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Parameters of the Dorsal Bundle Extinction Effect: Previous Extinction Experience

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MASON, S. T. *Parameters of the dorsal bundle extinction effect: Previous extinction experience.* PHARMAC. BIOCHEM. BEHAV. 8(6) 655–659, 1978. – Lesion to the dorsal noradrenergic bundle using the selective neurotoxin 6-hydroxydopamine which depleted telencephalic noradrenaline to less than 5% of control values was found to cause prolonged responding in extinction of a continuously reinforced (CRF) operant lever pressing response (a further replication of the dorsal bundle extinction effect). The parameters involved in causing this effect were investigated, particularly the role of previous extinction experience. Although resistance to extinction was seen the first time animals were placed in extinction, it disappeared when they were retrained on CRF and extinguished a second time. Experience of extinction as part of the acquisition process, brought about by training on a successive visual discrimination, also prevented the development of over-responding in subsequent extinction. These results are discussed in the context of related demonstrations of the absence of the dorsal bundle extinction effect after partially reinforced acquisition training.

Noradrenaline Locus coeruleus Dorsal bundle Learning and memory Extinction CRF Visual discrimination learning

DEPLETION of forebrain noradrenaline (NA) by injection of the selective neurotoxin 6-hydroxydopamine (6-OHDA) into the fibres of the dorsal bundle has been found to alter extinction behaviour in a number of instances [6]. After the initial demonstration by Mason and Iversen [6] using a food rewarded runway task similar effects have been seen in extinction of continuously reinforced (CRF) lever pressing [7,29], extinction of a complex motor manipulative task [8,9], extinction of a go/no-go alternation [30], extinction of one-way [1] and two-way [18] active and passive [15] avoidance tasks, in extinction of an exploratory response [16] and also replicated in the original runway situation [19]. However, there are situations in which resistance to extinction does not occur. These are generally schedules involving partial reinforcement where not every lever press/runway response is rewarded. Absence of the dorsal bundle extinction effect (DBEE) has been found after variable interval (VI) training [21], partially reinforced runway training [19], a partially reinforced variable ratio schedule [14] and possibly after fixed ratio (FR) schedules [20]. The common element of all of these acquisition schedules is that they involve experience of extinction as part of the acquisition process itself. Contrasted to these are the situations where DBEE is found, which are usually continuously reinforced tasks where extinction has never been experienced on the task until the start of the extinction phase proper. It was thus of interest to see if previous experience of extinction was a determinant in the dorsal bundle extinction effect. Two paradigms were utilised. In Experiment 1 lesioned and control animals were trained on CRF and extinguished, this extinction hence representing their first such experience. They were then retrained on CRF and extinguished for a second time, this time having already experienced extinction previously. The second experiment incorporated extinction experience as part of the acquisition training by using a successive visual discrimination where extensive experience with extinction was given during the unrewarded S minus periods. Extinction after this acquisition training was examined in the presence of the S plus, in the presence of the S minus and in a schedule of S plus/S minus similar to acquisition.

EXPERIMENT 1

METHOD

Surgery

Ten male Albino Woodlyn rats weighing 300 g were anaesthetised with Nembutal (50 mg/kg intraperitoneal), placed in a stereotaxic apparatus (David Kopf) and two holes drilled in the skull through which a 34 ga cannula was lowered bilaterally to the following coordinates, AP + 2.6 mm from interaural line ML ± 1.1 from midline and DV + 3.7 mm from interaural line with the animal's skull in the plane of König and Klippel [4]. This corresponds to the course of the dorsal noradrenergic bundle in the mesencephalon. Four micrograms of 6-OHDA (weight expressed as base, 6-OHDA HBr, Regis) dissolved in two microliters of 0.9% saline with 0.3 mg/ml ascorbic acid antioxidant were infused bilaterally at the rate of 1 microlitre per min over two min and the cannula left in for an extra minute to

permit diffusion of the drug. Ten control animals received saline-ascorbic infusion. Animals were allowed two weeks after the operation before behavioural testing started to permit completion of anterograde degeneration. The first week was on ad lib food and water but during the second week the animals were reduced to 90% of free-feeding weight and acclimatised to receiving 15 g of laboratory chow per day.

Procedure

Biochemical. Following completion of behavioural testing all treated and a randomly selected five control animals were sacrificed by cervical fracture and their brains dissected on ice into the following regions [22,23], cortex-hippocampus, hypothalamus, and striatum. The areas were then assayed for endogenous catecholamines by the method of McGeer and McGeer [17]. This served to confirm that the 6-OHDA injection had indeed produced the expected pattern and extent of amine depletion.

Behavioural. Animals were lever shaped in operant test chambers (BRS/LVE) as described elsewhere [7,10] and immediately placed on a continuously reinforced (CRF) schedule for the next 10 days. Each daily session was of 20 min duration. At the end of acquisition training the animals were placed into extinction in which a lever press no longer produced either a food pellet or the click of the automatic feeder. An extinction session consisted of placing the animal in the test chamber until no lever response had been emitted for two consecutive minutes. The number of lever presses emitted and the time taken to reach this criterion were recorded. The animal was then removed from the chamber for the day. Extinction testing continued for two days. The animals were then retrained on CRF for a further 10 days and extinction repeated exactly as before.

RESULTS

Biochemical

The post-mortem amine assays are shown in Table 1 and confirm that the 6-OHDA injection had produced severe and permanent depletion of forebrain NA. The hippocampus was reduced to 3% of controls and the hypothalamus to 23% of control with only slight damage to striatal dopamine.

Behavioural

The terminal level of CRF performance and subsequent extinction for the control and lesioned animals is shown in Fig. 1. Both groups were performing at an equivalent high response rate on the last day CRF training (shown in the upper left panel of Fig. 1) and no statistically significant difference was found between them (control mean = 194, lesioned mean = 190 responses in the 20 min session). However, upon being placed into extinction for the first time the lesioned animals showed the usual DBEE and responded significantly more than controls (control mean on Day 1 of extinction = 27.7, lesioned mean = 69.8, $t(18) = 2.91$, $p<0.01$). By Day two of the first extinction period both groups had reduced to the same low level of responding and no significant difference was seen between them. Following 10 days of CRF retraining the rewarded CRF response rate was again similar for the two groups (control mean = 178, lesioned mean = 170). This time, in the second extinction no significant difference emerged between control and lesioned animals on either the first or the second day of testing (right panel in Fig. 1).

TABLE 1

Region	Control (N=5)	Lesioned (N=10)	%
Noradrenaline			
Hippocampus-cortex	355	9	3
Hypothalamus	2560	590	23
Dopamine			
Striatum	10270	8220	80

Amine assay data on animals used Experiment 1. Values are means of ten lesioned and five control animals in nanograms per gram wet weight of tissue.

% is the percent of control concentrations remaining in lesioned tissues.

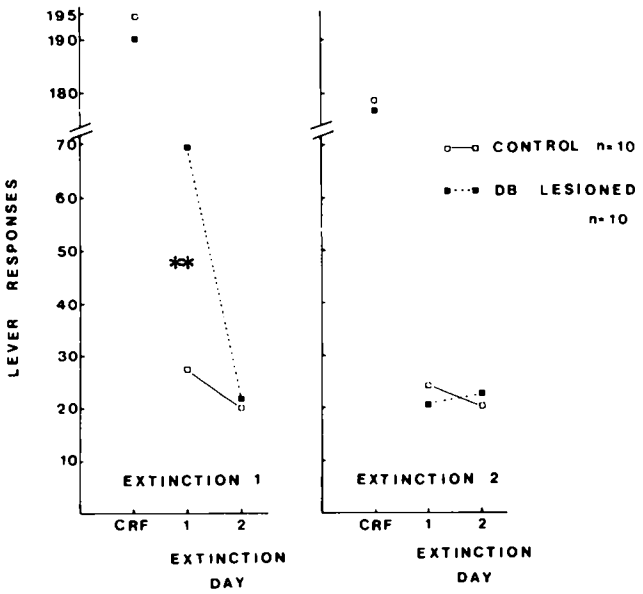

FIG. 1. Extinction of control and dorsal bundle 6-hydroxydopamine lesioned (DB Lesioned) animals trained on a CRF schedule and then tested on the first and second experience of extinction. Values are mean number of lever presses emitted in the daily extinction session for ten control and ten DB lesioned rats over the two days of extinction testing. Values above the break in the axis are terminal rewarded CRF rates on the day immediately prior to extinction testing. **Indicates that the control and lesioned animals differ at the 1% significance level.

DISCUSSION

Experiment one demonstrated the DBEE, but only on the first experience of extinction.

To test further this effect of prior extinction experience on the DBEE a schedule was used in which experience of extinction was given during the acquisition process itself, namely a successive visual discrimination.

EXPERIMENT 2

METHOD

Surgery

Twenty-seven male albino rats received intracerebral injections of 6-OHDA into the dorsal bundle as previously described. Twenty-seven control animals received saline-ascorbic infusion. Animals were allowed two weeks after the lesion for anterograde degeneration to become complete and food deprived as described in Exp. 1.

The apparatus was similar to that described in Exp. 1.

Procedure

Behavioural. The 27 control and 27 lesioned animals were trained for 10 days on a successive light/dark visual discrimination described elsewhere [7,11]. Briefly, this consisted of 45 sec period which could be either S plus or S minus. A lever response during the S plus produced a food pellet on a CRF schedule, a response during the S minus had no consequence and was not rewarded. The stimuli used as the S plus and S minus were counterbalanced across control and lesioned groups with the stimulus conditions being either illumination of the houselight and stimulus lights in the test chamber or these lights being off. Following this the rats were randomly divided into three groups of nine controls and nine lesioned rats. Group 1 was then extinguished in a single session in the presence of the S plus. That is, the stimuli did not change as they had during the rewarded training and only the previous S plus was constantly present. Group 2 was similarly extinguished in the presence of the previous S minus, and Group 3 was extinguished on a schedule that was indistinguishable from one used in rewarded training except that no food pellet or click of the feeder occurred. This latter group, thus, received exposure to both the previous S plus and the previous S minus during extinction. The animal was left in the test chamber until no lever press had occurred for two consecutive min and the time to reach this criterion was recorded as well as the total number of lever responses emitted during this period. For Group 3, lever presses were divided into those emitted in the presence of S plus and those emitted in the presence of the S minus and subtotals recorded every 45 sec. No food or click of the feeder was ever presented to any group during extinction.

RESULTS

Biochemical

The results of the assays of amine concentration in randomly selected control and lesioned animals are shown in Table 2 and serve to confirm that severe and extensive depletion of forebrain NA had occurred with no effect on dopamine in any area measured.

Behavioural

The terminal level of performance after 10 days of successive visual discrimination was equivalent for control and lesioned animals in each of the three groups destined for different extinction conditions. The percent performance, obtained by dividing the S plus responses by the total number of responses in S plus and S minus, did not differ significantly between control and lesioned animals. Group 1 control mean = 76.7%, lesioned mean = 79.0%; Group 2 control mean = 73.7%, lesioned mean = 74.8%; Group 3 control mean = 75.2%, lesioned mean = 79.0%. The time course of extinction within the single extinction session is shown in Fig. 2 for the lesioned and control animals extinguished on the original training schedule of S plus and S minus (Group 3). Although behaviour was controlled by the stimuli as shown by the greater responding initially in the previous S plus compared to the S minus periods, no difference was seen between control and lesioned animals. The mean total responses during this session were 124 for controls and 122 for lesioned rats. The time prior to reaching the extinction criterion also failed to differ with a mean control time of 749 sec and lesioned value of 708 sec. A similar lack of difference was seen in the groups extinguished in the presence of the S plus only and the S minus only. No sign of resistance to extinction was seen in the lesioned groups compared to controls either in the time to criterion or the number of lever presses.

TABLE 2

Region	Control (N=4)	Lesioned (N=8)	%
Noradrenaline			
Hippocampus	251	27	11
Cortex	268	12	4
Cerebellum	176	232	131
Hypothalamus	1103	780	61
Dopamine			
Cortex	43	36	84
Hypothalamus	307	336	109
Striatum	777	875	112

Amine assay data on animals used Experiment 2. Values are means of four contrl and eight lesioned animals in nanograms per gram wet weight of tissue.

% is the percent of control concentrations remaining in lesioned tissues.

DISCUSSION

Experiment 2 thus further confirms the role of previous extinction experience as a parameter determining the DBEE, even if that extinction experience is given during acquisition training. This finding is similar to other demonstrations that the DBEE does not occur after partially reinforced acquisition training, which also involves experience of extinction as part of the acquisition schedule.

GENERAL DISCUSSION

Depletion of forebrain NA using 6-OHDA injection into the fibres of the dorsal bundle was again shown to cause resistance to extinction after CRF training (Exp. 1), confirming numerous previous reports [1, 6–9, 10, 13–16, 18, 19, 29, 30]. However, this was shown to apply only to the first time the animals experienced extinction. After identical training given following the first extinction period no such resistance to extinction was seen in the second extinction period. A similar finding was shown following experience of extinction during the acquisition schedule itself (Exp. 2). One mechanism suggested to explain the DBEE, due to Gray [2,3], implicates the dorsal bundle in coding for frustrative non-reward. This has been expounded

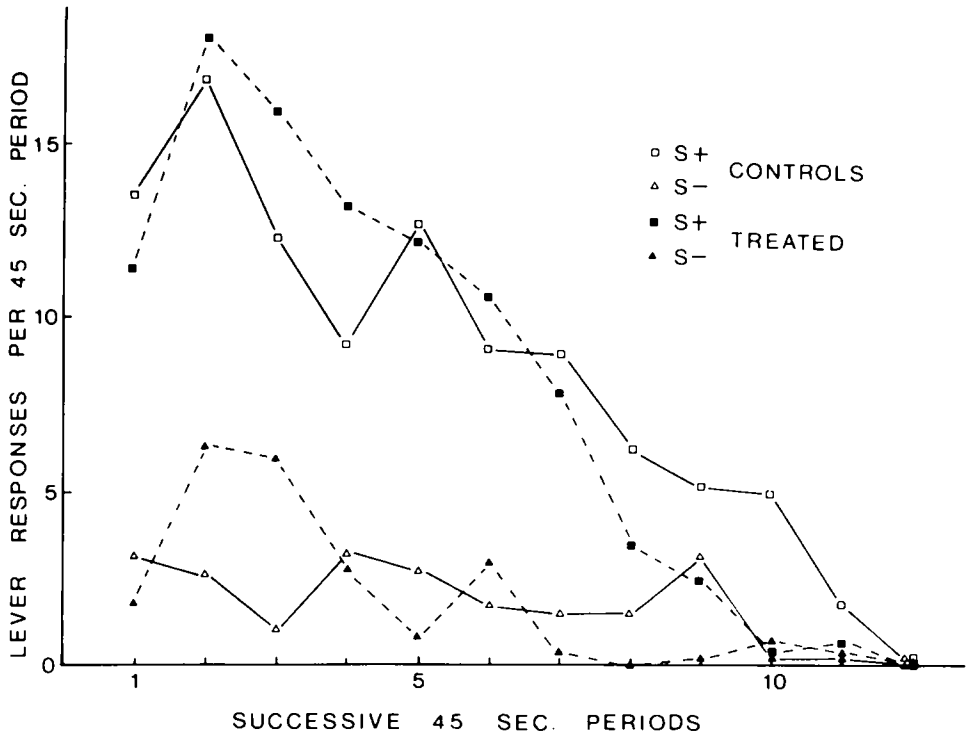

FIG. 2. Intra-session extinction curves for control and DB lesioned rats trained on a successive visual discrimination and then extinguished in the presence of both the S plus and the S minus as on the original training schedule. Values are means of nine control and nine treated animals being the mean number of responses emitted in successive 45 sec periods throughout the course of extinction.

at length elsewhere [2, 3, 14] and explicitly tested several times with generally negative results [13,14]. Suffice it to say that the frustration theory appears to predict that the effect of dorsal bundle lesion acts during the extinction period itself and as such, given an equal level of reinforced responding prior to extinction, would be expected to occur every time the animal was placed into extinction and not just the first extinction experience.

One theory which may offer a mechanism for the present effect is couched in attentional terms. It suggests [7,25] that the dorsal bundle has a role in filtering out irrelevant stimuli and that animals without such a mechanism sample more environmental stimuli than normal. One view of the determinants of extinction rate [5,26] holds that is the number of stimuli that have become associated with reward that is important. If this is true it could explain both the resistance to extinction seen after CRF training [7,25] and the disappearance of this effect after previous extinction experience which alters stimulus sampling in a way described elsewhere [24, 27, 28]. A similar mechanism might also explain the absence of DBEE after successive visual discrimination and could be advanced for its absence after other partially reinforced schedules [14, 19, 20, 21]. Whatever the theoretical mechanism involved, the current study has established that prior extinction experience is indeed a significant parameter in the determination of the dorsal bundle extinction effect.

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