the anti-anxiety drugs by way of its projection to the septo-hippocampal system.

Introduction

The dorsal noradrenergic bundle (DB) carries fibres from the locus coeruleus to innervate wide areas of the forebrain, including the neocortex, septal area, hippocampus and amygdala. Its behavioural functions are in dispute (Mason & Iversen, 1979; McNaughton & Mason, 1980). According to one proposal, it forms part of a neural system that mediates anxiety and the behavioural effects of drugs (benzodiazepines, barbiturates and ethanol) which reduce anxiety (Gray, 1977). A specific version of this view holds that it is in particular the noradrenergic projection to the septo-hippocampal system which performs these particular functions (Gray, 1983; Gray, McNaughton, James & Kelly, 1975). From this hypothesis, one may derive the general prediction that the behavioural effects of destruction of the DB should resemble those produced by administration of the anti-anxiety drugs or by damage to the septal area or hippocampal formation.

There is an extensive literature on the behavioural effects of each of these three reference treatments (Gray, 1977; Gray et al., 1975; Grossman, 1978; O'Keefe & Nadel, 1978; Gray & McNaughton, 1983). Where the effects of the anti-anxiety drugs, septal lesions and hippocampal lesions are all known, there is a substantial overlap between them (Gray, 1983). We have recently shown that concordance of the effects of the three reference treatments is able successfully to predict the behavioural effects of DB destruction in tasks involving the omission of anticipated reward (Owen, Boarder, Gray & Fillenz, 1982).

In the present paper we apply the same logic to tests of reactions to novelty; and ask whether the behavioural effects of DB destruction are the same as the known effects of the anti-anxiety drugs and lesions to the septal area and hippocampus. For this purpose we have used four tasks: spontaneous alternation in a T-maze; the response to stimulus change in this apparatus; and low- and high-stress open field tests.

Surgical and Biochemical Methods

Surgical and biochemical methods have been fully described (Owen et al., 1982). The subjects were male Sprague-Dawley rats weighing 300-320 g at the time of surgery. In each experiment half of the subjects were injected with 6-hydroxydopamine (6-OHDA) in the vicinity of the DB according to Owen et al.'s (1982) 'lesion 2' procedure, while the other half underwent a sham operation in which the vehicle-filled cannula was lowered to the same co-ordinates, but nothing injected. Co-ordinates were 5.1 mm posterior to bregma, 1.1 mm lateral and 5.2 mm deep from dura. 6-OHDA-HBr (Sigma) was dissolved in the vehicle (1 mg ascorbate per ml of

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0.9% saline) in the ratio 6 mg/ml, and 2μl was injected bilaterally at the rate of 0.5μl/min. At the end of the experiment the brains were assayed for regional levels of noradrenaline (NA), dopamine (DA) and 5-hydroxytryptamine (5-HT). The results of these assays are given by Owen et al. (1982); see their Tables I and III. The level of NA was reduced by 91% or more in the hippocampus, by about 50% in the septal area and by 30-44% in the hypothalamus; there were no significant changes in the levels of striatal or hypothalamic DA or hippocampal 5-HT.

Experiment 1

If a rat is allowed to make two successive free choices in a T-maze, it manifests a strong tendancy to enter on the second trial the arm opposite to the one chosen on the first. This behaviour ('spontaneous alternation') is controlled in the main by spatial features of the animal's enviroment (Douglas, 1966; O'Connell, 1964; Rosen & Stein, 1969). The level of spontaneous alternation is reduced by anti-anxiety drugs (Cox, 1970; Granjean & Battig, 1962; Hughes & Greig, 1975; Iwahara, Oishi, Yamazaki & Sakai, 1972; McNaughton & Feldon, 1980) and by both septal and hippocampal lesions (see Gray & McNaughton, 1983). We thus have a strong prediction that spontaneous alternation should be reduced by DB lesions.

Apparatus

The wooden T-maze had goal arms (65 × 18 × 15 cm), which were fixed in a constant position with respect to the testing chamber. The floor section joining the two arms was also fixed. One arm had walls painted black and the other was white. The rest of the maze was unpainted wood. The start arm (65 × 18 × 15 cm), which contained the start box (28 cm), and the section of the wall facing the exit could be interchanged to reverse the orientation of the start arm with respect to the goal arms. The mouths of the goal arms and the exit from the start box were fitted with perspex guillotine doors. The entire maze was roofed with perspex. Illumination was provided by a 15W lamp placed 150 cm directly above the choice point.

Procedure

The 16 sham-operated (SO) and 16 DB-lesioned rats were placed on ad lib food for 2 weeks after completing Owen et al.'s (1982) Experiment 2, in which they were tested for acquisition and extinction of a running response in the alley. They were brought to the testing room in groups of four. A subject was placed in the start box and after 10 s the start door was raised. When the entire body of the animal, excluding the tail, had entered a goal arm the goal door was closed and, after 10 s, the animal was removed to a holding box. Care was taken not to rotate the animal with respect to the room during handling. The subject remained in the holding box for 1 min while the apparatus was reset; the trial was then repeated. Each animal received one such test on each of two days with 1 free day after each test day. No animal failed to make a choice within 6 min. The orientation of the start arm with respect to the goal arm on the initial trial of each test day was randomised across animals within test days and within animals across test days.

Results and Discussion

Rats with dorsal bundle lesions alternated at a rate of 47%, whereas controls showed the usual rate of 75%. The difference between the groups was statistically significant ($d = 2.32, p < 0.01$, one-tail binomial test). This effect is similar to those of the anti-anxiety drugs and septal and hippocampal lesions, and thus confirms our prediction. However, when more searching analyses of the effects of the latter three treatments have been undertaken, it has been reported that, although they all reduce spontaneous alternation, they may do so in different ways, each affecting alternation of body turn cues and spatial cues to different extents (Dalland, 1970; McNaughton & Feldon, 1980). Thus further data are required to determine whether the effect of DB lesions on spontaneous alternation reported here resembles more closely those of the anti-anxiety drugs, septal lesions or hippocampal lesions.

Experiment 2

If a rat is exposed to a T-maze in which one arm is white and one black, and is then retested after the brightness of one arm has been changed so that both are now black or both white, it manifests a strong tendency to choose the changed arm (Dember & Millbrook, 1956; O'Connell, 1964). Ison, Glass and Bohmer (1966) showed that this tendency is abolished by the barbiturate, sodium amylobarbitone. No exactly similar experiment has been performed using animals with septal or hippocampal lesions. However, Gaffan (1972) abolished the response to stimulus change by section of the

fornix-fimbria, thus severing all septo-hippocampal connections. Comparable findings have also been reported after hippocampal lesions in experiments in which a previously closed arm in a maze is opened. Under these conditions, animals with hippocampal damage show lesser tendency than controls to explore the novel part of the maze (Cohen, 1970; Means, Leander & Isaacson, 1971). In the present experiment we used Ison et al.'s (1966) procedure to investigate the effects of DB lesions alone and in combination with the adminstration of sodium amylobarbitone on the response to stimulus change.

Apparatus

The T-maze used in Experiment 1 was slightly modified. Grey poster-board inserts were placed in the start arm and black and white ones, as required, in the goal arms. Illumination was provided by a 45 W lamp placed below the level of the T-maze and aimed at the ceiling above the choice point.

Procedure

The 16 SO and 16 DB-lesioned rats were placed on ad lib food for 2 weeks after completing an experiment in which they had been tested for acquisition and extinction of a running response in the alley (Note 1). The subjects were brought to the testing room in groups of four. A subject was placed in the start box and after 10 s the start door was raised. The perspex doors to the goal arms remained closed so that the animal could see that one arm was black and one white, but could not enter the arms. The subject was removed after 3 min and returned to its home cage for 30 s, during which time the goal doors were raised and goal inserts were changed so that the arms were both white or both black. The subject was replaced in the start box and after 10 s the start door was raised. The subject was removed immediatley after its entire body, excluding tail, was in one arm. The location of the black arm during initial exposure to the apparatus (left or right) and the colour of the changed arm were counterbalanced across animals and drug condition (see below).

Each animal received one test on each of three days with two free days after each test day. On the second and third tests each subject received an intraperitoneal injection of either 20mg/kg sodium amylobarbitone (Lilly) or an equal volume (1 ml/kg) of saline, ten minutes before testing. Subjects received the opposite drug condition on day 3 to that which they had received on day 2. Results for days 2 and 3 were pooled for analysis.

Results and Discussion

Table 1 presents the results of this experiment. The effects of the lesion were very similar in the no-drug and saline conditions ($\chi^2 = 0.15$, df = 2) and were pooled for subsequent analysis. The effects of the drug and lesion did not interact significantly ($\chi^2 = 1.93$, df = 1, $0.2 p < 0.1$; see Fienberg, 1970). A test of sham animals alone showed that choice under amylobarbitone was reduced close to chance levels (d = 1.56, $p = 0.059$, one-tail binomial test). A test of undrugged groups alone showed that the dorsal bundle lesion significantly reduced the response to stimulus change (d = 3.1, $p = 0.001$, one-tail binomial test). Thus both lesion and drug groups respond at chance levels while intact undrugged animals choose the changed arm significantly more often than would be predicted by chance ($p > 0.01$; Beyer, 1966).

The numbers of unlesioned animals choosing the changed arm in both the control and drugged conditions are within 10% of the values reported by Ison, Glass & Bohmer (1966), and although the effect of the drug does not quite achieve the 5% level of significance the conditions used clearly replicate those of their experiment. The effect of the dorsal bundle lesion shown here is thus similar to that reported for the drug. The chance behaviour of the drug-lesion group might be taken to indicate that both treatments abolish activity in a single system. However, the drug × lesion interaction is not significant, and even if it were, deviation below chance would not be observed if this value represents a ceiling. Thus, the present experiment indicates similar qualitative effects of amylobarbitone and dorsal bundle lesions on the response to stimulus change and is consistent with, but not conclusive evidence for, interference by both treatments with a common system.

Table 1: *Effects of Dorsal Bundle Lesions on the Response to Stimulus Change in the T-Maze With or Without Injection of Sodium Amylobarbitone. Values are Number of Animals out of 16 Choosing Changed Arm (% in brackets).*

	No Drug	Saline	Amylobarbitone
Sham	13(81)	12(75)	9(56)
Lesion	7(44)	8(50)	9(56)

Experiment 3

In this experiment we investigated the effects of DB lesions on behaviour in a table-top open field test, in which the level of stress imposed on the animal is relatively low. Under these conditions the anti-anxiety drugs reliably decrease rearing, as do sepal lesions (Kemble & Nagel, 1975; Laughlin, Donovick & Burright, 1975; Vergnes & Penot, 1976). Hippocampal lesions have somewhat more variable effects, but they too have been reported to reduce rearing (Murphy, Race & Brown, 1975; Strong & Jackson, 1970). The effects of these three treatments on locomotion ('ambulation') in such a test are less concordant with one another. Gray's (1983) review draws the following conclusions. The anti-anxiety drugs generally give rise to an initial increase in ambulation, followed by a more rapid decline in ambulation with continued exposure to the open field than is seen in controls; but these effects are less marked, the lower the level of stress in the open field test. Septal lesions generally give rise to the opposite temporal pattern of change, i.e., an initial decrease in ambulation followed by increased ambulation with continued testing. Hippocampal lesions give rise to increased ambulation more consistently. The dependence of the changes seen after septal and hippocampal lesions on the level of stress in the open field is not known. In the light of these findings, we may predict with some confidence that DB lesions will reduce rearing, but no firm prediction is possible for ambulation.

Method

Apparatus

The table was 125 × 75 cm covered in white plastic and marked off in 25 cm squares. Illumination was provided by a 15 W light placed 150 cm above the centre of the table. Ambulation and rearing were recorded on push buttons, connected to a NOVA computer located outside the testing room. The experimenter sat 1 m from one corner of the table.

Procedure

Two separate replications were run. In one, 12 SO and 12 DB lesioned rats were tested 4 days after they had served in Experiment 1 of the present report. In the second 12 SO and 12 DB-lesioned rats were used 2 weeks after operation and before receiving any other behavioural test. The subjects were brought into the room in groups of four. A subject was placed on the corner of the table nearest to the experimenter's chair and the number of lines on the table crossed by the animal's body, excluding the tail, were counted in minute bins over 10 minutes. Total rearing and defecation were also scored. Each animal received only one such session. The ambulation data were subjected to a square root transform to achieve normality of distribution and submitted to analysis of variance with extraction of orthogonal polynomial components of effects involving minutes (Snedecor & Cochran, 1967).

Results and Discussion

Despite the different experimental histories of the animals there were no differences in the results obtained in the two replications. In neither case was there any effect of the lesion on ambulation or on its rate of habituation (Figure 1; largest

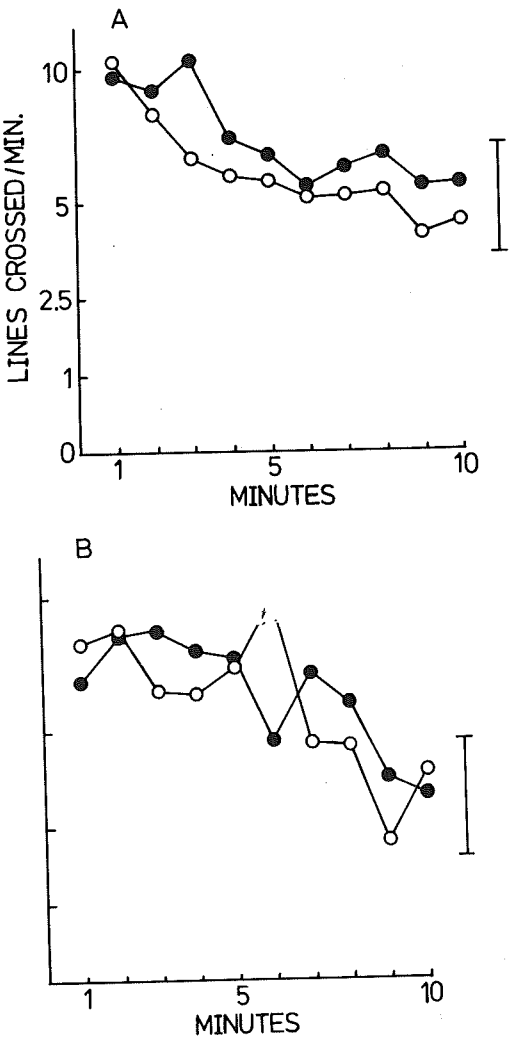

Figure 1. Ambulation on the table open field after dorsal bundle lesion. Open circles sham, closed circles lesion. Scale is the result of square root transform. Bar is 2 standard errors. A. Naive animals. B. Animals which received a previous runway test.

Table 2: *Effects of Dorsal Bundle Lesions on Rearing and Defecation on a Table Top Open Field in Animals With or Without Previous Experimental Experience.*

	Sham	Lesion	t	df	p
Defecation					
Naive	0.21	0.29	1.00	22	—
Non-naive	0.38	0.28	0.99	22	—
Rearing					
Naive	1.31	0.16	2.63	22	<0.02
Non-naive	1.58	0.90	2.07	22	<0.05

Note: *Values in above table are Mean Rears or Boli/Minute.*

F ratio in either analysis = 1.2), or on defecation (Table 2). The level of defecation was low, confirming the low level of stress imposed by the test. In both experiments the lesion significantly reduced rearing (Table 2).

These findings confirm previous reports that DB lesions reduce rearing (Kovacs, Bohus & Versteeg, 1979; Leconte & Hennevin, 1981) but do not affect ambulation (Mason & Iversen, 1975; Wendlandt & File, 1979), although Kovacs et al. (1979) observed a reduction in ambulation. A separation between rearing (reduced) and ambulation (not reduced, and under some condition increased) has also been obtained with a number of anti-anxiety drugs (Thiebot et al., 1973; 1976).

The failure of the DB lesion to affect defecation is also consistent with other reports (Kovacs, et al., 1979; Wendlandt & File, 1979); however, given the low level of stress imposed by our procedure, this cannot be interpreted as evidence for unchanged emotional reactivity in the lesioned animals. The major prediction tested in the experiment — that DB lesions would reduce rearing — was confirmed.

Experiment 4

The low stress open field used in Experiment 3 shows only small effects of anti-anxiety drugs on ambulation (see Gray, 1983) although it does show large effects of septal lesions (e.g. Kemble & Nagel, 1975). The lack of effect of DB lesions in this experiment could therefore be due to a similar action to that of the drugs in such tests. However, higher stress forms of the test do show effects of the anti-anxiety drugs, as was described in the introduction to Experiment 3. Experiment 4 was undertaken to investigate the effects of DB lesions on ambulation under conditions where an effect of anti-anxiety drugs would also be expected. For completeness with the previous experiment rearing and defecation were also measured.

Apparatus

The open field consisted of a 43 cm radius circular arena with walls 35 cm high. It was marked off into 20 approximately equal areas by circular and radial lines (Broadhurst, 1960). Four loudspeakers placed at equal distances around the field provided white noise with an intensity of 75 db down onto the centre of the field and six 100 W light bulbs set in reflectors and placed approximately 150 cm from the centre of the field provided an illumination of 2.1 - 2.2 wg ft lamberts (40-500 lumens) measured by reflection from a sheet of white paper placed in the centre of the field.

Procedure

Thirty-two sham and 32 lesion animals were placed on ad lib food for at least two weeks after completing a previous experiment in which they had been tested for acquisition and extinction of a running response in a straight alley.

Ten minutes before testing subjects received an injection of 15 mg/kg sodium amylobarbitone (Lilly) or an equal volume (1ml/kg) of 0.9% saline. They were then brought singly into the testing room, in which the white noise generator was running continuously and placed immediately into the open field. Areas entered by all four paws of the rat and rears in those areas were recorded on a standard chart of the apparatus using a different coloured pen for each 0.5 minute period in the 2 minute test session. At the end of the session the rat was removed and the number of fecal boli in the apparatus was recorded.

Ambulation and defecation data were subjected to a square root transform and rearing data to a logarithmic transform to normalise their distribution and were then submitted to analysis of variance (with extraction of orthogonal polynomial trend components for rearing). The 2 standard error markers in Figure 2 are based on the error term of the analysis and are appropriate to between groups comparisons. Regression coefficients associated with the polynomials were also extracted. Since the only significant polynomials in the ambulation data were linear, Figure 2A represents ambulation as the appropriate group means with the relevant linear regression lines, derived from the analysis of variance, drawn through the points.

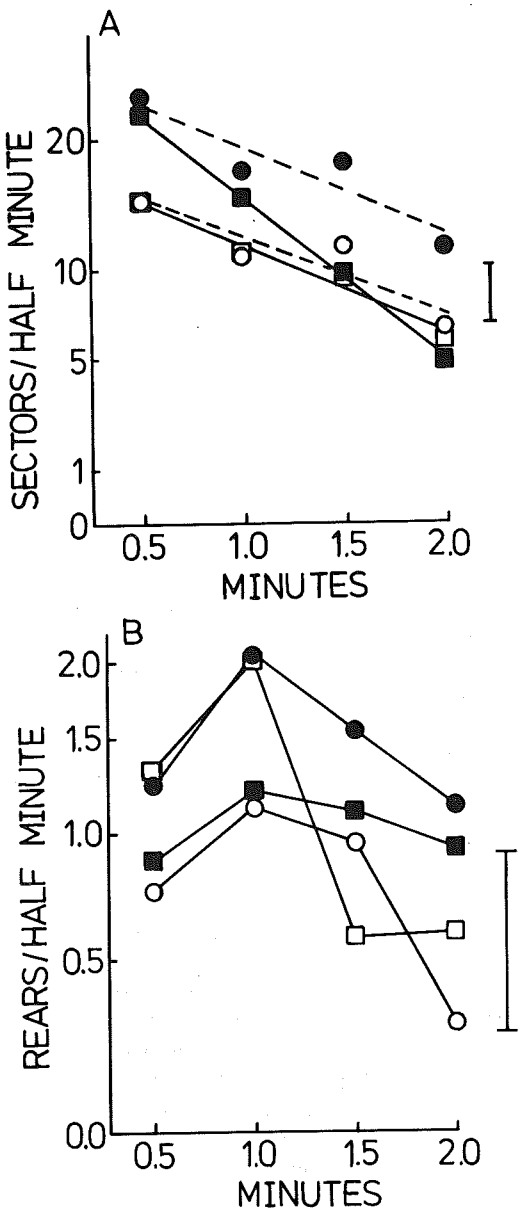

Figure 2.A. Ambulation in the Broadhurst open field. Circles and dotted lines sham, squares and solid lines lesion. Filled symbols drug, open symbols saline. Bar is 2 standard errors. Scale is the result of square root transform. B. Rearing in the Broadhurst open field. Symbols as in A. Scale is the result of log transform.

Results and discussion

As would be expected from the literature amylobarbitone produced an increase in ambulation during the first half minute in both sham and lesion animals (Figure 2A). The lesion-saline and sham-drug groups both show a slightly increased rate of habituation with respect to sham-saline animals (20% and 19% respectively), but the increase is most marked in the lesion-drug group (120%). The difference between this latter value and that which would be expected from additivity of the separate drug and lesion effects does not quite achieve significance (Linear trend of drug × lesion × time interaction: $F = 3.49$, df $= 1/111$, $p > 0.01$) while the overall effect of drug and of lesion is significant (Linear trends of drug × time and lesion × time interactions: $F = 7.39$, 7.79 respectively, df $= 1/111$, $p > 0.01$).

There is, then, an increase in initial levels of ambulation produced by amylobarbitone but not by dorsal bundle lesions; coupled with an increase in rate of habituation produced by both amylobarbitone and dorsal bundle lesions, which shows summation in the drug-lesion group. The hypothesis that this summation constitutes potentiation has marginal statistical support.

The data on rearing in the different groups are presented in Figure 2B. The only significant effect in the analysis was that of the linear trend of the drug × time interaction ($F = 5.86$, df $= 1/111$, $p > 0.05$) resulting from a lesser reduction of rearing with time in drugged than saline animals. This constitutes, in effect, an increase in rearing rather than the decrease that might be expected from the previous experiment. This difference is not due to rearing up the side walls of the present apparatus since rearing in the centre of the apparatus was changed in an identical manner. Again, in contrast to the results with the previous apparatus, dorsal bundle lesion had no significant effects.

Table 3: *Mean Defecation (Square Root Transform) Over the Entire Session in Animals Tested with Amylobarbitone and Dorsal Bundle Lesions in the Broadhurst (1966) Open Field. Values in Brackets are Reverse Transform Data, Not Mean of Raw Data.*

	SHAM	LESION
SALINE	1.27(1.11)	1.40(1.46)
DRUG	1.60(2.06)	1.13(0.78)

Mean defecation in the four groups is given in Table 3, both in the form of the transformed data analysed and with these scores reverse transformed back to bolus scores for comparison with Experiment 3.

Analysis of variance showed that there was a significant interaction of drug × lesion ($F = 5.97$, df $= 1/60$, $p > 0.025$). Inspection of the

Table 4: *Comparison of the Effects of Amylobarbitone and Dorsal Bundle Lesions on the Behaviours Investigated in the Present Paper.*

Test	Drug	Lesion	Effect of Lesion on Drug
Response to stimulus change	—(1)	—	none-ceiling?
Spontaneous alternation	—(2)	—	
Table Open Field:			
Ambulation	+0—(3)	0	
Rearing	—(4)	—	
Defecation	0(4)	0	
Broadhurst Open Field:			
Initial ambulation	+	0	none
Habituation of ambulation	(+)	(+)	summation or potentiation
Initial rearing	0	0	none
Habituation of rearing	—	0	none
Defecation	+	0	drug effect blocked

(1) Replication of Ison et al (1966)
(2) Granjean & Battig (1962); MnNaughton & Feldon (1980)
(3) See Gray (1983)
(4) Note 2

table suggests that this interaction results from an increase in defecation in the drug-sham group relative to saline-sham coupled with blockade or even reversal of this effect in the lesioned animals. Post hoc testing with Newman-Keuls statistic revealed a significant difference between the drug-sham and drug-lesion group ($q=3.84$, $p=4$, $n=60$, $p>0.05$); no other comparisons achieved acceptable significance.

General Discussion

With respect to the major prediction (Gray, 1983; Gray et al., 1975) under test in these experiments — that the behavioural effects of DB lesions would resemble those of the anti-anxiety drugs (Gray, 1977) and of septal and hippocampal lesions (O'Keefe & Nadel, 1978; Gray & McNaughton, 1983) — our results are largely confirmatory (see Table 4). They suggest, furthermore, that this prediction is more likely to be supported, the greater the agreement between the observed effects of the three reference treatments, anti-anxiety drugs, septal and hippocampal lesions. Thus, these all reduce spontaneous alternation and rearing, as did DB lesions in Experiments 1 and 3 respectively. Reduction in the response to stimulus change in Dember and Millbrook's (1956) design has been reported only for fornix lesions (Gaffan, 1972) and the barbiturate, sodium amylobarbitone (Ison, Glass & Bohmer, 1966), as confirmed in Experiment 2, but there are no contrary data from other experiments. This response too was blocked by DB lesions in Experiment 2. Further experiment with septal and hippocampal lesions and with other anxiolytics, particularly the benzodiazepines, would be required to confirm this point. In contrast to these positive effects of the DB lesion, we found no change in ambulation in Experiment 3 but the three reference treatments have mixed effects among themselves in this case. This pattern of results is consistent with the hypothesis that the anti-anxiety drugs affect behaviour, at least in part, by impairing the noradrenergic input to the septo-hippocampal system. It also allows us to reverse the direction of prediction: if the pattern of results noted above is general, both septal and hippocampal lesions should block the response to stimulus change in Dember & Millbrook's (1956) design.

Experiment 4 does not bear directly on this hypothesis since it involves a task in which the reference treatments have different effects. However, it does bear on the original theoretical basis for that hypothesis: that both anti-anxiety drugs and dorsal bundle lesions are reducing anxiety. As discussed by Gray (1983) there is a critical difference between responses to aversive events, including omission of expected reward, and responses to stimuli which predict those events. It is the latter which he presumes are critical for the action of anti-anxiety drugs. The status of novel stimuli is less clear.

By analogy with their effects in relation to aversive events we can describe the effects of antidanxiety drugs on spontaneous alternation

and on response to stimulus change as reduced avoidance of the more familiar of two alternatives. That is to say we see reduced inhibition on the second trial in relation to a stimulus presented on the first trial. Whether one would wish to call the process involved conditioned familiarity in the sense that one can refer to conditioned fear or conditioned frustration is a moot point.

In the stressed open field as used in Experiment 4 low initial ambulation scores and high defecation are usually taken as indices of high 'emotionality' (Whimbey & Dennenberg, 1967). In this context the effects of amylobarbitone in Experiment 4 are paradoxical: increased initial ambulation with increased defecation. Equally, DB lesions do not reproduce either of these effects, although they appear to block the appearance of the second. The increased habituation of ambulation produced by amylobarbitone is reproduced by the drug and the combination of the treatments produces summation, or perhaps even potentiation. However, habituation of ambulation, as opposed to initial levels of ambulation, is not clearly related to 'emotionality' more than to 'exploration'. Whatever the interpretation put on these data, then, it seems that a simple explanation in terms of a common action of anti-anxiety drugs and DB lesions in relation to anxiety would be hard to find.

A lack of concordance between the effects of DB lesions and anti-anxiety drugs also occurs with tasks involving shock (see McNaughton & Mason, 1980). One possibility, therefore, is that the stressed open field test activates similar systems to those involved in responses to shock, while the unstressed open field test, and the two T maze tests involve separate systems similar to those involved in responses to the omission of reward.

Further work needs to be done to clarify the theoretical basis of these observations. The present results, however, support the empirical generalisation that where the effects of anti-anxiety drugs, septal lesions and hippocampal lesions are the same in tasks involving nonreward novel stimuli then the effects of DB lesions also be the same.

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