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Individual Differences in Novelty-Induced Activity Do Not Predict Strength of Amphetamine-Induced Place Conditioning

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ERB, S., AND L. A. PARKER. *Individual differences in novelty-induced activity do not predict strength of amphetamine-induced place conditioning.* PHARMACOL BIOCHEM BEHAV **48**(3) 581–586, 1994.—A rat's level of activity while in a novel chamber has been shown to predict the likelihood that rat will learn to self-administer low doses of amphetamine (10). In a series of four experiments employing the place conditioning paradigm, a rat's level of activity when placed in a novel chamber was used to predict its sensitivity to the rewarding properties of low doses of amphetamine. In phase 1 of each experiment, rats were divided into high responders (HRs) and low responders (LRs) on the basis of activity level while in a novel chamber. In phase 2, rats were given place conditioning trials (one to four trials) with amphetamine (0.75–10 mg/kg). Although amphetamine-induced place preferences were consistently demonstrated, activity in a novel chamber did not predict the strength of a preference formed for an amphetamine-paired place. The failure of these experiments to support similar investigations using the self-administration paradigm [e.g., (10)], suggests that caution be used in generalizing between paradigms believed to measure similar processes.

Individual differences Amphetamine Place conditioning Place preference Activity Novelty
Dopamine Reward Reinforcement Rat

PIAZZA, Deminiere, Le Moal, and Simon (10) have recently provided information regarding the factors responsible for the considerable variability in the speed with which rats learn to self-administer low doses (10 μg/kg) of amphetamine. They reported that the level of activity that a rat displays when placed in a novel chamber predicts the likelihood that rat will self-administer amphetamine (5,10). Rats that demonstrate a high activity response (HR), but not rats that demonstrate a low activity response (LR), while in a novel environment, rapidly learn and maintain amphetamine self-administration.

Another paradigm that is used to measure the capacity of a drug to serve as a rewarding stimulus is that of place conditioning. Within this paradigm, there is also considerable variability in the strength of conditioning [e.g., (11)]. If both paradigms measure the efficacy of a drug to serve as a reward, then individual differences in novelty-induced activity level should also predict the ability of amphetamine to produce a place preference.

Four experiments are reported below which assessed the ability of a rat's reaction to novelty to predict the strength of amphetamine-induced place conditioning. If it is assumed that place conditioning assesses the same rewarding properties of drugs as self-administration, then the same variables that modify self-administration should also modify place conditioning. However, as will be evident, novelty-induced activity level did not predict the strength of place conditioning in the experiments reported below.

GENERAL METHOD

Subjects

Male Sprague-Dawley rats were obtained from Charles River Labs, St. Constant, Quebec, weighing 270–320 g on the day of the first test. They were housed singly in stainless steel mesh cages and maintained on a 12 L : 12 D schedule, with the lights on at 0800 h and the lights off at 1800 h; all testing was conducted in the light phase. A 1-week adaptation period preceded each experiment during which the rats were handled daily. Food and water were available ad lib throughout the experimentation.

Apparatus

The chambers employed in all experiments were wooden chambers (large chamber: 70 × 25 × 29 or small chamber:

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35 × 25 × 29 cm) painted flat black with distinctive floor textures. The floor texture cues consisted of one of: soft corrugated black plastic, 5 cm wide black sandpaper strips located 5 cm apart on the black wooden floor chamber or wire mesh grid (0.625 cm wide). These cues have been employed in previous place-conditioning experiments in our laboratory and tend to be equally preferred as assessed by group means [e.g., (4,8,9)].

The location and activity level of each rat during each minute of testing was measured by a videotracking apparatus (Videomex V; Columbus instruments) as reported by Parker (8). The movement of the white rat (the widest part of its image at any given time) against the black background of the chamber was monitored by a videocamera located in the ceiling. The signal was analyzed by the videotracking apparatus and sent to an IBM computer. During the phase 1 novelty test, the Videomex monitored the movement of the rat in the chamber. The activity measure consisted of a frequency count of the number of times that the rat entered eight equidistant zones within the chamber. During the phase 2 place preference test, the Videomex monitored the amount of time spent in each chamber.

General Procedure

Phase 1. In Experiments 1–4, the novel test apparatus consisted of either a large black wooden chamber (70 × 25 × 29 cm) or a small black wooden chamber (35 × 25 × 25 cm), depending upon the experiment, with a sheet of soft black corrugated plastic floor matting (0.25 cm thick) placed across the floor. Each rat was placed in the apparatus for a 60–120-min period (depending upon the experiment) and the movement of the rat was automatically recorded by the videotracking apparatus. The rats were run in squads of four or eight, depending upon the experiment. On the basis of the phase 1 activity scores, the rats were classified as high responders (HR) or low responders (LR) by a median split and assigned to the phase 2 place conditioning conditions. An ANOVA was conducted with the factor of novelty response, to assess whether the HRs and LRs differed significantly after assignment, and the factor of squad order, to assess whether the time of day of testing influenced the level of activity during the novelty test. In no experiment did the time of day (as indicated by the order of the squad of rats run beginning at 0900 daily) significantly effect activity scores nor did this variable interact with novelty response. However, in all experiments ($p < 0.001$) the HRs were significantly more active than the LRs on the basis of the phase 1 groupings.

Phase 2. In each of Experiments 1–4, between 3–7 days after the phase 1 trial, the phase 2 conditioning trials began. On each conditioning trial, the rats were injected intraperitoneally (IP) with *d*-amphetamine sulfate or with physiological saline solution, 5 min prior to placement into a conditioning chamber (35 × 25 × 29 cm, black wooden box) with the grid floor or into a conditioning chamber (35 × 25 × 29 cm, black wooden box) with the sandpaper strip floor for a 30-min period. The order of injections and the floor paired with amphetamine were counterbalanced among the HR and the LR groups. The rats received 1–4 cycles (amphetamine/saline) of conditioning trials, depending upon the experiment; each pair of trials occurred on consecutive days and 1–2 days intervened between pairs of trials. Between 2–3 days after the final conditioning trial, the rats were tested for their chamber preference for a 15-min period. During the place preference test, the barriers between the chambers were removed and the rats were allowed to explore the chambers for 15 min. The amount of time spent in each chamber was recorded by the videotracking apparatus.

EXPERIMENT 1

In Experiment 1, the novelty-induced HRs and LRs received four conditioning trial cycles with 1.5 mg/kg of amphetamine during the phase 2 place conditioning.

Method

During the phase 1 novelty test, 47 rats were individually tested in the large novelty test chamber (70 × 25 × 29 cm) for a 60-min period as described in the general procedure section. On the basis of a median split of their activity scores, they were classified as HRs ($n = 23$) or LRs ($n = 24$) and assigned to phase 2 place conditioning groups. During phase 2 place conditioning, the rats received four cycles of conditioning trials as described in the General Procedure section. The dose of amphetamine was 1.5 mg/kg, injected IP at a volume of 2 ml/kg. Three days after the final conditioning trial, the rats were given a 15-min test of their preference for the amphetamine-paired side.

Results and Discussion

Figure 1 presents the mean amount of time (s) that the HRs and LRs spent in the amphetamine-paired minus the saline-paired chambers during the preference test of Experiment 1. Although both groups displayed a preference for the amphetamine-paired chamber, $t(23) > 3.8$, $p < 0.01$, when compared with the population mean (0), the LRs and the HRs did not significantly differ from one another. Additionally, the correlation between the phase 1 activity in the novel chamber and the place conditioning difference scores was not significant ($r = -0.07$). The phase 1 novelty response was not related to the strength of amphetamine-induced place conditioning.

EXPERIMENT 2

In Experiment 2, the novelty-induced HRs and LRs were assigned to separate groups that received 1, 3, or 10 mg/kg of amphetamine during phase 2. Deminiere et al. (5) emphasized that the difference between HRs and LRs is expected to be

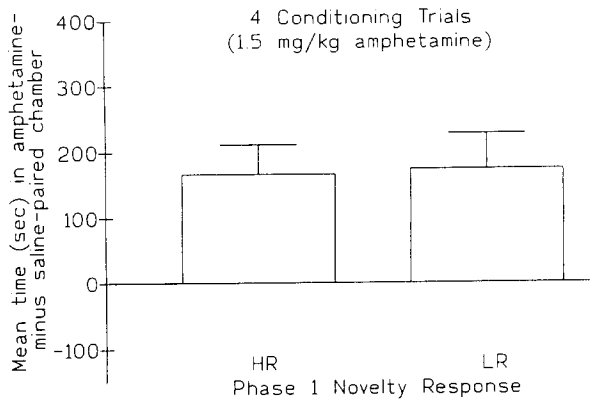

FIG. 1. Mean amount of time (s) spent in the amphetamine-paired minus the saline-paired chamber by the HRs and LRs in Experiment 1.

evident only at low doses of amphetamine; "high doses of amphetamine tend to override individual differences in vulnerability" (5). Therefore, the difference between HRs and LRs should be greatest at the lower doses than at the higher doses.

Method

During the phase 1 novelty test, 70 rats were individually tested as in Experiment 1. On the basis of a median split of their activity scores, they were classified as HRs or LRs and assigned to phase 2 place conditioning groups. During phase 2 place conditioning, the rats received four cycles of conditioning trials. The doses of amphetamine were 1 mg/kg (n = 22), 3 mg/kg (n = 24), or 10 mg/kg (n = 24), all at a volume of 2 ml/kg. Between 2-3 days after the final conditioning trial, the rats were given a 15-min test of their preference for the amphetamine-paired side. Additionally, the total activity of the rats during the preference test was monitored to determine whether the HRs were more active during testing than the LRs.

Results and Discussion

Figure 2 presents the mean amount of time (s) that the HRs and LRs spent in the amphetamine-paired minus the saline-paired chambers during the preference test of Experiment 2. The 2 by 3 ANOVA of the difference scores with the factors of novelty response (HR, LR) and dose of amphetamine (1, 3, and 10 mg/kg) revealed only a significant dose effect, $F(2, 64) = 3.3$, $p < 0.05$; by subsequent Newman-Keuls analyses, 10 mg/kg of amphetamine produced a stronger preference than did 1 mg/kg. The interaction between novelty responsiveness and dose was not significant. At no dose level did the HRs differ significantly from the LRs. Additionally, the correlations between phase 1 activity and phase 3 place preference difference scores were not significant for any dose group (1 mg/kg, $r = -0.05$; 3 mg/kg, $r = -0.23$; 10 mg/kg, $r = 0.01$) or across all the groups ($r = -0.23$).

When preference for the amphetamine-paired chamber was compared with the population mean by mean of t-tests ($p < 0.01$, to correct for experimentwise error), all groups except LRs conditioned with 1 mg/kg demonstrated a preference for the amphetamine-paired chamber. Although this finding is consistent with the prediction that the LRs would develop a weaker place preference than would the HRs, it should be considered with caution given that the difference between LRs and HRs was not significant at this dose level.

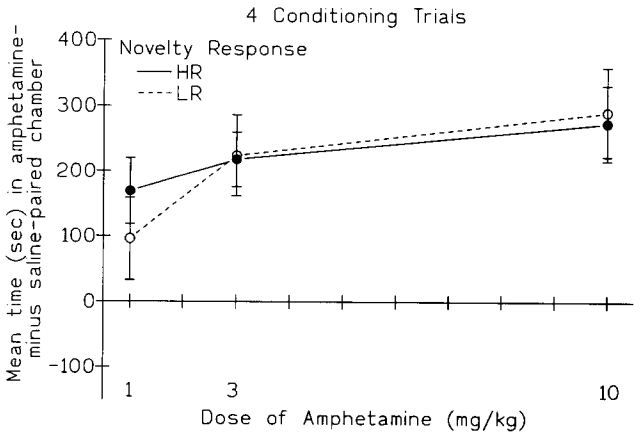

FIG. 2. Mean amount of time (s) spent in the amphetamine-paired minus the saline-paired chambers by HRs and LRs conditioned with 1, 3, or 10 mg/kg amphetamine in Experiment 2.

In order to assess the consistency of the level of activity in the HR and LR groups, the total number of line crossings during the place preference test (among both chambers) was assessed in a 2 by 3 between groups ANOVA with the factors of novelty response (HR, LR) and dose of amphetamine (1, 3, and 10 mg/kg). The only significant effect was that of novelty response, $F(1, 64) = 4.4$, $p < 0.05$; group HR ($\bar{X} = 183.1$) displayed greater activity than group LR ($\bar{X} = 161.9$) during the place preference test, demonstrating consistency in the activity of HRs and LRs between phase 1 and phase 2.

EXPERIMENT 3

Piazza et al. (10) emphasize that the initial response to amphetamine is most sensitive to the variable of novelty responsiveness. Using the self-administration paradigm they found that after four exposures to amphetamine, the difference between HRs and LRs in acquisition of self-administration was no longer evident. In Experiments 1 and 2, it is conceivable that after four conditioning trials, the LRs may have become sensitized to the rewarding properties of amphetamine, such that the HRs and the LRs no longer differed in responsiveness to amphetamine reward. In fact in Experiment 2, although the HRs and LRs conditioned with 1 mg/kg of amphetamine did not significantly differ from one another, when compared against the baseline, only the HRs demonstrated an amphetamine-induced place preference. Experiment 3 employed a single conditioning trial with a dose of 1 mg/kg of amphetamine in an attempt to measure the initial rewarding response to amphetamine at a near threshold place preference. Such a manipulation was expected to enhance the difference in place preference conditioning between HRs and LRs.

Additionally, in other investigations of the role of novelty-induced activity as a predictor of the behavioral effects of amphetamine, the novel test chamber size differed from that of Experiments 1 and 2. Piazza et al. (10) employed a circular chamber (170 cm long by 10 cm wide) to assess novelty-induced activity level, and Hooks et al. (6,7) employed a rectangular novelty test chamber (39 × 25 × 24 cm) that was smaller than that employed in the above experiments. It is, therefore, possible that our failure to demonstrate differences in strength of place conditioning in the HRs and LRs was the result of assessment of novelty-induced activity in a larger chamber than those used by other investigators. Because both Piazza et al. (10) and Hooks et al. (7) demonstrated that novelty-induced activity predicts rats' responsiveness to amphetamine in chambers with very different stimulus characteristics, it is inconceivable that specific chamber cues are responsible for the appropriate assignment to HR and LR groupings. However, it is conceivable that the size of the chamber would modify the likelihood that a rat would explore a novel environment (2). Therefore, in Experiment 3, we employed a chamber with dimensions (35 × 25 × 29 cm) very similar to those of the chamber employed by Hooks et al. (6).

Additionally, Piazza et al. (11) administered a 120-min rather than a 60-min novelty test, although Hooks et al. (6) divided the rats on the basis of 60-min novelty response. Therefore, in Experiment 3, the phase 1 novelty test was continued for a 120-min period. The rats were assigned to HRs and LRs on the basis of their 120-min activity score, but the

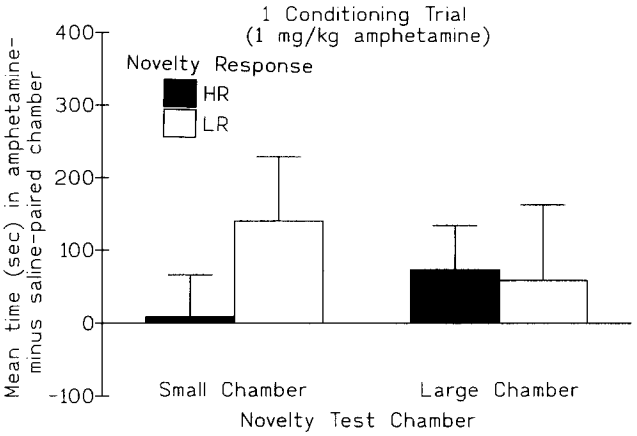

FIG. 3. Mean amount of time (s) spent in the amphetamine-minus the saline-paired chambers by HRs and LRs, divided on the basis of novelty response in a small or large novel chamber, after one conditioning trial with 1 mg/kg amphetamine in Experiment 3.

data was also analyzed with the groups composed of scores from the first 60 min of testing; the two analyses revealed the same pattern of results.

Method

During phase 1 of Experiment 3, 48 rats were given a 120-min novelty test in either the small chamber (n = 24) or in the large chamber (n = 24). Each group of rats was classified as HRs or LRs on the basis of their 120-min activity scores and assigned to phase 2 conditions. During phase 2, they were given a single cycle of conditioning trials with a dose of 1 mg/kg, IP, of amphetamine administered in a volume of 1 ml/kg. Three days later, rats were given a 15-min place preference test.

Results and Discussion

Figure 3 presents the mean amount of time (s) spent in the amphetamine-paired minus the saline-paired chamber by phase 1 HRs and LRs divided on the basis of novelty response in the small or large novel chamber. The 2 by 2 ANOVA of the difference scores with the factors of novelty response (HR, LR) and novelty chamber size (small, large) revealed no significant main effects or interactions. The HRs and LRs did not differ, regardless of whether they were tested in the small or large chamber during phase 1 novelty test.

No group significantly differed from the baseline preference for the amphetamine-paired chamber; however, the preference of the LRs tested in the small chamber approached significance ($p < 0.10$). Furthermore, a comparison of pooled difference scores with baseline revealed a preference for the amphetamine-paired chamber, $t(47) = 1.8, p < 0.05$.

Finally, the correlation between phase 1 activity in the novel chamber and the phase 3 difference scores was not significant for the group tested in the small chamber (r = 0.09), the group tested in the large chamber (r = 0.11), or the combined groups (r = 0.07).

Even when the strength of amphetamine-induced place preference conditioning was at a near threshold level after a single conditioning trial, HRs and LRs did not demonstrate a difference in sensitivity to amphetamine-induced place conditioning.

EXPERIMENT 4

The factor of novelty responsiveness has been demonstrated not only to predict the likelihood that rats would self-administer amphetamine (10), but also to predict rats' sensitivity to motor-activating properties of amphetamine (7) and their sensitivity to amphetamine sensitization effects (6,10). Therefore, in Experiment 4 the ability of both novelty-induced activity and amphetamine-induced activity to predict amphetamine-induced place conditioning were assessed.

Method

During phase 1, 48 rats received two 120-min novelty tests; one test was given in the large test chamber with the soft plastic floor mat and another was given in the small test chamber with an astroturf floor. Following each 120-min novelty test, rats were injected IP with 1 mg/kg amphetamine, at a volume of 1 ml/kg, and were immediately returned to the test chamber where their activity was monitored for an additional 60 min. This provided the opportunity to divide the rats, on the basis of a median split, into HRs and LRs on the basis of four activity measures: novelty response in the large chamber, amphetamine response in the large chamber, novelty response in the small chamber, and amphetamine response in the small chamber.

During phase 2, rats received either one (n = 16), two (n = 16), or four (n = 16) cycles of conditioning trials as described in the General Procedure section. The dose of amphetamine was 0.75 mg/kg at a volume of 1 ml/kg. We reasoned that this procedure would allow us to measure threshold place conditioning effects that would be more sensitive to the HR/LR factor. Twenty-four hours following their final conditioning trial, rats received a 15-min place preference test.

Results and Discussion

Novelty-induced HRs and LRs. Figure 4 presents the mean amount of time (s) spent in the amphetamine-paired minus the saline-paired chambers by phase 1 HRs and LRs, divided on the basis of novelty response. The difference scores in each section of Fig. 4 were entered into a 2 by 3 ANOVA with the

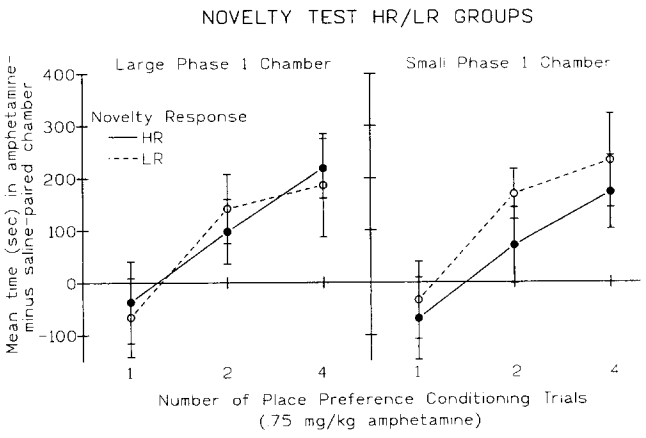

FIG. 4. Mean amount of time (s) spent in the amphetamine-minus saline-paired chambers by HRs and LRs, divided on the basis of novelty response in the large or the small novel chamber, after one, two, or four conditioning trials with amphetamine (0.75 mg/kg) in Experiment 4.

factors of novelty response (HR, LR) and number of conditioning trials (1, 2, and 4). For both sections, the only significant effect was that of trials, $F(1, 42) > 6.1$, $p < 0.01$; by subsequent Newman-Keuls analyses, the rats demonstrated greater preference for the amphetamine-paired chamber after two or four trials than after one trial ($p < 0.05$). The interaction between novelty response and trials was not significant. The HRs and LRs did not significantly differ from one another at any level of conditioning trials.

When compared against baseline, after one trial, no group displayed a place preference. After two trials, only the LRs (tested in both chambers) displayed a place preference ($p < 0.05$). After four trials, all groups displayed a place preference ($p < 0.05$).

The correlations between the phase 1 novelty test activity scores and the phase 3 difference scores were not significant for any group. The correlation coefficients are presented in Table 1.

To assess the consistency of the activity measure, the total activity of the rats during place preference testing (in both chambers) was analyzed as a 2 by 3 between-groups ANOVA with the factors of novelty response and number of conditioning trials for the groups based on novelty response in the large chamber and in the small chamber. For both analyses, only the novelty response effect was significant, $F(1, 42) > 4.2$, $p < 0.05$; the HRs were more active during preference testing than the LRs, suggesting that the phase 1 classification was maintained during the preference testing.

The pattern of results of the novelty induced HRs and LRs in Experiment 4 is extremely consistent with those of previous experiments. After two or four conditioning trials, but not one conditioning trial, rats developed a preference for a chamber paired with a low dose of .75 mg/kg of amphetamine. However, HRs and LRs never significantly differed in the strength of their amphetamine-induced place preference. The failure to demonstrate a difference between HRs and LRs is not a function of sensitization to the rewarding properties of amphetamine in the LRs due to the phase 1 exposure to amphetamine, because a single conditioning trial was insufficient to produce a place preference in either the HRs or the LRs.

Amphetamine-induced HRs and LRs. Figure 5 presents the mean amount of time (s) spent in the amphetamine-paired minus the saline-paired chambers by HRs and LRs, divided on the basis of the 60-min amphetamine challenge test. The 2 by 3 ANOVA of the difference scores for the amphetamine challenge response (HR, LR) and number of conditioning trials (1, 2, or 4) revealed only a significant trials effect, regardless of the size of the phase 1 test chamber, $F(2, 42) > 6.8$, $p < 0.01$. By Newman-Keuls analyses, the groups given two or four conditioning trials demonstrated a greater preference for the amphetamine-paired chamber than the groups given one conditioning trial ($p < 0.05$). HRs did not significantly differ from LRs after an equivalent number of conditioning trials, regardless of the size of the phase 1 novelty test chamber.

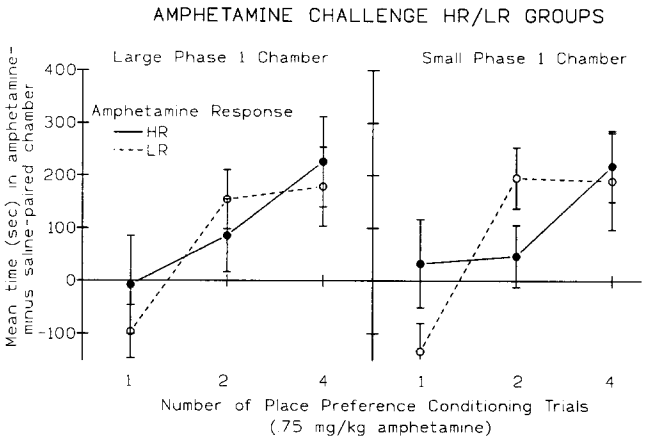

FIG. 5. Mean amount of time (s) spent in the amphetamine-minus the saline-paired chambers by HRs and LRs, divided on the basis of amphetamine challenge response in the large or the small novel chamber, after one, two, or four conditioning trials with amphetamine (0.75 mg/kg) in Experiment 4.

When each group was compared against baseline by *t*-tests, one conditioning trial resulted in a place *aversion* ($p < 0.05$) in the LR group, based on amphetamine response in the small chamber, but no other groups differed from baseline. After two conditioning trials, the LRs, based on amphetamine response in both chambers, displayed a place *preference* ($p < 0.05$); however, the HRs did not significantly differ from baseline. After four trials, all groups displayed a place preference ($p < 0.05$).

The correlations between the phase 1 amphetamine challenge test activity scores (in both the large and small chambers) and the place preference difference scores during phase 3 were significant only for the groups given one conditioning trial ($p < 0.05$). The correlation coefficients for each group are presented in Table 2.

Amphetamine-induced activity level appears to be related to the strength of place conditioning produced with a low (0.75 mg/kg) dose of amphetamine and a single conditioning trial. However, after two trials, the correlation between these two measures was no longer significant. In fact, when compared with baseline, the results suggest that after one trial, the

TABLE 1

TABLE OF CORRELATIONS BETWEEN PHASE 1 ACTIVITY IN NOVEL CHAMBER AND PHASE 3 PREFERENCE TEST DIFFERENCE SCORES

	Number of Conditioning Trials		
	1 Trial	2 Trials	4 Trials
Phase 1 novelty test	(n = 16)	(n = 16)	(n = 16)
Large chamber	0.23	−0.04	−0.08
Small chamber	0.01	−0.20	−0.12

TABLE 2

TABLE OF CORRELATION COEFFICIENTS BETWEEN ACTIVITY DURING PHASE 1 AMPHETAMINE CHALLENGE TEST AND PHASE 3 PLACE PREFERENCE DIFFERENCE SCORE

	Number of Conditioning Trials		
	1 Trial	2 Trials	4 Trials
Amphetamine challenge test	(n = 16)	(n = 16)	(n = 16)
Large chamber	0.54*	−0.44	0.31
Small chamber	0.48*	−0.27	0.26

*$p < 0.05$.

LRs displayed a place aversion (on the basis of small chamber testing), and after two trials they displayed a place preference; yet, the HRs display no place conditioning after one or two trials. It is, thus, likely that amphetamine-induced activity, but not novelty-induced activity, is related to amphetamine-induced reward, as assessed by the place conditioning paradigm.

GENERAL DISCUSSION

In a series of four experiments, the factor of reactivity to novelty was found to be unrelated to the strength of amphetamine-induced place conditioning. This was surprising because reactivity to novelty has been demonstrated to predict the likelihood that rats will self-administer amphetamine (10). If amphetamine-induced place conditioning and amphetamine self-administration are both measures of the rewarding properties of amphetamine, then the failure of reactivity to novelty to predict the strength of one measure, but not the other, is problematical for the general model that reactivity to novelty predicts sensitivity to amphetamine reward (10).

The manipulations employed in the present series of experiments measured near threshold and suprathreshold preferences for an amphetamine-paired chamber. Such manipulations are consistent with reports in the self-administration literature that the factor of novelty responsivity is most sensitively detected during early training trials with low doses of amphetamine (10). Yet, in the above experiments, the strength of the place preference measure of amphetamine reward did not differ between rats that displayed high activity or low activity in response to a novel environment.

It is conceivable that task demands of the two paradigms purported to assess the rewarding properties of amphetamine may be differentially affected by individual differences in activity level. A high baseline activity level may directly facilitate, disrupt, or have no effect upon the demonstration of the learned response depending upon the paradigm. In the self-administration paradigm, an active response is required for the rats to learn the task, and it is conceivable that the HRs would be more likely to produce such an active response than the LRs. Therefore, HRs may learn to self-administer amphetamine faster than LRs because they have a higher level of baseline activity, not necessarily because they are more sensitive to the rewarding effects of amphetamine.

In the place conditioning paradigm, the rats need not respond during conditioning trials to associate the cues of the chamber with the rewarding properties of the drug. During the place preference test, the HRs might be expected to demonstrate a weaker place preference than the LRs, because they would be more likely to explore both chambers. In fact, a number of investigators have reported that during the place preference test, rats demonstrated a *reduced* activity level in the preferred chamber relative to the nonpreferred chamber, presumably a behaviour that would serve to prolong contact with the preferred chamber cues (1,8,12). Conceivably, the higher baseline activity of the HRs could operate in a manner that would reduce contact with the preferred cues.

On the other hand, novelty responsiveness may predict sensitivity to drug reward. This sensitivity may be reflected in the enhanced sensitivity of rats to respond for amphetamine in the self-administration paradigm. In the place conditioning paradigm, it is also possible that the HRs learned stronger amphetamine-induced place preferences, but their higher baseline responding interfered with the demonstration of these stronger preferences.

In summary, both the self-administration and the conditioned place preference paradigms are purported to measure drug reward; however, only the self-administration paradigm appears sensitive to individual differences in reactivity to novelty. Therefore, caution must be exerted in generalizing between measures of drug reward. Carlezon and Wise (3) recently reached a similar conclusion. They demonstrated sensitization to the effects of phencyclidine on intracranial self-stimulation, but not to its effect on general locomotor activity. Task specificity may have accounted for these contrasts in the effects of amphetamine and phencyclidine, and should be considered in any model of individual vulnerability to drug addiction.

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