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Sign-tracking (autoshaping) in rats: A comparison of cocaine and food as unconditioned stimuli

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A series of experiments was performed to determine whether sign-tracking would occur in rats with intravenous (i.v.) cocaine as the unconditioned stimulus. In Experiment 1, a retractable lever paired with food produced strong sign-tracking, but a lever paired with one of three doses of i.v. cocaine did not elicit any approach or contact behavior. Experiment 2 demonstrated that doses of cocaine that did not elicit sign-tracking would function as a positive reinforcer for a lever contact operant. In Experiment 3, an artificial *consummatory response* was added to make the cocaine reinforcement episode more behaviorally comparable to that occasioned by food. Although the rats readily performed this response when it was required to receive cocaine infusions, they still did not contact a lever that signaled the availability of these infusions. It appears that cocaine is different from other positive reinforcers (e.g., food, water, warmth, or intracranial stimulation) in that it will not produce sign-tracking in rats.

Sign-tracking, or *autoshaping*, first reported by Brown and Jenkins (1968), often occurs when a spatially localized conditioned stimulus (CS) reliably signals an appetitive unconditioned stimulus (US). In the most commonly studied variation of the procedure, pigeons are presented with brief illuminations of a keylight that are paired with food. After several such keylight–food pairings, the pigeons begin to approach and peck the keylight. However, there is no contingency in effect that requires the pigeon to peck the key in order to receive the food. In addition, the pigeons will continue to peck the key even when doing so cancels food delivery (Williams & Williams, 1969). This pecking is considered to be a Pavlovian conditioned response (CR) but is likely influenced by operant factors as well (Hearst & Jenkins, 1974; Locurto, 1981; Schwartz & Gamzu, 1977; Tomie, Brooks, & Zito, 1989; Wessels, 1974; Williams, 1981).

Although the topography of the CR differs depending on the species used and other experimental parameters (e.g., type of reinforcer), the essential behaviors involved in sign-tracking include approaching and usually contacting the CS that is paired with the appetitive US (Hearst & Jenkins, 1974). Animals will approach and contact localized stimuli that signal food (Brown & Jenkins, 1968), water (Jenkins & Moore, 1973), heat in warmth-deprived subjects (Wasserman, 1973), reinforcing intracranial stimulation (ICS; Peterson, 1975; Peterson, Ackil, Frommer, & Hearst, 1972; Wilkie & McDonald, 1977), and access to a copulation partner (Burns & Domjan, 1996, 2000). Sign-tracking has been reported many times and in a variety of different species, including pigeons, rats, goldfish, horses, monkeys, and humans (for reviews, see Hearst & Jenkins, 1974; Schwartz & Gamzu, 1977; Tomie et al., 1989).

Autoshaping and human drug abuse share important features in common (Newlin, 1992, 2002; Tomie, 1995, 1996, 2001). In both situations, (1) spatially and temporally discrete stimuli (e.g., a keylight vs. a heroin syringe) reliably predict an appetitive US (e.g., food vs. heroin), (2) skeletal motor responses are directed at the CS (and often at the US itself), and (3) the behavior is relatively insensitive to control by response contingencies (Newlin, 1992, 2002; Tomie, 1995, 1996, 2001). Thus, sign-tracking may model the CRs elicited by drug-paired stimuli in human drug abusers. However, not until recently have there been sign-tracking experiments that used a drug of abuse as the US.

Tomie and his associates (Tomie, 2001; Tomie, Festa, Sparta, & Pohorecky, 2003) found that rats exposed to response-independent pairings of retractable lever insertions with presentations of a bottle containing an ethanol/saccharin solution pressed the lever at a significantly higher rate than control rats who received the lever insertions and bottle presentations independently of each other. When the saccharin was faded out of the solution, rats' leverpressing behavior declined somewhat but still remained substantially higher than control levels. Tomie (2001) also found that pairings of a retractable lever with access to an amphetamine/saccharin solution elicited leverpressing in rats. Interestingly, those rats that drank the largest volumes of the ethanol/saccharin or amphetamine/saccharin solution also made the most leverpressing responses. Krank (2003) found that rats would approach a small cue light that was paired with access to a saccharine/ethanol solution. These rats approached the cue light significantly more often than the rats receiving unpaired presentations of the cue light and the solution did.

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Although theses studies (Krank, 2003; Tomie, 2001; Tomie, Festa, et al., 2003) are consistent with the hypothesis that drugs can serve effectively as USs in sign-tracking procedures with rats, they are somewhat hard to interpret, because sign-tracking was always acquired with saccharin present in the drug solution. It is not clear to what extent the acquisition of sign-tracking was a function of the CS–saccharin association, rather than the CS–drug association, and it appears to be difficult, if not impossible, to induce rats to begin drinking significant quantities of drug solutions that do not contain sweetening agents (Tomie, 2001). One way to resolve this problem is to use intravenous (i.v.) infusions of the reinforcing drug as the US, instead of sweetened oral solutions.

There have been many reports of autoshaping procedures being used to facilitate rats' acquisition of i.v. cocaine or heroin self-administration (Campbell & Carroll, 2001; Campbell, Morgan, & Carroll, 2002; Carroll & Lac, 1993, 1997, 1998; Carroll, Morgan, Lynch, Campbell, & Dess, 2002; Gatham, LaBounty, Wyvell, & Carroll, 1996; Lynch & Carroll, 1999; Lynch, Roth, Mickelberg, & Carroll, 2001; Roth, Casimir, & Carroll, 2002; Specker, Lac, & Carroll, 1994). However, these studies do not show that Pavlovian (i.e., response-independent) CS–US contingencies produced the sign-tracking, because, in all of these studies, a retractable lever was inserted into the chamber and was followed by drug infusion after a brief period of time had elapsed *or* if the rat had contacted the lever. This means that an operant contingency was in effect from the outset of training. Moreover, after 60 infusions were delivered in this manner, the retractable lever remained inserted for the remainder of the session, during which leverpresses were operantly reinforced with drug infusions. Because the rats were exposed to this experimental arrangement from the first session, it is possible, and even likely, that leverpressing in subsequent sessions was a result of the operant contingency, which reinforced leverpresses, and not of the Pavlovian lever–drug association. Finally, neither unpaired nor truly random control groups were studied, making its impossible to isolate the influence that the Pavlovian contingency had on behavior.

The present experiment was performed to (1) determine whether sign-tracking would occur in rats with i.v. cocaine as the US and (2) compare behavior elicited by cocaine-paired stimuli with behavior elicited by food-paired stimuli. In rats, sign-tracking has been demonstrated with appetitive USs such as food (Atnip, 1977; Davey & Cleland, 1982a, 1982b; Davey, Oakley, & Cleland, 1981; Locurto, Terrace, & Gibbon, 1976; Stiers & Silberberg, 1974), water (Davey & Cleland, 1982b), reinforcing ICS (Peterson, 1975; Peterson et al., 1972; Wilkie & McDonald, 1977), and access to bottles containing ethanol/saccharin or amphetamine/saccharin solution (Krank, 2003; Tomie, 2001; Tomie, Festa, et al., 2003). Since cocaine is readily self-administered by rats, it is hypothesized that rats should approach and contact a lever that signals cocaine, just as they approach and contact a lever signaling the appetitive USs listed above. Such a demonstration could support the premise that sign-tracking is involved in human drug-related behavior (Newlin, 1992, 2002; Tomie, 1995, 1996, 2001). On the other hand, if rats fail to approach and contact a lever paired with i.v. cocaine, this research would suggest that there are potentially important differences between cocaine and the other appetitive USs that have produced sign-tracking in rats.

EXPERIMENT 1

The two-retractable-lever procedure originally employed by Peterson et al. (1972) has proven very effective in generating strong sign-tracking in rats when food was the US (Davey & Cleland, 1982b; Peterson et al., 1972; Stiers & Silberberg, 1974). In this arrangement, insertion of one lever is paired with food, whereas insertion of the other lever is not. Insertion of the first lever comes to elicit robust lever contacting (sign-tracking), whereas insertion of the other lever provides a within-subjects control measure of nonconditioned lever contact behavior. The first experiment sought to determine whether sign-tracking would occur with this procedure when cocaine was the US.

For three groups of rats, retractable lever insertions were paired with an infusion of i.v. cocaine. Rats received one of three doses of cocaine: 0.125, 0.25, or 0.5 mg/kg/infusion. Cocaine self-administration studies performed in this laboratory have shown that doses within this range function effectively as positive reinforcers when made available at approximately the frequency at which infusions would be received in the present experiment (e.g., Kearns, Weiss, & Panlilio, 2002; Weiss, Kearns, Cohn, Schindler, & Panlilio, 2003). This experiment also included a group of rats trained with a food US, permitting direct comparisons between the behaviors of rats trained with a cocaine US and those trained with a food US.

Method

Subjects. Sixteen naive adult male Long-Evans rats maintained at approximately 80% of their free-feeding weights ($M = 384.2$ g $\pm$ 7.7 *SEM*) served as subjects. The rats were individually housed in plastic cages with cedar chip bedding and metal wire tops. They had unlimited access to water in their home cages and were fed approximately 12 g of laboratory rat chow immediately after their training sessions. The colony room had a 12:12-h light:dark cycle, with lights on at 0800 h.

Surgery. The rats receiving cocaine USs were surgically prepared with chronic indwelling jugular vein catheters, using a procedure described in detail by Panlilio, Weiss, and Schindler (1996). In brief, under ketamine (60 mg/kg) and xylazine (10 mg/kg) anesthesia, approximately 3 cm of Silastic tubing (0.044 mm ID, 0.814 mm OD) was inserted into the right jugular vein. This Silastic tubing was connected to 5 cm of vinyl tubing (Dural Plastics: 0.5 mm ID, 1.0 mm OD) that was passed under the skin around the shoulder and exited the back at the level of the shoulder blades. The vinyl tubing was threaded through a 10-mm^2 section of Tygon tubing that served as a subcutaneous anchor. Four stainless steel jeweler's screws were implanted in the skull, to which a 20-mm plastic screw was cemented with dental acrylic. The rats in the food group were left undisturbed in their home cages.

After surgery, the rats were given 5–7 days to recover in their home cages. Catheters were flushed daily with 0.1 ml of a saline solution containing 1.25 U/ml heparin and 0.08 mg/ml gentamycin. After the last training session, catheter patency was determined by infusing 0.15 ml of a solution containing 30 mg/ml ketamine and 4 mg/ml xylazine. A catheter was determined to be patent if ataxia was observed within 10 sec of this infusion. One rat in the 0.5-mg/kg group was eliminated from the study (and replaced with another) because of a nonfunctional catheter.

Apparatus. Training took place in a Coulbourn Instruments test chamber (28.5 × 25.5 × 39.5 cm) enclosed in a Coulbourn Instruments sound attenuation shell that was equipped with an exhaust fan. The two side walls of the chamber were made of Plexiglas, and the front and rear walls were aluminum. The grid floor consisted of 0.7-cm-diameter steel rods spaced 1.3 cm apart. The chamber was continuously illuminated by a 100-mA houselight mounted on the rear wall of the sound attenuation shell. Two retractable levers (Scientific Prototype; 3.2 × 1.9 cm) were located on the front wall approximately 2 cm from the left or the right side walls and approximately 2.5 cm above the floor. When fully inserted, each lever extended 1.2 cm into the chamber. Each lever was connected to a Med-Associates drinkometer circuit so that lever contacts could be measured. The food trough was located on the front wall directly between the two levers. Food was delivered via a Coulbourn Instruments Model E14-12 food dispenser.

Cocaine (NIDA, Bethesda, MD) in a saline solution (2.56 mg/ml) was delivered through Tygon tubing that was suspended through the ceiling and wrapped in a metal spring. This tubing was attached to a 10-ml syringe that was driven by a Med Associates syringe pump located outside of the sound attenuation shell. Cocaine was infused at a rate of 3.19 ml/min. Dose per infusion was manipulated by varying the duration of infusion. Thus, infusion durations in the present study were approximately 0.3, 0.6, and 1.2 sec for the 0.125-, 0.25, and 0.5-mg/kg doses, respectively (durations varied very slightly from animal to animal, due to differences in bodyweight).

Procedure. The rats were randomly assigned to one of four groups on the basis of which US they received: cocaine, 0.125 mg/kg/infusion; cocaine, 0.25 mg/kg/infusion; cocaine, 0.5 mg/kg/infusion; or food. For each rat, one lever was designated CS+ and the other CS− (counterbalanced over the left and the right levers). For the first 2 days, the CS+ and CS− levers were presented alone to determine *operant-level* baseline contact rates for each lever and to habituate the rats to the chamber. Although it is possible that these lever-only sessions might have created latent inhibition, previous studies employing this procedure (e.g., Locurto et al., 1976; Peterson et al., 1972; Stiers & Silberberg, 1974) have shown that this potential latent inhibition did not noticeably interfere with acquisition of sign-tracking. Presentations of each lever lasted 15 sec and were controlled by separate variable-time (VT) 90-sec schedules (range: 45–157 sec). While one lever was inserted into the chamber, the timer associated with the VT schedule for the opposite lever was paused. Thus, only one lever could be in the chamber at any time. A session consisted of 40 presentations of each lever and lasted approximately 80 min.

The rats in the food group were magazine trained on the next 2 days. Forty food pellets were delivered according to a VT 90-sec schedule. All the rats reliably ate each food pellet soon after delivery by the end of the second magazine-training session. The rats in the cocaine groups received equivalent training with their respective USs alone during these 2 days. That is, these rats received 40 cocaine infusions of the appropriate dose according to a VT 90-sec schedule. At the moment the infusion pump was operated, the feeder was also activated, but no food was delivered (because the tube from the feeder to the food trough was diverted to a cup located behind the front wall of the chamber). Thus, the rats receiving cocaine and those receiving food had a comparable auditory stimulus accompanying presentation of the US.

On the 5th day, pairings of the CS+ with the US began. As before, the CS+ lever was inserted into the chamber for 15 sec. Now, at the moment it began to retract, a single food pellet (for the food group) or an infusion of cocaine (for the cocaine groups) was delivered. As before, cocaine infusions were accompanied by feeder clicks, but not food. CS+ lever presentations were controlled by a VT 90-sec (range: 45–157 sec) schedule. The intertrial interval was inclusive of the infusion durations. The CS− lever was also presented for 15-sec trials according to a separate VT 90-sec schedule, but no US was delivered when it was retracted. As previously, only one lever could be in the chamber at any given time. A session consisted of 40 presentations of each lever, and training continued for 20 sessions. Lever contacts were recorded by the drinkometer circuits connected to the levers. The last 4 sessions were video recorded by a miniature infrared camera (Defender Security, Model 82-2995), whose lens was placed over a 2.2-cm (diameter) hole drilled in the ceiling of the chamber. This allowed for an observation of the rat's location within the chamber, as well as the topography of responding on the levers.

Data analysis. For all statistical tests, $\alpha = .05$. For each lever, the percentage of trials with a least one lever contact was averaged across two-session blocks. This contact measure was subjected to a repeated measures analysis of variance (ANOVA) for each group. If the F statistic for the main effect of stimulus or the stimulus × block interaction was significant for a particular group, paired t tests were used to compare the CS+ contact measure with the CS− contact measure for each block. Holm's (1979) sequentially rejective Bonferroni procedure was used to control the Type 1 error rate at .05 for this collection of t tests.

The videotapes from each subject's final session were analyzed to see whether the rats spent differentially more time in the vicinity of the CS+ or the CS− lever without necessarily contacting it. A modification of the approach–withdrawal score used by Wasserman, Franklin, and Hearst (1974) was used. By dividing the floor of the chamber into four equal-sized quadrants, the total amount of time a rat spent in the same quadrant as a particular lever (CS+ or CS−) while that lever was fully inserted was recorded. The approach–withdrawal score was this amount of time divided by the total amount of time that a lever was fully inserted over the whole session. Thus, if a rat spent all of the time that the CS+ lever was inserted in the quadrant of the chamber where the CS+ lever was located, the approach–withdrawal score for the CS+ lever would be 1.0. If the amount of time spent in a given quadrant while the CS+ lever was inserted was evenly distributed across the four quadrants, an approach–

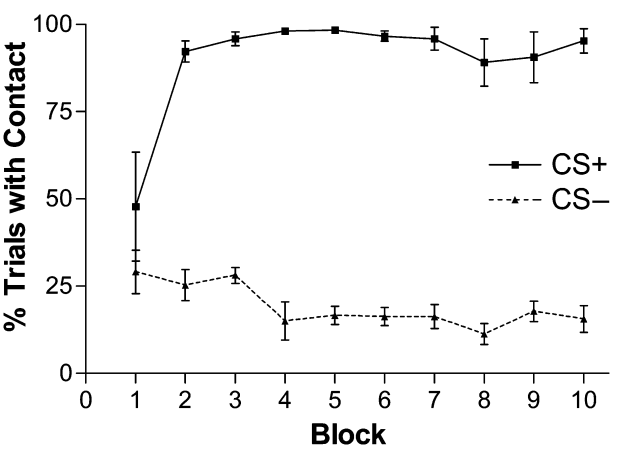

Figure 1. Mean percentages (±*SEM*s) of trials with at least one lever contact in rats ($n = 4$) trained with food unconditioned stimulus (US) over successive two-session blocks.

withdrawal score of .25 would be observed. A repeated measures ANOVA was performed on the approach–withdrawal scores from all four groups. Paired-sample *t* tests were then used to compare the CS+ and the CS− approach–withdrawal scores for each group.

Results and Discussion

During the operant-level baseline sessions, the mean percentage of trials with a contact was between 12% and 25% for the CS+ lever and between 15% and 22% for the CS− lever for all the groups. There was no significant difference (paired-sample *t* tests; all *p*s > .20) between the CS+ and the CS− lever contacts for any group.

For the 4 rats trained with food, Figure 1 presents the mean (±*SEM*) percentage of CS+ and CS− trials with at least one lever contact over the 20 sign-tracking training sessions presented in 10 blocks of 2 sessions each. A repeated measures ANOVA revealed significant differences for the effects of stimulus [CS+ vs. CS−; $F(1,3) = 2{,}866.17$, $p < .0001$] and block [$F(9,27) = 8.85$, $p < .02$] and for the stimulus × block interaction [$F(9,27) = 13.91$, $p < .0001$]. Paired-sample *t* tests indicated that the rats contacted the CS+ lever on a significantly higher ($p < .005$) percentage of trials than they contacted the CS− lever on all blocks except the first one. The rats in the food group were frequently observed biting, licking, and pawing the CS+ lever. Thus, this experiment replicated the results of many previous studies that have demonstrated sign-tracking in rats with a food US.

The results from the three cocaine groups are presented in Figure 2. Repeated measures ANOVAs indicated that there was no significant effect of stimulus (CS+ vs. CS−) and no significant stimulus × block interaction for any of the cocaine groups (all *p*s > .20). The effect of block was significant ($p < .001$) for the 0.125-mg/kg cocaine group only. Overall, the rats in the cocaine groups contacted the CS+ lever at approximately the same low rates that they contacted the CS− lever. A procedure that was very effective in eliciting vigorous and specific contacts on the CS+ lever when food was the US failed to produce this behavior when cocaine was the US.

It is possible that the rats in the cocaine groups approached the CS+ lever without actually contacting it. To evaluate this possibility, approach–withdrawal scores (that reflected the proportion of time a rat spent in the CS+ or the CS− quadrant of the chamber when these respective levers were inserted) were computed from videotapes of the rats' final training session. Figure 3 presents the mean approach–withdrawal scores for the CS+ and CS− levers for all four groups. A repeated measures ANOVA revealed that the effect of group was significant [$F(3,12) = 10.47$, $p < .01$], the effect of stimulus was almost significant [$F(1,3) = 4.403$, $p = .06$], and the group × stimulus interaction was significant [$F(3,12) = 5.30$, $p = .01$]. The rats in the food group spent almost all of the time that the CS+ lever was inserted in the chamber in the CS+ quadrant. In contrast, during CS− lever insertions, they spent approximately the amount of time that would be expected

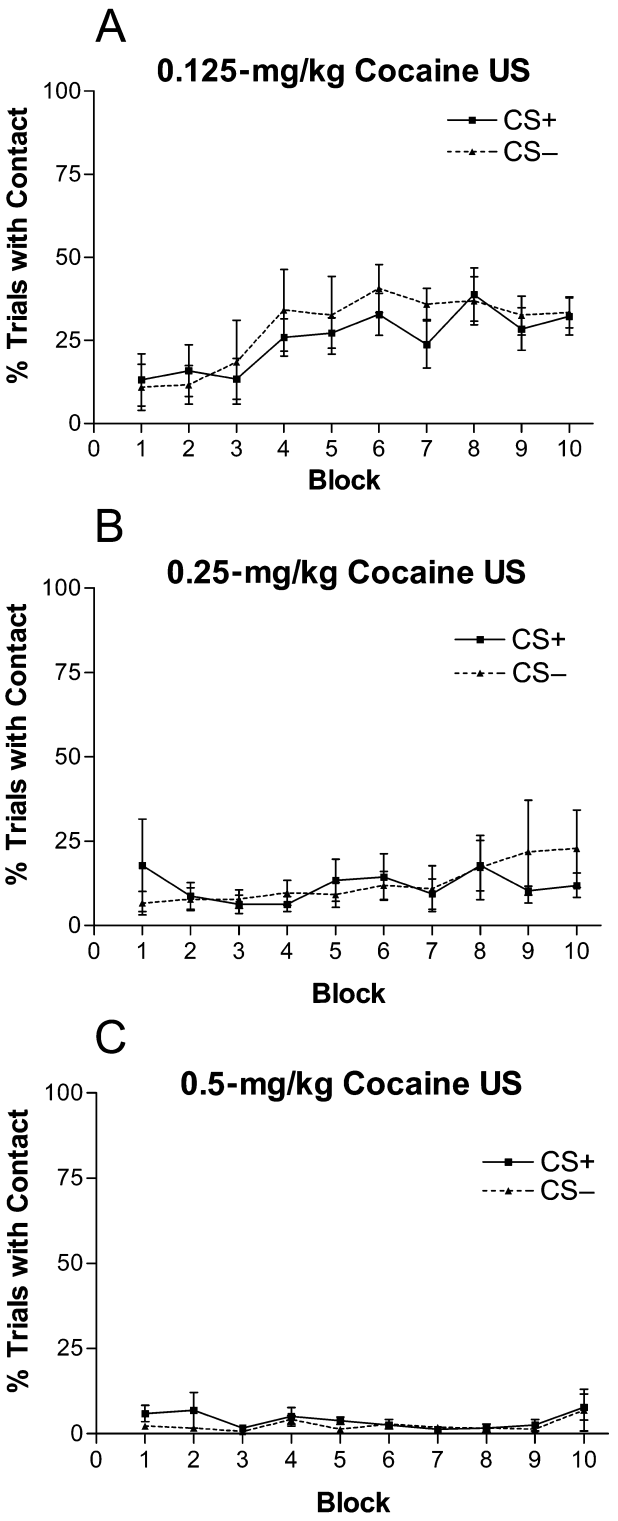

Figure 2. Mean percentages (±*SEM*s) of trials with at least one lever contact in rats trained with a 0.125-mg/kg (panel A), 0.25-mg/kg (panel B), or 0.5-mg/kg (panel C) intravenous cocaine unconditioned stimulus (US; *n* = 4 for each group) over successive two-session blocks.

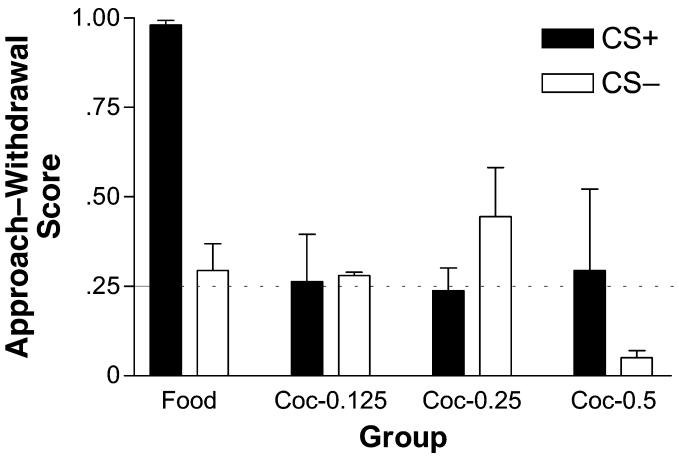

Figure 3. Mean (±*SEM*) approach–withdrawal scores for rats trained with a food, 0.125-mg/kg cocaine, 0.25-mg/kg cocaine, or 0.5-mg/kg cocaine unconditioned stimulus (US). An approach–withdrawal score greater than .25 indicates approach to the conditioned stimulus (CS), whereas a score less than .25 indicates withdrawal from the CS (n = 4 for all groups).

by chance in the CS− quadrant. A paired-sample t test indicated that this difference in approach–withdrawal scores between the two levers for the food group was significant [$t(3) = 10.64$, $p = .002$].

However, there were no significant differences between the approach–withdrawal scores for the two levers in any of the cocaine groups (all ps $> .35$). The rats in the 0.125-mg/kg cocaine group had mean approach–withdrawal scores very near the .25 chance level for both levers. The mean approach–withdrawal score for CS+ in the 0.5-mg/kg cocaine group would have been much lower had it not been for 1 rat who spent almost the entire session in the CS+ quadrant regardless of whether any lever was present. The rest of the rats in this group spent much of the session in the rear half of the chamber (i.e., in neither the CS+ nor CS− quadrant). Thus, the more sensitive approach–withdrawal measure also failed to provide any evidence of sign-tracking when cocaine was the US, whereas it illustrated robust sign-tracking when food was the US.

Experiment 1 demonstrated that three different doses of i.v. cocaine failed to produce sign-tracking in rats with a procedure that rapidly and reliably produced robust sign-tracking in rats when food was the US. A plausible explanation for the failure to observe sign-tracking in the cocaine groups is that the infusions of cocaine were not appetitive stimuli that would function as positive reinforcers. This possibility was examined in Experiment 2.

EXPERIMENT 2

Experiment 2 was performed to examine whether the cocaine infusions used as the US in Experiment 1 would function as positive reinforcers for an operant response. This was accomplished by using the same procedure as that in Experiment 1, with the exception that an operant contingency now required rats to contact the S+ lever[1] to receive an infusion. As before, contacts on the S− lever had no consequences. A higher contact rate on the S+ lever than on the S− lever would show that the dose of cocaine was reinforcing (Yokel, 1987).

Method

Subjects and Apparatus. Twelve naive adult male Long-Evans rats served as subjects. The rats were maintained at 80% of their free-feeding weights (M = 382.2 g, SEM = 4.6). Housing and maintenance conditions, as well as surgical procedures, were the same as those described in Experiment 1. All experimental equipment was the same as that in Experiment 1.

Procedure. The rats were randomly assigned to one of three groups on the basis of the dose of cocaine they would receive: 0.125, 0.25, or 0.5 mg/kg/infusion. For each rat, one lever was designated S+ and the other S−, with the left and the right levers counterbalanced over rats in each group. As for the groups in Experiment 1, to measure operant-level rates, during the first 2 days, the rats were placed in the chamber, and the S+ and the S− levers were presented alone according to separate VT 90-sec schedules. For the next two *magazine-training* sessions, with the levers retracted, the rats received 40 noncontingent infusions of cocaine according to a VT 90-sec schedule.

On the 5th day, training sessions with the operant contingency were instituted. The procedure used was the same as that in Experiment 1, with the exception that a contact on the S+ lever was now required by the subject to receive an infusion. S+ trials lasted 15 sec and trials were separated by 90-sec intertrial intervals. A cocaine infusion, along with the click stimulus, was presented at the moment a contact was made on the S+ lever. The lever remained inserted into the chamber for the entire 15-sec trial regardless of when a contact was made (if at all). Only one infusion could be earned per S+ trial. If a lever contact did not occur on the S+ lever, it was retracted at the end of 15 sec, and no infusion was delivered. The S− lever was also inserted for 15-sec trials that were presented according to a sep-

arate VT 90-sec schedule. Contacts on the S− lever were recorded but had no programmed consequences. As before, only one lever could be in the chamber at any given time. A session consisted of 40 presentations of each lever, and training continued for 20 sessions.

Data analysis. Lever contact data were analyzed in the same manner as that in Experiment 1.

Results and Discussion

For all the groups, the mean percentages of trials with a contact during the operant-level baseline sessions were 4%–14% for the S+ lever and 12%–18% for the S− lever. During these sessions, there were no significant differences in contact rates between the S+ and the S− levers for the 0.125-mg/kg or the 0.5-mg/kg group (paired sample *t* tests; both *p*s $> .37$). The rats in the .25-mg/kg group displayed a slight, but significant ($p = .02$), unconditioned preference for the S− lever (14% vs. 18% of the trials with S+ and S− lever contacts, respectively).

Figure 4 presents the mean percentages (±*SEM*s) of S+ and S− trials with at least one lever contact over the 10 self-administration blocks for the rats receiving a 0.125-, 0.25-, or 0.5-mg/kg cocaine reinforcer. For the 0.125-mg/kg group, there was no significant effect of stimulus [$F(1,3) = 0.859, p > .85$] or stimulus × block interaction [$F(9,27) = 0.517, p > .8$]. However, there was a significant effect of block [$F(9,27) = 3.68, p < .01$], with the rats increasing their contact rates on both levers slightly over sessions. The rats in the 0.125-mg/kg group contacted the S+ and the S− levers at approximately the same rate, suggesting that the 0.125-mg/kg dose did not function as a reinforcer.

For the 0.25-mg/kg group, there were significant effects for stimulus [$F(1,3) = 26.97, p < .02$] and block [$F(9,27) = 9.01, p < .0001$ and a significant stimulus × block interaction [$F(9,27) = 3.131, p < .02$]. Paired-sample *t* tests indicated that the rats contacted the S+ lever on a significantly ($p < .005$) higher proportion of trials than they contacted the S− lever on Blocks 9 and 10. For the 0.5-mg/kg group, the effects of stimulus [$F(1,3) = 19.60, p < .03$] and block [$F(9,27) = 3.48, p < .01$] and the stimulus × block interaction [$F(9,27) = 5.41, p < .001$] were all significant. The difference between the S+ lever and the S− lever was marginally significant ($p = .006$) on the 10th block.

This experiment demonstrated that the 0.25- and 0.5-mg/kg cocaine infusions were effective reinforcers for a lever contact operant. These results cast doubt on the possibility that the failure to obtain sign-tracking in the 0.25- or 0.5-mg/kg cocaine groups in Experiment 1 was due to the fact that those cocaine infusions were not reinforcing. Nevertheless, it should be noted that the rats in the cocaine groups of Experiment 1 received a noncontingent cocaine infusion on every CS+ trial, whereas the rats in the 0.25- and 0.5-mg/kg cocaine groups of the present experiment self-administered an infusion only on about 80% and 45%, respectively, of the S+ trials. Although it is possible that receiving a noncontingent infusion on every trial leads to cumulative tissue levels of cocaine that make further infusions nonreinforcing or even aversive, there is evidence from the present experiment that is inconsistent with this conjecture.

The rats in the 0.5-mg/kg group of Experiment 2 self-administered approximately 9 mg/kg/session (45% of 40 trials = 18 infusions × 0.5 mg/kg/infusion), which is very close to the 10 mg/kg/session administered noncontingently to the 0.25-gm/kg group in Experiment 1 (40 infusions × 0.25 mg/kg/infusion). In addition, 1 of the 4 rats in the 0.25-mg/kg group of the present experiment self-administered an infusion on 90%–98% of the trials on each of the last five sessions of training. These two results suggest that the cocaine should have functioned as an appetitive US at least for the 0.25-mg/kg group in Experiment 1.

The use of a yoking procedure, in which a rat in one group (the Pavlovian group) receives response-independent lever–cocaine pairings only on those trials on which its yoked partner (in the operant group) self-administers an infusion, would have permitted a direct comparison between groups, with frequency of cocaine infusion held constant. However, this yoked paradigm would have raised other concerns, because the pairing of lever insertion and cocaine infusion would be intermittent in the Pavlovian group. Such an arrangement would have been at variance with the primary goal of Experiment 1—creating optimal conditions for the generation of sign-tracking.

EXPERIMENT 3

A potentially important difference between food and cocaine as USs is that a consummatory response chain is required by the rat to ingest food, but not to ingest cocaine (Wise, 1987). The rat must move to the food trough, pick up the food pellet, chew it, and swallow it. In contrast, the rat does not have to do anything to ingest the cocaine infusions—it passively receives them. Support for the potential importance of a consummatory response here comes from studies showing that the topography of the sign-tracking CR often resembles consummatory responses directed at the US. For example, the form of pigeons' keypecks on food-paired keylights resembles that of their pecks at food, whereas their keypecks directed at water-paired keylights resemble normal drinking movements (Jenkins & Moore, 1973). Similarly, rats direct eating-like consummatory responses at food-paired levers, whereas they direct drinking-like responses at fluid-paired levers (Davey & Cleland, 1982b).

Experiment 3 was performed to see whether requiring rats to perform an artificial consummatory response to receive cocaine would produce sign-tracking to a cocaine-paired lever. This strategy has been successful in making behavior reinforced by an ICS more closely resemble behavior reinforced by food (Gibson, Reid, Sakai, & Porter, 1965; Hawkins & Pliskoff, 1964; Pliskoff, Wright, & Hawkins, 1965). For example, it had long been considered difficult or impossible to maintain behavior reinforced by

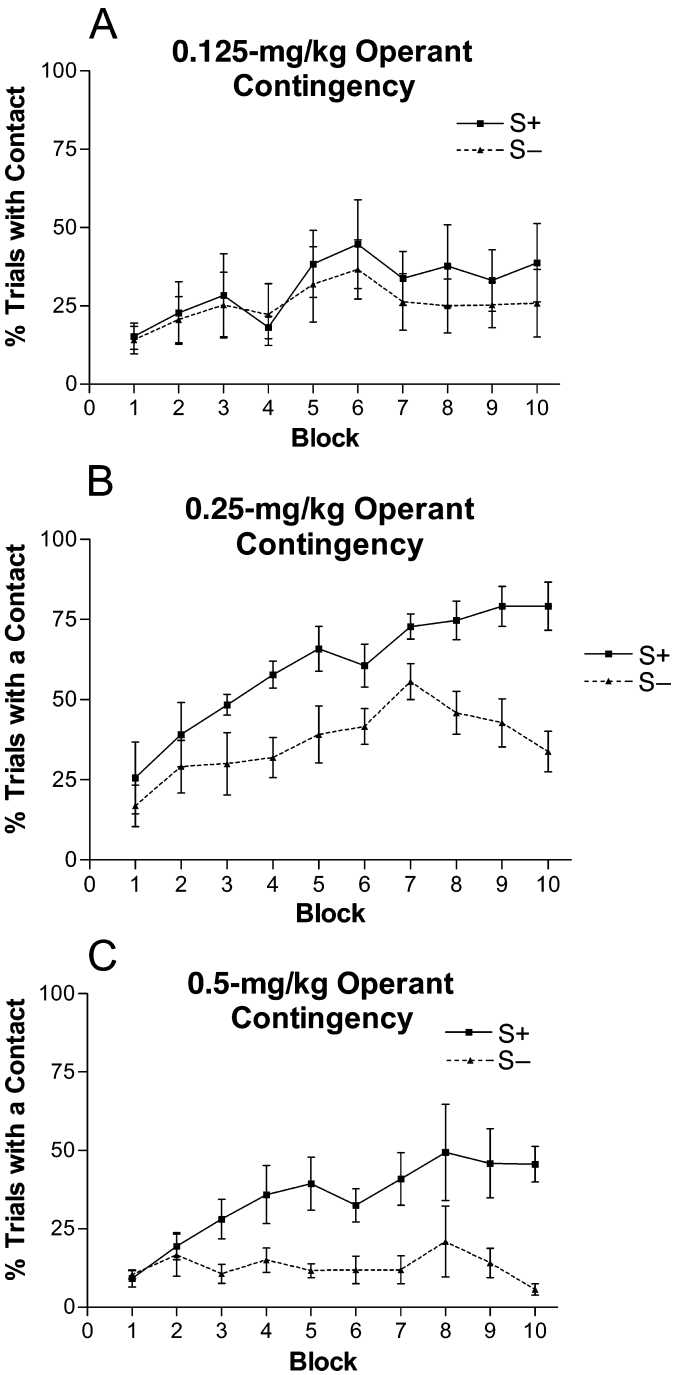

Figure 4. Mean percentages (±*SEM*s) of trials with at least one contact for rats trained on an operant contingency with a 0.125-mg/kg (panel A), 0.25-mg/kg (panel B), or 0.5-mg/kg (panel C) intravenous cocaine reinforcer ($n = 4$ for each group) over successive two-session blocks.

an ICS on the types of intermittent schedules often employed with food—especially when these schedules allowed only for infrequent reinforcement. However, Pliskoff et al. (1965) were able to generate robust responding on fixed-interval (FI) 10-min, a fixed-ratio (FR) 100, a variable-interval 4-min, and other schedules of reinforcement when rats were required to perform an arbitrary consummatory response to receive the ICS reinforcer. More-

over, the cumulative records from the rats trained on these schedules exhibited the characteristic patterns of responding associated with each type of schedule when food is the reinforcer (e.g., FI "scallops," FR bursts, etc.).

In Pliskoff et al.'s (1965) procedure, responses on the operant lever, which was always inserted in the chamber, were reinforced by the insertion of a second, retractable lever on which leverpresses were reinforced by an ICS on a continuous reinforcement schedule. After the rat produced 20 ICS reinforcers by pressing the lever 20 times, this lever was retracted. Requiring the rats to press this second lever to receive the reinforcer was designed to approximate the chain of consummatory responses involved when food is used as the reinforcer. Response rates and patterns on the operant lever more closely resembled food-reinforced responding when this response chain was added. This suggests that performance of this artificial consummatory response shares some functional similarities with the chain of behaviors the rat engages in when it receives a food pellet.

The present experiment adapted Pliskoff et al.'s (1965) procedure to the sign-tracking situation. Insertions of one lever (the CS lever) preceded insertions of a second lever (the consummatory lever). Contacting the first lever had no consequences, whereas contacts on the second lever were reinforced with infusions of cocaine. Unlike the cocaine groups in Experiment 1, the rats no longer passively received the cocaine infusions. They now had to move to a specific place in the chamber and make contact with a specific physical stimulus in order to receive the cocaine US, just as they have to move to the food trough when food is the US in the sign-tracking paradigm. In addition, because the rats in the present experiment self-administered their cocaine, they could control their rate of intake—unlike in Experiment 1, in which infusions were presented noncontingently. Thus, there could be little question about whether the dose of cocaine administered was reinforcing.

Method

Subjects and Apparatus. Four naive adult male Long-Evans rats served as subjects. The rats were maintained at 80% of their free-feeding body weights (M = 373.3 g, SEM = 12.0). Housing and maintenance conditions, surgical procedures, and all experimental equipment were the same as those in Experiment 1.

Procedure. For all the rats, the left lever was designated the *CS* lever, and the right lever was designated the *consummatory* lever. The rats were first trained to self-administer cocaine by contacting the consummatory lever. The consummatory lever was inserted into the chamber for 15-sec trials separated by intertrial intervals lasting 90 sec on average (range: 45–135 sec). A session consisted of 40 trials. Initially, each leverpress was followed immediately by a 0.5-mg/kg infusion of cocaine and a feeder click (but no food). This FR-1 schedule of self-administration remained in effect for the duration of the 15-sec trial. Thus, the subject could self-administer multiple infusions per trial. However, if the subject did not contact the lever on a given trial, the lever was retracted, and no infusions were presented on that trial. The rats were trained on this procedure until they made at least one contact on at least 40% of the trials in a single session (i.e., at least 16 trials out of 40). For all the rats, it took between 7 and 17 sessions to meet this criterion. Then the self-administration schedule was gradually increased over sessions from FR-1 to FR-5. At the same time, the unit dose of cocaine was gradually decreased from 0.5 to 0.2 mg/kg.

The rats were trained on this FR-5 schedule until they met a criterion of self-administering at least one infusion on at least 60% of the trials (i.e., 24 out of 40) in a single session. It took between 13 and 26 total sessions for all the rats to reach this criterion. Then trials consisting of pairings of the CS lever with the consummatory lever commenced. The CS lever was inserted into the chamber for 15-sec intervals. Contacts on this lever were recorded but had no programmed consequences. When the CS lever was retracted, the consummatory lever was inserted for a 15-sec period, during which the FR-5 self-administration schedule operated as previously. CS-lever–consummatory-lever pairings were separated by 90-sec intertrial intervals (range: 45–135 sec) and each session consisted of 40 trials. Training on this procedure continued for 20 sessions.

Following this training, these rats continued on the procedure described above, but with food as the reinforcer instead of cocaine. To accomplish this, they were given three sessions in which only the consummatory lever was inserted according to a VT 90-sec schedule (as described above) to establish lever contacting for food on the FR-5 schedule. All the rats met the criterion of completing at least one FR-5 ratio on at least 60% of the trials within these three sessions. Then they were given eight sessions of CS-lever–Consummatory-lever pairings exactly as before, but now food was the reinforcer instead of cocaine.

Data analysis. For each lever, the percentages of trials with a least one lever contact were averaged across two-session blocks. This contact measure was subjected to a repeated measures ANOVA followed by paired-sample t tests, as described in Experiment 1. A t test was also used to compare, for each lever, the percentage of trials with at least one contact during the final block of training with the cocaine reinforcer with the percentage for each of the blocks of training with the food reinforcer. Approach–withdrawal scores were computed from videotapes of the rats' final training sessions with cocaine, as described in Experiment 1.

Results and Discussion

Figure 5 presents the mean percentages ($\pm SEM$s) of trials with at least one lever contact on the CS lever and the consummatory lever over successive two-session blocks. The left section of the figure presents data for the sessions in which cocaine was the reinforcer, and the right section presents data for the sessions in which food was the reinforcer. Throughout training, the rats contacted the consummatory lever on approximately 55%–75% of the trials, on average. In contrast, with the exception of the first two blocks, the rats contacted the CS lever on only approximately 10%–20% of the trials. A repeated measures ANOVA performed on the cocaine data indicated that the effects of stimulus [$F(1,3) = 41.92$, $p = .008$] and the stimulus × block interaction [$F(13,39) = 6.85$, $p = .039$] were significant. The effect of block was not significant [$F(9,27) = 1.19$, $p = .34$]. Paired-sample t tests indicated that the rats contacted the consummatory lever on a significantly higher ($p < .005$) proportion of trials than they contacted the CS lever on Blocks 7 and 10.

During the food phase of Experiment 3, the rats contacted the consummatory lever on almost every trial on all the sessions, plus they also contacted the CS lever on almost every trial during the last two blocks. This indicates that the CS lever elicited sign-tracking CRs when food

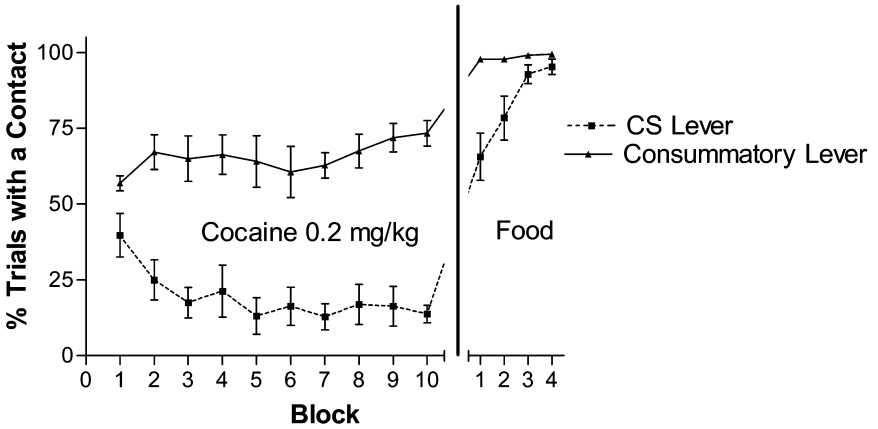

Figure 5. Mean percentages (±*SEM*s) of trials with at least one contact for rats ($n = 4$) trained on a procedure that required a lever contact *consummatory response* on a second lever over successive two-session blocks. Data to the left of the solid vertical line is from trials in which intravenous cocaine of 0.2 mg/kg was the reinforcer. Data to the right of the line is from trials in which food was the reinforcer.

was contingent on contacting the consummatory lever. A repeated measures ANOVA performed on the food data showed that the effects of stimulus [$F(1,3) = 13.49$, $p = .034$] and block [$F(3,9) = 12.56$, $p = .001$], and the stimulus × block interaction [$F(3,9) = 9.85$, $p = .003$] were significant. Paired-sample t tests showed that a difference between the consummatory lever and the CS lever contacts approached significance only on Block 1 of food training.

For each lever, the percentage of trials with a contact during each of the food session blocks was compared with that contact measure from the final block of training with cocaine. Paired t tests indicated that the rats contacted the CS lever during all of the food blocks on a significantly higher ($p < .01$) proportion of trials than they did during the final block of training with cocaine. The rats contacted the consummatory lever on a significantly higher percentage of trials only on Blocks 2–4 of food training, as compared with the final session of cocaine training.

It is possible that the difference in CS contact rates between the cocaine and the food phases could be related to a difference in the consistency of the CS–reinforcer contingency between phases. That is, in the food phase, the rats were reinforced with a food pellet for pressing the consummatory lever on almost every trial, thereby creating a near-perfect contingency between CS lever insertion and food. In contrast, during the cocaine phase, the rats self-administered an infusion on only 55%–75% of the trials, thereby creating a less than perfect contingency between the CS lever and cocaine. Nonetheless, even with

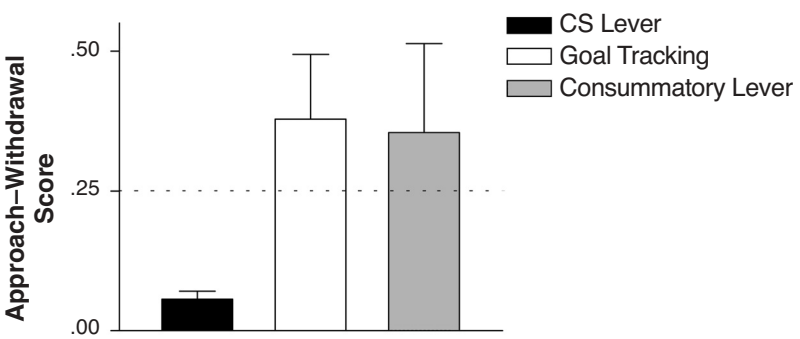

Figure 6. Mean (±*SEM*) approach–withdrawal scores for rats required to perform a consummatory response chain. The black and gray bars present mean approach–withdrawal scores for the conditioned stimulus (CS) lever and the consummatory lever, respectively. The white bar presents an approach–withdrawal score that represents the mean proportion of the total CS lever time that the rats spent in the quadrant of the chamber where the consummatory lever was located (but not inserted).

this partial reinforcement schedule, it would be expected that CS lever contact rates would be higher than the 10%–20% that was observed (which was comparable to the CS− lever control contact rates observed across groups in Experiment 1). For example, Davey and Cleland (1982a), using a sign-tracking procedure with rats that was very similar to that used in the present study, found that rats would contact a lever on over 90% of trials even when only half of the lever insertions were paired with food (i.e., a 50% partial reinforcement schedule was used).

The black bar in Figure 6 presents approach–withdrawal scores for the CS lever from the rats' final training session with cocaine. Even with this more sensitive measure (i.e., more sensitive than the lever contact measure), there was no evidence that the rats sign-tracked the CS lever during the cocaine phase of Experiment 3. In fact, the mean approach–withdrawal score for the CS lever, .06, was significantly lower than .25, the score that would be expected by chance [$t(3) = 3.684$, $p < .05$]. However, this is not evidence that the CS lever acquired aversive properties. Instead of sign-tracking, it appears that the rats *goal-tracked* (Boakes, 1977) during CS lever presentations.

The white bar in Figure 6 presents an approach–withdrawal score modified to reflect goal-tracking. This score is the proportion of the total time that the CS lever was inserted that the rats spent in the quadrant of the chamber where the consummatory lever was located. The mean proportion of .38 is significantly higher [$t(3) = 3.23$, $p < .05$] than .25, the proportion of time that would be expected if the rats had evenly distributed their time in each quadrant. This finding is important because it suggests that the rats' behavior was controlled by CS lever presentations, with this learning expressed as goal-tracking, rather than sign-tracking. The mean approach–withdrawal score for the consummatory lever, .34 (checkered bar in Figure 6), was actually lower, but not significantly lower ($p > .6$), than the mean goal-tracking score (.38). This is consistent with the observation that the rats usually self-administered one or more infusions soon after insertion of the consummatory lever and then quickly moved away from the lever.

In summary, when food was the reinforcer for touching the consummatory lever, the rats contacted the CS lever on almost every trial, often biting and gnawing the CS lever, just like the food rats in Experiment 1. In contrast, when cocaine was the reinforcer, the CS lever was contacted on very few trials—in fact, on about the same percentage of trials (10–20%) as the 0.125-mg/kg and 0.25-mg/kg cocaine groups in Experiment 1 contacted the CS+ lever. There was no evidence that the rats approached the CS lever either. Thus, it appears that requiring rats to perform an artificial consummatory response chain—a strategy that has proven very effective in making rats' intracranial self-stimulation behavior more like their food-reinforced behavior (Gibson et al., 1965; Hawkins & Pliskoff, 1964; Pliskoff et al., 1965)—does not make it any more likely that rats will contact a cocaine-paired lever.

Clearly, there are differences, in terms of both topography and etiology, between natural consummatory responses and the artificial consummatory response employed here. It is possible that the FR-5 response chain did not adequately model natural consummatory responses in the rat. Indeed, it is informative to note that in studies in which sign-tracking has been produced with saccharin/alcohol or saccharin/amphetamine solutions as the US (Krank, 2003; Tomie, 2001; Tomie, Festa, et al., 2003), the drinking consummatory response of the rat was necessary to ingest the US. Moreover, in an innovative adaptation of the autoshaping procedure, Tomie and associates (Tomie, Di Poce, Derenzo, & Pohorecky, 2002; Tomie, Sparta, et al., 2002; Tomie, Wong, Apor, Patterson-Buckendahl, & Pohorecky, 2003) have found that when a sipper bottle containing alcohol is used as the CS, very high levels of sign-tracking, as well as alcohol consumption, can be produced when food is the US. This indicates that robust autoshaping of drug intake can occur when natural consummatory responses are directed at the US.

On the other hand, sign-tracking has been reported with other USs that do not require a consummatory response. Peterson et al. (1972) found that rats would approach and contact a lever signaling a reinforcing ICS, where no consummatory response is required, almost as frequently as they did a lever that signaled food. Woodruff and Williams (1976) found that pigeons would peck a key predicting water even when the water was delivered through a cannula implanted in the upper mandible, thus eliminating the need for a consummatory response to ingest the water. On the basis of this evidence, it appears that the requirement of a consummatory response chain to ingest the US may not be a necessary condition for sign-tracking to occur. Further research might shed light on the importance of consummatory responses in sign-tracking.

GENERAL DISCUSSION

In summary, in Experiment 1, a lever paired with doses of i.v. cocaine that maintained self-administration did not elicit sign-tracking in rats. In contrast, when food was the US, strong sign-tracking was observed. In Experiment 2, the rats readily self-administered two of the three doses of cocaine used as USs in Experiment 1, indicating that for these two doses, at least, the failure to observe sign-tracking did not occur because the cocaine US was not reinforcing. Requiring rats to perform an artificial consummatory response chain, which has been successful in making rats' intracranial self-stimulation behavior more closely resemble food-reinforced behavior (Hawkins & Pliskoff, 1964; Pliskoff, et al., 1965), did not result in sign-tracking to a cocaine-paired lever in Experiment 3.

Previous research has demonstrated that CSs paired with a wide variety of appetitive stimuli will elicit sign-tracking in animals (see the introduction). The results of the present study are important because they show that cocaine will not generate sign-tracking in a procedure in

which food produces very strong sign-tracking. This suggests that simply being a reinforcing appetitive stimulus is not a sufficient condition for a particular US to generate sign-tracking. Unfortunately, the present series of experiments has not been able to pinpoint what the essential difference is between i.v. cocaine and appetitive stimuli that do work effectively in sign-tracking studies.

One potential explanation for the difference found between food and cocaine is that the direct effects of cocaine (i.e., sensory or motor effects) interfered with the rats' ability to approach and contact the cocaine-paired lever. Support for this hypothesis comes from the observation that the rats were often observed engaged in cocaine-induced stereotypy (i.e., repetitive movements of the head, running in circles, etc.). However, Experiment 2 of the present study demonstrated that the potential direct effects of cocaine did not prevent the rats from contacting a lever when an operant contingency required them to do so. It is unlikely that the direct effects of cocaine would interfere with a lever contact CR but would not interfere with lever contacting when it is an operant reinforced by cocaine. Moreover, Wise, Yokel, Hansson, and Gerber (1977) showed that amphetamine-induced stereotypy does not interfere with operant leverpressing for intracranial stimulation. Finally, research from our own laboratory (Weiss et al., 2003) has indicated that rats are capable of leverpressing at high rates despite self-administering amounts of cocaine comparable to those administered in the present study.

It is possible that the temporal and spatial arrangements of stimuli in the present study created a bias that made sign-tracking especially likely to be observed when food was the US, but not when cocaine was the US. Specifically, the food trough was located on the front wall of the chamber directly between the two levers. Thus, in learning to eat from the food trough, the rats would have also increased the amount of time that they spent in the vicinity of the two levers. In contrast, the rats could have received the i.v. cocaine infusions when they were anywhere in the chamber—even in locations distant from the levers. This discrepancy might explain the rapid acquisition of the lever-contacting response when food was the US and the failure to acquire the lever-contacting response when cocaine was the US.

However, there are three lines of evidence that make this possible explanation seem unlikely. First, as was noted previously, Peterson et al. (1972) showed that rats would sign-track a lever paired with a reinforcing ICS—a US that, like i.v. cocaine, could be received by the rat anywhere in the chamber. Second, and perhaps more convincingly, Jenkins's experiments with the *long box* (described in Hearst & Jenkins, 1974) demonstrated that sign-tracking will occur in pigeons even when the location of food delivery is quite distant (nearly 3 ft) from the location of the CS. Finally, if the spatial relation between the levers and the food trough is responsible for the observed sign-tracking with food, this should have been true for both the CS+ and the CS− levers, since they were located the same distance from the food trough (and these designations were counterbalanced over the right and the left levers). However, the rats in the food group of Experiment 1 came to contact the CS+ lever on over 95% of the CS+ trials, while only contacting the CS− lever on about 15% of the CS− trials—which was approximately the same rate that they contacted either lever during the operant-level baseline sessions (i.e., before any food was ever received in the chamber).

It is possible that sign-tracking was not observed when cocaine was the US but was observed when food was the US because of differences in the immediacy of the effects of the two types of USs. For the food group in Experiment 1, the feeder operated at the moment the CS+ lever began retracting. The presence of the food pellet is detected by the rat almost instantaneously. Similarly, for the cocaine groups, the infusion pump was activated at the moment the CS+ lever was retracted. However, there may be a delay between pump activation and the onset of the reinforcing effects of the cocaine. This could result in there being an important functional difference between the two procedures. Specifically, if there is a delay in the onset of the effects of cocaine, the CS–US interval is effectively longer when cocaine is the US than when food is the US. This potential lack of temporal contiguity might have disrupted the acquisition of sign-tracking in the cocaine groups.

However, it should be noted that when food is the US, sign-tracking has been observed in rats with trace intervals of up to 8 sec between lever retraction and food delivery (Messing, Kleven, & Sparber, 1986).[2] Thus, even if there is a delay in the onset of the reinforcing effects of cocaine, sign-tracking might still be expected to be observed if that delay is 8 sec or less. However, we do not know how long this potential delay is, since there have been no studies with rats (that we could find) that have measured the latency between infusion and the onset of the reinforcing effects of cocaine. If this potential delay was considerably longer than 8 sec, it is not surprising that sign-tracking was not observed. Future research that systematically varies the intervals between lever retraction and infusion (perhaps even presenting the infusion before lever insertion) might shed light on this issue.

The results of the present study are surprising because experiments in which the conditioned place preference procedure has been employed have demonstrated that rats will come to approach distinctive contexts that are paired with cocaine (for a review, see Bardo, Rowlett, & Harris, 1995). In fact, Newlin (1992) has described conditioned place preference as "an awkward form of autoshaping," because, in both procedures, exteroceptive stimuli are paired with a response-independent appetitive CS and this pairing produces a skeletal CR that involves approach toward the reward-paired stimuli. However, despite these two similarities, there are vast differences between place conditioning and sign-tracking in terms of both the procedure used and the resultant behavior. As Newlin (1992) noted,

in place conditioning, the CS is diffuse (e.g., one compartment of a chamber that has distinctive visual, tactile, and perhaps olfactory characteristics), and CS durations are very long (often 20 min or more) as compared with most other Pavlovian procedures. In contrast, the CS used in sign-tracking studies is spatially and temporally discrete (e.g., lever presentation or keylight illumination lasts only several seconds). Moreover, in place conditioning, there are very few total trials and usually no more than 1 or 2 per day. In sign-tracking there are typically 25–50 trials presented within a session that lasts 1–2 h. There are also large differences in the behavior that is conditioned in the two procedures. In conditioned place preference, the rat simply comes to spend more time on one side of the chamber than on the other, and this difference in time spent is often subtle. In sign-tracking, on the other hand, the CS elicits vigorous and focused activity that often involves the animal's manipulating (e.g., biting, grasping, etc.) the CS in some way.

The *behavior systems* (Timberlake, 1983, 1994, 2001; Timberlake & Lucas, 1989) approach to learning and behavior may shed light on the differences observed between food and cocaine reported here. According to behavior systems theory, animals come equipped with repreexisting functional systems that direct different types of naturally occurring behavior. For example, there is a *feeding system* that is activated by food and food-related stimuli and controls feeding responses. There is a *defensive system* that is activated by threatening stimuli and includes *fight or flight* responses. These and other behavior systems have evolved to meet the specific biological needs of the organism. All learning occurs within the context of a particular behavior system that determines the speed of acquisition, relevant stimuli, the form of conditioned responding, and so on.

In sign-tracking in rats with food as the US, the food itself and the food-paired lever activate the feeding system. Because of the physical characteristics of the lever and the temporal proximity of lever insertion and food, the focal search and handle/consume modes of the feeding system control the rat's behavior. Ultimately, ingestive action patterns, such as licking, biting, and gnawing, are directed at the lever (Timberlake & Lucas, 1989). This same basic framework can be applied to instances of sign-tracking in rats in which the US was a liquid, including saccharine/ethanol or saccharine/amphetamine solutions (Krank, 2003; Tomie, 2001; Tomie, Festa, et al., 2003).

It is likely that sign-tracking reported with an ICS as the US involves the feeding behavior system as well. Peterson et al. (1972) implanted their electrodes in the lateral hypothalamus, which is well known to be intimately related to feeding behavior (Berridge & Valenstein, 1991; Hoebel & Teitelbaum, 1962; Margules & Olds, 1962). Wilkie and McDonald (1977) compared several different stimulation sites and found that the lateral hypothalamus was the most effective site for producing sign-tracking. Substantial levels of conditioned responding were also observed when electrodes were implanted in the raphe nucleus, the substantia nigra, or the amygdala. Research has shown that all of these areas are also related to feeding (raphe nucleus, Klitenick & Wirtshafter, 1989, Wirtshafter, 2001, and Wirtshafter & Krebs, 1990; substantia nigra, Parker, Inglis, & Winn, 1993, Winn, 1991, and Winn, Farrell, Maconick, & Robbins, 1983; amygdala, Montgomery & Singer, 1975, and White, 1973).

The behavior systems approach has also been applied to instances of sign-tracking involving USs not related to feeding or drinking. For example, Wasserman (1973) demonstrated that chicks placed in a cold environment would approach and peck a keylight that signaled the activation of a heat lamp. In contrast, the chicks would engage in sprawling and wing extension behavior during heat lamp activation. Timberlake and Lucas (1989), citing Hogan (1974), noted that in their natural environment, young chicks peck their mother hen to induce brooding, thereby receiving warmth. From this, it is inferred that a keylight paired with heat engages modules of the behavior system that guides that chick's interactions with its mother, whereas the heat lamp itself engages modules related to natural *sunning* behavior (i.e., sprawling and wing extension). The behavior systems theory has also been used to explain sign-tracking when a sexual reinforcer was the US (Domjan, 1994).

However, it is not clear what behavior system in the rat, if any, is activated by infusions of i.v. cocaine. Behavior systems are viewed as preorganized, functional systems of behavior that have evolved because they enable animals to adapt to their natural environment in ways that promote their survival and reproduction. Since it is doubtful that rats ingest cocaine in their natural environment, it is unlikely that there would be a behavior system that was evolved because it directs and guides behavior related to the procurement of cocaine. It is possible that cocaine activates components of multiple, and perhaps conflicting, behavior systems.

For example, it has been suggested that drugs of abuse have important effects on brain systems related to social behavior (Panksepp, Knutson, & Burgdorf, 2002). Cocaine may also activate components of the behavior systems related to avoidance behavior (e.g., the defensive system), since cocaine likely has aversive properties in addition to its reinforcing properties (Spealman, 1979). In an interesting demonstration of the conflicting approach and avoidance behaviors that cocaine can produce, Geist and Ettenberg (1997) reported that rats would alternately move toward and retreat from a goal box (in a runway design) where they received cocaine. Similar conflict behavior also appeared in rats that received both food and electric shock in the goal box. The simultaneous activation of incompatible behavior systems, or the failure to activate behavior systems that include approach and contact responses as important components, might underlie the failure to observe sign-tracking in rats when i.v. cocaine is the US.

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NOTES

1. Following convention, in the operant procedure the lever associated with the availability of cocaine is designated S+ instead of CS+, and the other lever is designated S−, rather than CS−.

2. We have replicated this result using a 5-sec delay between lever retraction and food delivery. After completing the training described in Experiment 2, the rats in the 0.125-mg/kg group were trained with a food US on the same procedure as that used for the food group in Experiment 1, with the exception that the food pellet was delivered 5 sec after the CS+ lever was retracted. The results were nearly indistinguishable from those presented in Figure 1—the rats came to contact the CS+ lever on over 90% of the trials, while only contacting the CS− lever on 10%–20% of the trials. Although the rats did not receive cocaine during this training, they were connected to the tether and infusion apparatus for the duration of each session, and their catheters were flushed daily. Thus, this experiment demonstrates that having surgery, being connected to the tether and infusion apparatus, and daily catheter flushing does not interfere with sign-tracking when food is the US, even under the more demanding conditions of a 5-sec delay between lever retraction and food delivery.

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