

Some Effects of Chlordiazepoxide and Chlorpromazine on Response Force in Extinction¹

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FOWLER, S. C. *Some effects of chlordiazepoxide and chlorpromazine on response force in extinction.* PHARMAC. BIOCHEM. BEHAV. 2(2) 155-160, 1974. — A total of 52 male Wistar rats were continuously reinforced with food pellets for paw-pressing a silent, isometric, force-sensing manipulandum. Subsequently, extinction was introduced and the effects of chlordiazepoxide (CDP, 2.5, 5.0, 10.0 mg/kg) and chlorpromazine (CPZ, 1.0, 2.0, 4.0 mg/kg) upon response force, response rate, and resistance to extinction were observed. CPZ reduced these three extinction measures in a dose-related manner. In accord with predictions from frustration theory, CDP (5.0 mg/kg) increased resistance to extinction. However, contrary to the theory, CDP did not attenuate the extinction-related force increase. This latter result prompted an analysis of the pattern of force emission during a session of reinforced responding. Force for the first response was found to be very near extinction levels. This result, combined with the observation that the first response of a session is virtually uncued by reinforcement, suggested that high extinction force may result from a generalization decrement and not from unconditioned frustration effects.

Response force Extinction Frustration Chlordiazepoxide Rat Chlorpromazine

A NUMBER of investigators have noted the similarity between the behavioral effects of punishment on the one hand and extinction on the other [12,19]. Drugs, such as ethyl alcohol and sodium amytal, are effective in reducing the decremental effects of either extinction or punishment [3, 9, 12, 19]. These results have given rise to the hypothesis that both the fear engendered by punishment and the frustration produced by extinction are derived from a common emotional reaction subserved by a common physiological system [7, 8, 19]. According to this view, a drug such as chlordiazepoxide (CDP), which possesses fear- and anxiety-reducing properties as measured by approach-avoidance conflict procedures [11, 13, 18], should, under certain circumstances, also attenuate frustration just as it lessens fear. The present experiment, therefore, examines the effects of CDP on extinction, and in so doing, tests some predictions derived from Amsel's theory of frustration [1,2]. Frustrative nonreward was defined by the extinction of a bar-press response; resistance to extinction and peak force of response served as the primary dependent variables.

According to Amsel's theory [1,2] frustrative nonreward has two major consequences. First, a primary, unconditioned emotional reaction occurs. It serves to augment

the prevailing motivational state, and may act to increase behavioral output, at least momentarily. The second type of frustration, anticipatory frustration, develops relatively more slowly by means of a classical conditioning process whereby the apparatus cues preceding frustrative nonreward come to elicit conditioned frustration. Although evidence for unconditioned frustration and anticipatory frustration has come mainly from the double runway and the single runway, respectively, the theory may also be useful in explaining some free-operant analogs of the runway procedures. More specifically, if CDP does have antifrustration properties, as hypothesized earlier, predictions of its effects are easily derived from Amsel's theory. If previously observed extinction-related increases in bar-press force [13,15] are a result of unconditioned frustration, and if CDP reduces this "primary emotional reaction," then the drug, in appropriate doses, should attenuate the force rise. Moreover, CDP should enhance resistance to extinction by lessening anticipatory frustration, which the theory offers as a partial explanation for the eventual cessation of responding in extinction.

Because the foregoing hypothesis rest so heavily upon the assumed specific antifrustrational action of CDP, the experiment also examined the effects of another tranquiliz-

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ing drug, chlorpromazine (CPZ), which does not possess specific fear-reducing properties [10]. Thus CPZ is not expected to affect frustration *per se*, but, by virtue of its neuroleptic action [11], CPZ can be expected to reduce overall behavioral output. A comparison of performances under the influences of these two agents should afford a stronger test of the hypotheses offered above.

In addition to these theoretical considerations, an examination of drug effects on force emission is of interest in its own right. Although previous work in this area has been concerned with drug effects on precision of continuous lever positioning [4] or with discriminative force emission [6], the results clearly suggest that such non-discrete measures *vis a vis* rate or latency measures of behavior can be quite sensitive to pharmacological manipulations.

METHOD

Animals

The animals were 52 male Wistar rats purchased from Charles River Breeders, Inc. They were approximately 100 days old at the start of the experiment. A 22-hr food deprivation schedule was gradually introduced during the first 2 weeks in the laboratory. This regimen was maintained throughout the experiment, with the 1 hr daily feeding occurring approximately 1/2–1 hr after a session ended. Water was continuously available in the individual home cages.

Apparatus

Programming of contingencies and recording of data were accomplished by means of a small digital computer PDP-12-A, (Digital Equipment Corp.) interfaced with conventional, reed relay equipment. The system serviced 2 simultaneously operative Skinner boxes, each with Sanborn force transducers (Model FTA-100) being used as manipulanda. The portion of the transducers available to the 2 concurrently run animals was a disc 18 mm in diameter, the surface of which was 60 mm above the grid floor. Each manipulandum was positioned outside the box (approximately 3 cm from an opening in the wall to the center of the disc), but within reach of the animal's paw. Since downward excursion of the disc was less than 0.4 mm for forces up to 200 g, the manipulandum was essentially isometric (cf., [13,17]); it was also silent in operation. Both boxes were 23 cm long × 20.5 cm wide × 19 cm high. In each box the food cup was mounted on the front panel at floor level, 7.5 cm to the right of panel midline, which also served as centerline of the manipulandum opening. The computer system was programmed to record peak force for all pressures 10.0 g or above.

Procedure

Animals were randomly distributed into the groups shown in Table 1. The largest number of animals were allocated to the saline control group in accord with Dunnett's suggestion that a design comparing 6 treatment groups of 6 animals each to a control group should have 15 animals in the control group [5].

Subsequent to routine magazine training, there were 3 daily shaping sessions (50 45-mg food pellets/session), which were programmed to reinforce on a CRF schedule any pressure on the manipulandum 10 g or above. The apparatus delivered reinforcement only upon termination

of a response. For the first shaping session, the manipulandum was completely inside the box; in the 2 subsequent sessions, it was gradually moved to its ultimate position outside the box. Shaping in this manner was undertaken to develop uniform response topography.

The experiment consisted of a conditioning phase and an extinction phase. Conditioning included 12 daily sessions (50 pellets each) of CRF training. On the tenth conditioning day, 40 min prior to a session, animals received intraperitoneal injections of the drugs and dosages shown in Table 1. Drugs were administered on the tenth conditioning session in order to obtain baseline results which, when compared to the drug effects in extinction, would provide a basis for judging whether the drug actions were specific to extinction responding.

Chlordiazepoxide hydrochloride (Librium, Hoffman-La Roche) was dissolved in 0.9% saline to yield an injection volume of 1 ml/kg at each of the 3 doses used. CPZ (Thorazine) was diluted with 0.9% saline to produce an injection volume of 1 ml/kg at each dose.

On the day immediately following the 12th session of conditioning a single 8 min session of extinction was given. During the extinction phase animals again received the drugs and dosages shown in Table 1 and in the manner described above. During extinction, responses activated the empty pellet dispenser.

Immediately after the extinction session, each rat was given 10 min access to 50 pellets in its food tray in the home cage. This procedure was designed to detect any obvious anorectic effects of the drugs. No animal failed to consume all the pellets in the allotted time.

RESULTS

Conditioning

Group means for response rate and peak force are presented in Table 1. On session 9, prior to the administration of drugs, no group differed significantly from the saline group.

For conditioning session 10 none of the drug treatments significantly affected response force, and only the highest dose of CPZ had a reliable influence on response rate. By conditioning session 12 this group had returned to preinjection baseline for rate of response.

Extinction

Despite the drug treatments, for all groups, response force in the 8 min extinction session displayed a significant increase over conditioning session 12 ($p < 0.05$ for each of the seven groups based on within-group, 2-tailed *t*-tests). However, as shown in Table 1, the degree of extinction-related force increase was drug-dependent. At 4.0 mg/kg, CPZ partially reduced the amount of force rise, while the intermediate dose of CDP (5.0 mg/kg) resulted in forces going even higher than those of the saline group.

As would be expected on the basis of subtraction of eating time during extinction, all groups, with the exception of the highest dose of CPZ, exhibited response rates significantly higher than their respective rates in conditioning session 12 ($p < 0.05$, within-group *t*-tests). Moreover, the highest dose of CPZ produced an extinction rate significantly lower than control (see Table 1).

Because they represent averages over 8 min of extinction, the rate data in Table 1 may not necessarily reflect true differences in terms of resistance to extinction. For

TABLE 1
GROUP MEANS OF MEAN PEAK FORCE AND AVERAGE RATE OF RESPONSE FOR THE INDICATED SESSION OF CONDITIONING AND EXTINCTION

Drug	N	Dose (mg/kg)	Session 9 No Drug		Session 10 + Drug		Session 12 No Drug		Extinction + Drug	
			Force (g)	Rate (R/min)	Force	Rate	Force	Rate	Force	Rate
Saline (Control)	15	—	21.9	10.2	21.8	10.4	21.9	10.0	38.6	24.6
Chlordiazepoxide (CDP)	6	2.5	23.2	10.7	26.3	10.9	23.2	10.5	45.8	23.7
	6	5.0	22.7	11.5	23.8	12.0	21.7	10.9	48.2*	33.0
	6	10.0	22.9	11.0	26.0	9.2	22.4	10.4	40.9	20.7
Chlorpromazine (CPZ)	6	1.0	24.2	10.0	23.5	7.8	23.0	9.4	40.4	23.5
	6	2.0	23.2	9.7	22.4	8.0	23.4	9.9	39.4	15.0
	7	4.0	20.1	10.3	20.0	5.1*	18.8	9.0	26.3	7.8*

* $p < 0.05$, based on Dunnett's test, comparing each treatment with a control group

this reason, extinction curves for the groups having effective doses of CDP and CPZ are compared to the saline group in Fig. 1. All 3 groups display decrements in responding as extinction progresses (Fig. 1-A). The CDP group is more resistant to extinction than the control group: over the last 4 min of responding, rate for the CDP group is significantly higher than that of the control group ($t = 2.481$, $p < 0.05$). For the CPZ group responding had almost ceased by the 4th min; and during the last half of extinction rate was significantly lower than that of the control group ($t = 3.245$, $p < 0.01$).

Unlike response rate, peak force for the 3 groups remained elevated throughout the 8 min extinction session. (See Fig. 1-B.)

DISCUSSION

In the appropriate dose, CDP increased resistance to extinction. This finding is consistent with results obtained by other investigators (e.g., [9]) and supports the hypothesis that CDP possesses antifrustrational properties which can act to reduce anticipatory frustration and thereby to prolong extinction. Further, this result also lends credence to the idea that CDP may act by releasing behavior from inhibition [11] which, in the present case, is engendered by extinction. The results for CPZ do not compromise these interpretations. Moreover, CPZ influenced response force, response rate and resistance to extinction in a manner consistent with the current theory of its behavioral effects [10]. CPZ reduced behavioral output, as reflected by rate of response in conditioning session 10 and by both rate and force in extinction. The fact that CPZ did not reliably influence response force but did depress rate during conditioning session 10 is consistent with results obtained by Falk [4], who reported that CPZ (2 mg/kg) produced a drop in "work rate" but had variable effects on motor control measures.

Contrary to expectations, however, CDP (5.0 mg/kg) did not attenuate the peak force rise in extinction. In fact, this dose produced mean peak forces significantly higher than those of the saline control group. Such a result calls into question the assumption that the changes in peak force attendant upon the introduction of extinction are an outgrowth of the unconditioned frustrative reaction postulated by Amsel [1,2] on the basis of runway data. It is also possible that CDP simply does not influence the unconditioned frustration, even while it is affecting anticipatory frustration. Yet this latter alternative seems unattractive on the grounds of parsimony.

It is noteworthy that the same kind of apparently contradictory results have arisen from runway experiments when the presumed antifrustrational agent was sodium amytal. Barry, Wagner, and Miller [3] and Gray [7] showed that sodium amytal reduces anticipatory frustration in the single goal-box runway. But with the very same dosages of sodium amytal Gray [7] did not obtain evidence for a reduction in unconditioned frustration as measured in the double runway.

A theoretical account offered by Staddon [16] is helpful in providing an explanation for why putative antifrustrational drugs reduce neither the speed in the second leg of an Amsel-Roussel runway nor peak force of a bar-press subsequent to reward omission. According to this view, reinforcement acquires "some measure of control over behavior that follows it"; and "if reinforcement is omitted the behavior to be expected will depend both on the kind of control exerted by reinforcement and on how similar the stimulus presented in lieu of reinforcement is to reinforcement" [16]. When applied to the present results, this account suggests that, during a conditioning session, reinforcement may have been operating as a cue to bring force emission comparatively closer to the reinforcement criterion of 10 g. High force in extinction is then seen as a

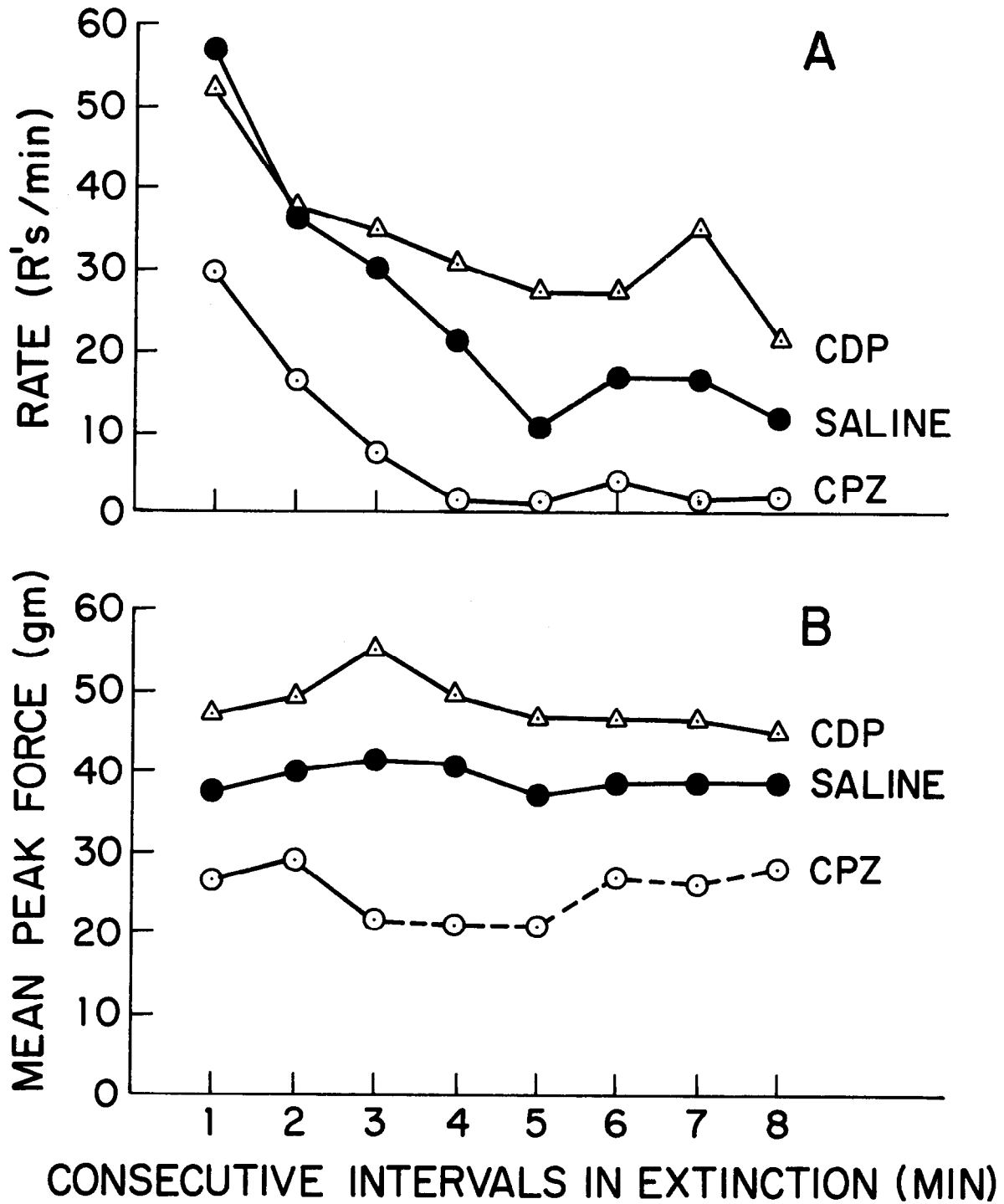


FIG. 1. Rate of response (Panel A) and mean peak force of response (Panel B) as a function of consecutive 1 min intervals in extinction after 12 conditioning sessions of continuous reinforcement. CDP is chlordiazepoxide 5.0 mg/kg and CPZ is chlorpromazine 4.0 mg/kg. In Panel B the broken lines joining the points on the CPZ curve indicate that these means are based only upon animals that emitted at least 1 response during the 1 min interval. For intervals 4, 5, 6, 7 and 8 the numbers of rats making at least one response were 4, 2, 3, 4, and 3, respectively.

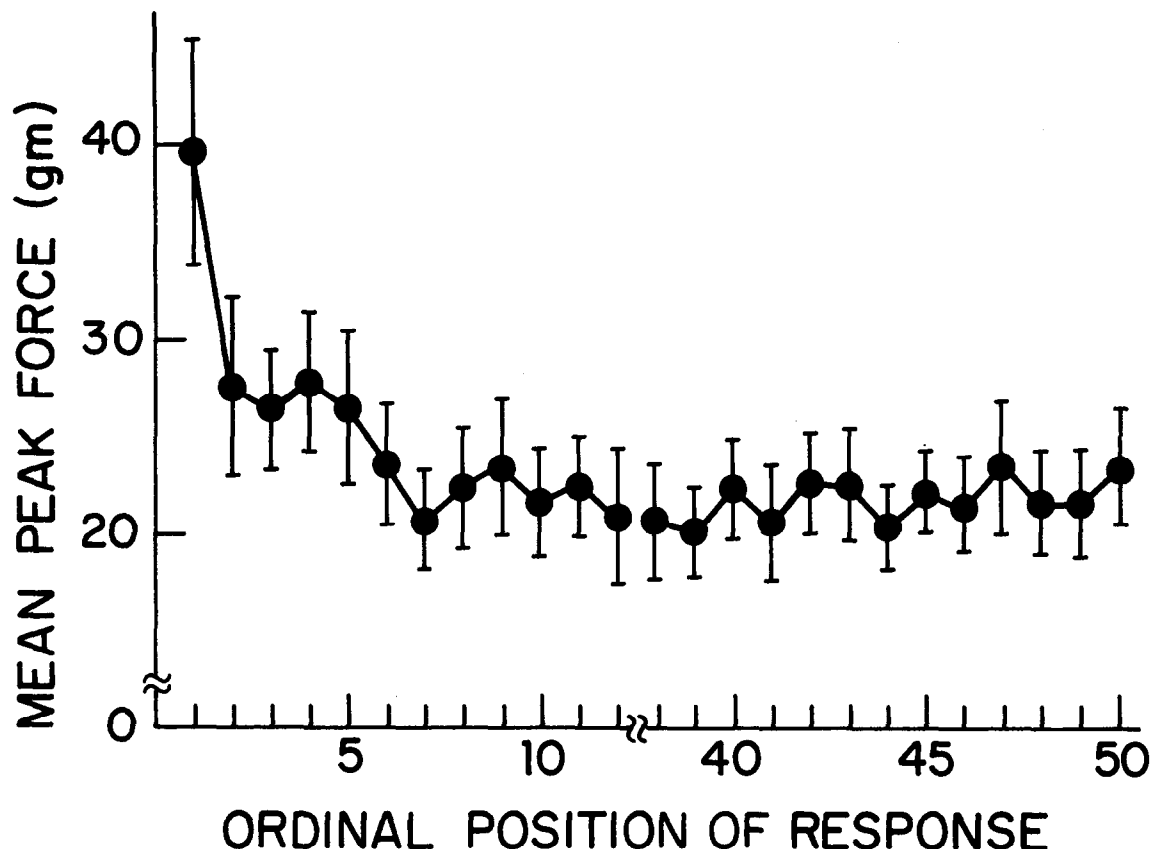


FIG. 2. Mean peak force as a function of ordinal position of response during the drug-free conditioning session 12. Each point is an average based on 52 animals. The vertical bars represent 95% confidence intervals.

deterioration of performance (generalization decrement) resulting from a removal of the salient cue – reinforcement.

Because the first response in a conditioning session is essentially uncued by reinforcement (the preceding reinforcement was 24 hr earlier), evidence in support of the foregoing account may be gleaned from an examination of peak force within a single session. Accordingly, such an analysis is presented in Fig. 2. Each point is mean peak force, averaged across all 52 animals for conditioning session 12. Thus, the point plotted at ordinal position 5 is the group average for the peak force of the fifth response emitted by each animal. The vertical lines represent the 0.95 confidence interval for each point. Figure 2 makes it quite clear that the first response of a session is most forceful. Furthermore, mean peak force for the first response of a session is very close to the level of force emission exhibited by the control group in extinction (see Table 1). Therefore, the occurrence of high forces throughout extinction may be interpreted as a continuation of the tendency to emit high force which ordinarily occurs at the beginning of a session of reinforced responding. Force emission does not decline in extinction because reinforcement is not available to cue the force changes depicted in Fig. 2.

Even though a CRF schedule was used, the within-session decrease in peak force shown in Fig. 2 is probably not a result of satiation. The major portion of the change in peak force occurs in going from the first response to the second, and by the sixth or seventh response peak force

exhibits no further tendency to decline. Therefore, it seems unlikely that a single 45-mg food pellet could produce sufficient satiation to account for the observed rapid decrease in peak force.

The foregoing analysis suggests that the drug related inter-group differences observed for peak force during extinction should appear in the peak force data for the first response of conditioning session 10 where drugs were also administered. The ordering of means is as expected; the values for CDP (5.0 mg/kg), CPZ (4.0 mg/kg) and saline are 41.0 g, 23.7 g and 36.5 g, respectively. However, the CDP group on this measure narrowly misses being significantly different from the saline control group (two-tailed *t*-test $0.05 < p < 0.10$), whereas the CPZ group is significantly below the saline control (same test, $p < 0.05$).

Despite this account of the present data, the force incrementing effects of CDP remain puzzling. The central motor effects of CDP may be involved [14]. Alternatively, the comparatively high forces produced by CDP may be interpreted as resulting from a reduction in reactive inhibition associated with each response when exertion is near maximal as in extinction (cf., [17]). Further experimentation with CDP and peak force of response should yield a solution.

Overall, the data point to a dissociation between response force and response rate during extinction. CDP appears to increase resistance to extinction by elevating rate late in extinction as predicted by frustration theory. Yet

the increase in response force attendant upon the introduction of extinction is not attenuated by this drug. The pattern of force emission within a session of CRF responding, i.e., high and then declining force over the first few

responses (see Fig. 2), suggests that force elevations in extinction may result from a type of generalization decrement rather than from unconditioned frustration effects.

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