Behavioral Neuroscience
2009, Vol. 123, No. 1, 137–144

0735-7044/09/$12.00 DOI: 10.1037/a0013805

Posttrial Corticosterone Administration Enhances the Effects of Incentive Downshift: Exploring the Boundaries of This Effect

Eliana Ruetti, Nadia Justel, and Alba E. Mustaca
Universidad de Buenos Aires and CONICET

Mauricio R. Papini
Texas Christian University

Posttrial administration of corticosterone was previously shown to enhance consummatory successive negative contrast (cSNC) in rats. The present series of experiments provides additional information that helps determine the boundaries of this effect. Posttrial corticosterone administration (1) enhances cSNC when rats experience a large downshift (32% to 4% sucrose), but not after a small downshift (8% to 4% sucrose; Experiment 1); (2) has no effect in an anticipatory negative contrast situation in which 4% sucrose precedes 32% sucrose in daily trials (Experiment 2); (3) does not support the development of a conditioned taste aversion to 4% sucrose, in the absence of an incentive downshift (Experiment 3); and (4) facilitates the extinction of consummatory behavior (Experiment 4). These results suggest that corticosterone facilitates the encoding of an egocentric aversive memory of the incentive downshift experience.

Keywords: corticosterone, consummatory successive negative contrast, anticipatory negative contrast, consummatory extinction, egocentric memory

Available evidence suggests that corticosterone administration modulates memory consolidation of emotionally significant events (Cahill & Alkire, 2003; McGaugh, 2000). For example, posttrial corticosterone administration enhances object recognition in a novel environment (Okuda, Roozendaal, & McGaugh, 2004), a result implying that the effects of corticosterone on memory consolidation require both high hormonal levels and emotional activation induced by the novelty of the training situation. Similar effects were reported with human participants exposed to emotionally arousing versus neutral pictures (Buchanan & Lovallo, 2001; see also Cahill, Gorski, & Le, 2003). Surprising reward reductions are also emotionally arousing and have effects similar to those induced by the presentation of aversive events such as electric shock (Papini & Dudley, 1997). For example, consumption of a 4% sucrose solution is disrupted in rats with previous access to 32% sucrose, in comparison with rats that received access to only 4% sucrose. This effect, called *consummatory successive negative contrast* (cSNC), dissipates after two to three additional trials with the downshifted solution (Flaherty, 1996).

The cSNC requires a comparison between the current downshifted solution and the reactivated memory of the preshift solution. Such comparison induces an approach–avoidance conflict that results from the competing tendencies to approach the sipper tube and consume the downshifted solution because of the food deprivation state and to avoid the sipper tube because of anticipated emotional rejection of the downshifted solution. This conflict makes cSNC susceptible to anxiolytic drug treatment, but mainly during the second postshift trial (Flaherty, Grigson, & Rowan, 1986). Moreover, corticosterone levels are elevated both before and after the second postshift trial, but not before or after the first postshift trial (Flaherty, Becker, & Pohorecky, 1985; Mitchell & Flaherty, 1998). The present research adds to the issue of whether the downshift experience in the cSNC situation results in the encoding of a glucocorticoid-mediated emotional memory of the frustrative reaction (called an *egocentric memory*; Papini, 2003; Papini, Wood, Daniel, & Norris, 2006).

The posttrial drug administration procedure has been used by Salinas, Introini-Collison, Dalmaz, and McGaugh (1997) to answer a similar question in a related training preparation: instrumental SNC (iSNC). In iSNC, the organism's behavior is measured before reaching the incentive (Crespi, 1942; Elliott, 1928). For example, the speed of running in a straight alley deteriorates after an incentive downshift in relation to the running speed of unshifted controls. Such response deterioration suggests the antic-

Eliana Ruetti, Nadia Justel, and Alba E. Mustaca, Laboratorio de Psicología Experimental y Aplicada, Instituto de Investigaciones Médicas, UBA-CONICET, Buenos Aires, Argentina. Mauricio R. Papini, Department of Psychology, Texas Christian University.

All the experimental procedures were approved by the Institutional Animal Ethics Committee, University of Buenos Aires. The research reported here was funded by Grant PIP 5552/05 from CONICET, and by grants PICT 25335/04 and PICT 38020/05 from the Agencia de Promoción y Desarrollo, Secretaría de Ciencia y Técnica, Argentina. The authors thank Jacob Norris and Leo Ortega for helpful comments on an earlier version of this article.

Correspondence concerning this article should be addressed to Mauricio R. Papini, Department of Psychology, Texas Christian University, Box 298920, Fort Worth, TX 76129. E-mail: m.papini@tcu.edu

ipation of a frustrating outcome (i.e., egocentric memory) that induces avoidance of the goal area and hence running speed reduction. Administration of oxotremorine, a muscarinic receptor agonist, into the amygdala immediately after the first six-trial downshift session enhanced iSNC in subsequent sessions (Salinas et al., 1997). Similar effects were obtained with systemic administration of the $GABA_A$ agonist muscimol (Salinas & McGaugh, 1995). Interestingly, postsession systemic administration of 4-OH amphetamine, an adrenergic drug with limited capacity to cross the blood–brain barrier (i.e., having mainly a peripheral adrenergic effect) also enhanced iSNC (Salinas, Williams, & McGaugh, 1996). In the latter experiment, rats exposed to a single six-trial session of downshift received 4-OH amphetamine or saline immediately after this session, and were then left undisturbed for a 6-day retention interval. Retest with the downshifted magnitude indicated little evidence of behavioral disruption in the downshifted saline group (i.e., poor retention of the downshift memory), but significant retention of behavioral disruption in the group treated with the adrenergic drug. An interpretation of these findings suggests that the release of stress hormones strengthens memory consolidation of the downshift event (McGaugh, 2000).

Bentosela, Ruetti, Muzio, Mustaca, and Papini (2006) reported data consistent with this hypothesis in the cSNC situation. Administration of corticosterone (3 mg/kg, sc) immediately after the first downshift trial (but not 3 hr after) led to an increase in the size and duration of the cSNC effect. Thus, temporal contiguity between the downshift experience and corticosterone administration is necessary for peripheral glucocorticoids to influence cSNC. The present experiments were designed to characterize the limits of the enhancing effects of posttrial corticosterone administration on cSNC.

Experiment 1

High circulating levels of corticosterone during and immediately after an emotionally arousing event, but not after relatively neutral events, are known to modulate memory consolidation and retrieval (Buchanan & Lovallo, 2001; Cahill et al., 2003; Cahill, Prins, Weber, & McGaugh, 1994; Okuda et al., 2004).[1] The cSNC is known to depend on the size of the discrepancy between the preshift and postshift incentive magnitudes (Papini & Pellegrini, 2006). Thus, by reducing the magnitude of the preshift sucrose concentration, it is possible to obtain smaller levels of consummatory suppression, including levels that do not provide any evidence of cSNC. If posttrial corticosterone enhances the emotional egocentric memory of the downshift event, and not just the cognitive memory of the incentive change (called *allocentric memory*; Papini, 2003), then it should be more effective with large incentive discrepancies than with small incentive discrepancies. In this experiment, groups were downshifted from either 8% or 32% sucrose to 4% sucrose. Their performance was compared to that of 4% unshifted controls. Corticosterone or vehicle was administered immediately after the first postshift trial.

Method

Subjects. The subjects were 49 male, experimentally naive Wistar rats, about 3 months old at the start of the experiment. One week before the start of the experiment, animals were placed in individual cages with free access to water and food. The average ad libitum weight was 380 g (range: 292–539 g). The amount of food was gradually reduced across days until the animals reached 85% of their ad libitum weights. This level of deprivation was maintained throughout the duration of the experiment by posttraining supplementary food administered at least 20 min after the end of the daily trial. Animals were kept in a daily light–dark cycle of 12 hr (lights on at 07:00 hr). Training trials were conducted between 10:00 and 15:00 hr to avoid the peak of the circadian release of corticosterone, which occurs at the onset of the dark period (Romero, 2002). The housing and testing rooms were maintained at constant temperature (around 22°C) and humidity (around 60–70%).

Apparatus. Rats were trained in four conditioning boxes (MED Associates, Fairfax, VT). Each box measured 24.1 cm in length, 29.2 cm in width, and 21 cm in height. The floor was made of aluminum bars (0.4 cm in diameter, 1.1 cm apart from center to center). In the center of a lateral wall there was a 5-cm hole, 3.5 cm deep, 1 cm above the floor level, through which a sipper tube could be introduced from the outside. When fully inserted, the sipper tube protruded 2 cm into the box. A photocell was located just in front of the tip of the sipper tube, inside this hole. Goal-tracking time (measured in 0.01-s units) was automatically recorded by a computer that measured the cumulative amount of time that the photocell was activated during the trial. Each box was enclosed in a sound- and light-attenuating cubicle equipped with a source of white noise and diffuse house light.

Procedure. Rats were randomly assigned to one of six groups differing in terms of the incentive magnitude during the preshift trials (Trials 1–10; 32%, 8%, or 4% sucrose solutions) and the drug treatment received immediately after the first postshift trial (corticosterone vs. vehicle): 32/cort ($n = 9$), 8/cort ($n = 8$), 4/cort ($n = 7$), 32/veh ($n = 8$), 8/veh ($n = 9$), or 4/veh ($n = 8$). During postshift trials (Trials 11–15), all rats received access to 4% sucrose. On each trial, the sipper tube was manually introduced into the box before rats were placed in the conditioning box. Trials lasted 5 min starting from the first interruption of the photocell located by the sipper tube.

Sucrose solutions (in weight per volume) were prepared by mixing the appropriate quantity of commercial sugar (320, 80, or 40 g) in 1 L of tap water. Immediately after Trial 11, all rats were injected (sc) with either corticosterone (3 mg/kg, in a volume of 2 ml/kg) or an equal volume dose of the vehicle (5% ethanol in isotonic saline). To prepare corticosterone (from Sigma-Aldrich Laboratories, Saint Louis, MO), ethanol 100% was diluted in 0.9% isotonic saline to a 5% ethanol concentration; corticosterone was then diluted in this vehicle to the target dose.

The following features apply to all the experiments reported in this article. Animals were tested in squads of four. The order of the squads was randomized across days. Each box was swept with a damp towel after each training trial. Goal-tracking times (recorded in 0.01-s units) were subject to analysis of variance (ANOVA). Post hoc least-significant difference (LSD) pairwise comparisons of

[1] For brevity, only "consolidation" will be used in the rest of this article, although it is noted here that it is currently difficult to disentangle the contribution of corticosterone to memory consolidation versus retrieval.

selected trials were included when necessary to determine the source of interaction effects. The value of alpha was set at the 0.05 level.

Results

A Contrast (32%, 8%, or 4% sucrose) × Drug (cort or veh) × Trial (1–10) analysis of preshift performance indicated only that goal-tracking times increased significantly across trials, $F(9, 387) = 33.18$, $p < .001$. No other effects reached significance (Fs < 1.52, ps > 0.08). Figure 1 shows the performance of all groups during the last preshift trial (Trial 10) and during all postshift trials (Trials 11–15). For the vehicle-treated groups, the 8–4 downshift was somewhat weaker than the 32–4 downshift, although both effects were rather small in size in comparison with previous experiments (e.g., Bentosela et al., 2006). The relatively small size of the cSNC effect implies that there was ample room to detect corticosterone-induced suppression of consummatory behavior. This effect was clearly visible in the 32–4 condition, but not in the 8–4 condition.

To determine the effects of post-Trial 11 corticosterone administration on cSNC, each trial was separately subjected to a one-way analysis of variance followed by four pairwise comparisons calculated with the LSD test. Each pairwise comparison involved the downshifted versus unshifted groups for each drug treatment. Thus, for example, the group downshifted from 32% to 4% sucrose and given the corticosterone treatment was compared to the 4–4 unshifted control also given corticosterone. Because both groups in these pairwise comparisons received the same drug condition, comparing each downshifted group to its appropriate unshifted control allowed for an assessment of cSNC size independent of the effects of corticosterone (or saline) on consummatory behavior (see Wood, Daniel, & Papini, 2005). The group effect was nonsignificant for Trial 10 ($F < 1$), but it reached a significant level for each of the postshift trials, Fs$(5, 43) > 2.63$, ps < 0.04. As is shown in Figure 1, corticosterone administered after a 32–4 downshift prolonged the cSNC effect from one trial in the vehicle groups ($p < .05$) to all five trials in the drug groups (ps < 0.02). The cSNC effect was weaker in the 8–4 groups, being present before the drug treatment ($p < .04$), but not in the vehicle controls ($p > .27$). Despite the presence of cSNC, posttrial treatment with corticosterone had no appreciable effect on the consummatory performance in the 8–4 condition (ps > 0.49). Vehicle-treated animals in the 8–4 condition also failed to exhibit any indication of cSNC (ps > 0.24).

These results confirm those reported by Bentosela et al. (2006) and extend their findings by suggesting that post-Trial 11 corticosterone affects cSNC only when there is a substantial discrepancy between the pre- and postshift solution concentrations. The effect of corticosterone in this experiment was relatively large, resulting in no evidence of complete recovery of consummatory behavior in the four trials that followed. In addition, post-Trial 11 corticosterone does not seem to affect consummatory behavior in unshifted controls, as is indicated by a Group (4/cort, 4/veh) × Trial (11–15) analysis (all Fs < 1). Finally, there was no evidence that corticosterone would impair recovery from cSNC after a relatively mild incentive downshift from 8% to 4% sucrose. Interestingly, the lack of a corticosterone effect in the 8–4 downshift condition was observed despite the presence of significant consummatory suppression on Trial 11. These results suggest that corticosterone enhances cSNC only when the downshift (and presumably its aversiveness) is substantial.

Experiment 2

Several procedures have been used to study incentive contrast effects (Flaherty, 1996). Unlike in cSNC, in which there is a single

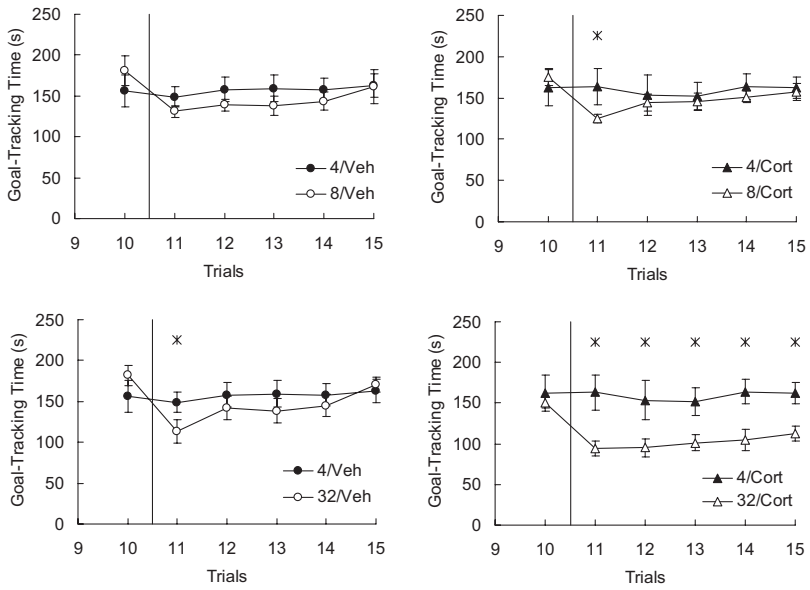

Figure 1. Results of Experiment 1. Goal-tracking times of independent groups of rats downshifted from 8% sucrose to 4% sucrose (top panels) or from 32% sucrose to 4% sucrose (bottom panels). The vertical line separates the last preshift trial (Trial 10) from the first postshift trial (Trial 11). Corticosterone (cort; 3 mg/kg, sc) or vehicle (veh; equal volume) was administered immediately after Trial 11. (Asterisks: $p < .05$; see text for details.)

transition from a large to a small incentive magnitude, in consummatory anticipatory negative contrast (cANC) each daily trial involves a magnitude transition. A trial contains two successive components separated by a brief midtrial interval. In the experimental group, animals have access to a small reward in the first component followed by access to a large reward in the second component. In the control group, animals have access to the small reward in both components. The cANC is observed in the first component (low incentive for both groups) when the performance of the experimental animals is significantly below that of the controls. Pharmacological manipulations suggest that cSNC and cANC depend on different underlying mechanisms (see Flaherty, 1996). For example, the benzodiazepine anxiolytic chlordiazepoxide (6, 12, and 20 mg/kg, ip), which reduces cSNC, has no effect on cANC (Flaherty & Rowan, 1988). On the basis of results like these, Flaherty (1996, p. 122) argued that cANC, unlike cSNC, "has nothing in common with animal models of anxiety." If posttrial corticosterone modulates performance in situations involving incentive shifts independently of the nature of the change, then it should also enhance cANC. No effects of posttrial corticosterone would be consistent with the hypothesis that this treatment modulates the consolidation of an egocentric memory of the successive downshift experience.

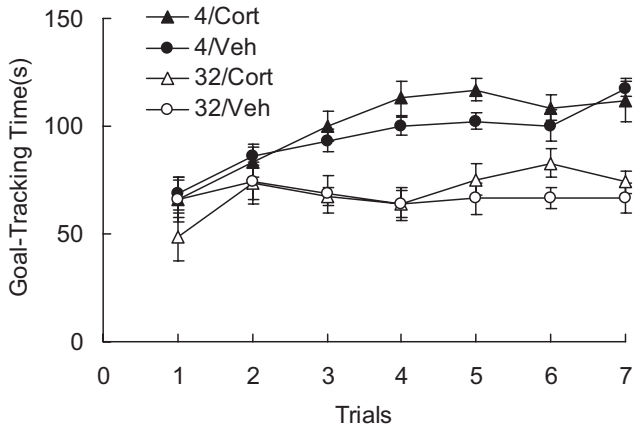

Figure 2. Results of Experiment 2. Goal-tracking times of rats trained in an anticipatory negative contrast situation with two daily components. In the first component (shown here), all rats had access to 4% sucrose. In the second component (not shown here), rats in different groups had access either to the same 4% sucrose or to 32% sucrose in independent groups. Group labels refer to the sucrose concentration received in the second component, either 4% or 32% sucrose. Corticosterone (cort; 3 mg/kg, sc) or vehicle (veh; equal volume) was administered immediately after the second component of the first training trial.

Method

Subjects and apparatus. The subjects were 38 male, experimentally naïve Wistar rats, about 3 months old at the start of the experiment. The mean weight for the entire sample was 416 g (range: 340–548 g). Other maintenance conditions, daily training times, and the conditioning boxes were as described for Experiment 1.

Procedure. The training consisted of seven daily trials in which rats had access to two solutions in a sequence. For all the rats, the first solution was 4% sucrose. This component lasted 3 min, counting after the first interruption of the photocell. The second component of the trial started after a midtrial interval of approximately 20 s. Animals were randomly assigned to one of four groups. Two groups received access to 32% sucrose: 32/cort ($n = 9$), 32/veh ($n = 10$), whereas two groups received access to 4% sucrose: 4/cort ($n = 9$), and 4/veh ($n = 10$). The second trial component also lasted 3 min, starting with the first interruption of the photocell. The main dependent measure was the goal-tracking time (recorded as is described for Experiment 1) during the first trial component, which involved access to 4% sucrose for all the groups. Immediately after the second component of the first trial, animals were administered either corticosterone (3 mg/kg, sc, in Groups 32/cort and 4/cort) or the vehicle (in Groups 32/veh and 4/veh). Drugs and sucrose solutions were prepared and administered as they are described for Experiment 1.

Results

Figure 2 shows the results of this experiment. A cANC effect rapidly developed over trials. Goal-tracking times for 4% sucrose were considerably lower during the first component of the task in animals exposed to 32% sucrose in the second component than in animals exposed to 4% sucrose again. However, post-Trial 1 corticosterone administration had no detectable effect on the development of this cANC effect. A Contrast (32% or 4% sucrose) × Drug (corticosterone or vehicle) analysis of Trial 1 scores indicated nonsignificant effects (Fs < 1.14, ps > 0.29). Thus, groups were matched before the treatment. A Contrast × Drug × Trial (2–7) for the trials following the posttrial treatment indicated a significant contrast by trial interaction, $F(5, 170) = 5.29$, $p < .001$, and significant main effects for contrast, $F(1, 34) = 48.09$, $p < .001$, and trial, $F(5, 170) = 3.65$, $p < .005$. None of the factors involving the drug treatment approached significance (Fs < 1.12, ps > 0.25). Importantly, the cANC effect was not evident in Trial 2 (Contrast × Drug: Fs < 1.94, ps > 0.17), a fact that provided a fertile ground for detecting any enhancing effect of posttrial corticosterone on goal-tracking time. The results of Experiment 2 suggest that corticosterone modulates the aversive memory of the downshift experience rather than memories associated with reward shifts in general.

Experiment 3

The posttrial injection procedure used in these and previous experiments (Bentosela et al., 2006) is essentially identical to the procedure used to induce conditioned taste aversions. In a typical taste aversion experiment, access to a taste solution (the conditioned stimulus, or CS) for a short period is immediately followed by the administration of a drug that causes an aversive effect (the unconditioned stimulus, or US). Aversive effects can be induced by a variety of drug USs, including lithium chloride (e.g., St. Andre, Albanos, & Reilly, 2007), opioid peptides (Wood, Norris, Daniel, & Papini, 2008), and nicotine (Iwamoto & Williamson, 1984), among others. Whereas there apparently is no available evidence that corticosterone induces taste aversion, the present experiment tested this potential confound. The rationale for this effect is as follows.

In a cSNC experiment, the downshifted solution (say 4% sucrose) has relatively more novelty for the downshifted animals than for the unshifted controls, which have tasted 4% during preshift trials. Experiments suggest that relative CS novelty is an important determinant of the ability of an animal to develop a taste aversion (Cannon, Best, & Batson, 1983). Extensively preexposed CSs exhibit a retardation of taste aversion acquisition, a phenomenon known as latent inhibition (Lubow, 1989). Thus, the enhancement of cSNC observed after post-Trial 11 administration of corticosterone could be related to the relative novelty of the 4% sucrose that could support a conditioned taste aversion rather than to the aversive emotional consequences of the incentive downshift experience. The development of such aversion would be impaired or retarded in the unshifted controls because of latent inhibition.

This hypothesis was tested in a two-group design with matched access to sucrose and drug administration across groups. Previous research shows that the administration of corticosterone after Trial 11 is ineffective if given 3 hr after the end of the trial rather than immediately (Bentosela et al., 2006). Therefore, a 3-hr interval was used to generate an unpaired condition. Matching exposure to the US across both paired and unpaired groups maximizes control for nonassociative factors (Daniel, Ortega, & Papini, 2008). Moreover, to control for the timing of the injection procedure in relation to the tasting of the sucrose solution, all animals were injected twice: immediately after the trial and 3 hr after the trial.

Method

Subjects and apparatus. The subjects were 16 male, experimentally naïve Wistar rats, about 3 months old at the start of the experiment. The mean weight for the entire sample was 432.7 g (range: 366–515 g). Other maintenance conditions, daily training times, and the conditioning boxes were as described for Experiment 1.

Procedure. Animals were randomly assigned to two groups ($n = 8$): paired and unpaired. On Trial 1, rats received access to 4% sucrose for 5 min, starting after the first interruption of the photocell. Immediately after the trial ended, all rats were injected with either corticosterone (3 mg/kg, sc) or the vehicle. To control for nonspecific effects of drug administration, both groups received a second injection 3 hr after the end of Trial 1. For the paired group, the second injection was the vehicle, whereas for the unpaired group, the second injection was corticosterone. Thus, the number of injections, their distribution in time relative to the training trial, and the administration of corticosterone or vehicle were equated across groups. A day later, animals were tested again in a 5-min trial of access to 4% sucrose. All other training parameters were as described for Experiment 1.

Results

Figure 3 shows the performance of the two groups in the two trials of this experiment, as a function of pairing condition. No differences were observed among the groups during both trials. Moreover, both paired and unpaired groups exhibited an increase of goal-tracking time on Trial 2, inrelation to Trial 1, suggesting that corticosterone generated no detectable taste aversion to the solution. A one-way analysis on Trial 1 scores indicated nonsignificant differences ($F < 1$). Similarly, a one-way analysis of Trial 2 performance, after the posttrial treatment a day earlier, also indicated no detectable group differences ($F < 1$). To control for possible individual differences on initial consummatory performance, we analyzed the results obtained on Trial 2 using the scores of Trial 1 as a covariate. Such analysis also failed to uncover group differences among the paired and unpaired conditions, $F(1, 15), = 2.03$, $p > .17$. Thus, there was no evidence supporting the hypothesis that posttrial corticosterone administration reduces consummatory behavior in the absence of a downshift event.

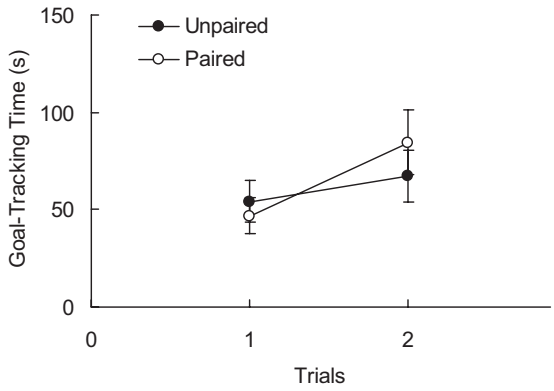

Figure 3. Results of Experiment 3. Goal-tracking times of rats exposed to two 5-min trials of access to 4% sucrose. After the first trial, all rats received two injections, one immediately after the trial and the second 3 hr later. In the paired group, the immediate injection was corticosterone, whereas the 3-hr injection was the vehicle. In the unpaired group, the immediate injection was the vehicle, whereas the 3-hr injection was corticosterone. Both groups were treated identically, except for the temporal contiguity between sucrose and corticosterone (3 mg/kg, sc). In the second trial, a day later, all rats received access to 4% sucrose for 5 min; no injections were administered.

Experiment 4

Consummatory extinction (cE) offers an alternative task to cSNC that should respond to the posttrial corticosterone treatment in much the same way. In cE, rats that had access to sucrose are eventually downshifted to an empty sipper tube. The behavior typically drops abruptly and then exhibits extinction (Mustaca, Freidin, & Papini, 2002). Appetitive extinction and SNC share some general behavioral and pharmacological properties. Instrumental appetitive extinction is also known to lead to increased plasma levels of stress hormones, including corticosterone, cortisol, and ACTH (e.g., Davis, Memmott, MacFadden, & Levine, 1976; Lyons, Fong, Schrieken, & Levine, 2000), whereas exogenous corticosterone facilitates extinction (Tomie, Tirado, Yu, & Pohorecky, 2004). Although nothing is known about endogenous levels of corticosterone during cE, such levels are elevated during cSNC (Flaherty et al., 1985; Mitchell & Flaherty, 1998). The cE is associated with a reduction in aggressive behavior during social interactions in male rats (Mustaca, Martinez, & Papini, 2000); similar changes were also reported in cSNC (Mustaca & Martinez, 2000). The cE and cSNC are also modulated in similar fashion by a variety of pretrial drug manipulations. For example, pretrial treatment with the opioid receptor antagonist naloxone (2 mg/kg, ip) enhances cE (Norris, Daniel, & Papini, in press) and cSNC

(Pellegrini, Wood, Daniel, & Papini, 2005), whereas benzodiazepine anxiolytics (e.g., diazepam, chlordiazepoxide, and lorazepam) attenuate both cE (Bialik, Pappas, & Pusztay, 1982; Flaherty, 1990; Soubrie, Thiebot, Simon, & Boissier, 1978; but see Miczek & Lau, 1975) and cSNC (e.g., Mustaca, Bentosela, & Papini, 2000; see Flaherty, 1990, for further evidence). Together, these results suggest that the emotional processes underlying cE and cSNC engage similar neurochemical changes. Here, the same posttrial corticosterone treatment shown to modulate cSNC was applied to cE.

Method

Subjects and apparatus. The subjects were 19 male Wistar rats, approximately 3.5 months old at the start of the experiment. These animals had participated in a previous experiment on cANC involving the consummatory procedure analogous to that described in Experiment 2. The mean weight for the entire sample was 487 g (range: 410–591 g). Other maintenance conditions, daily training times, and the conditioning boxes were as described for Experiment 1.

Procedure. Groups were matched in terms of prior experience. This experiment lasted nine daily trials. In the acquisition phase (Trials 1–5), all animals received 5-min trials of access to 4% sucrose, starting with the first interruption of the photocell. In the extinction phase (Trials 6–9), animals had access to the same sipper tube, but the bottle was empty. Immediately after the first extinction trial, rats in the corticosterone group ($n = 9$) were injected with corticosterone (3 mg/kg, sc), whereas rats in the vehicle group ($n = 10$) received an equal-volume injection of the vehicle. Drug and sucrose preparation were as described as for Experiment 1. To allow for within-trial analysis of behavior, goal-tracking times were recorded in 1-min bins.

Results

A Drug (corticosterone or vehicle) × Trial (1–5) analysis of acquisition scores indicated a significant trial effect, $F(4, 68) = 5.76$, $p < .001$, but nonsignificant drug or interaction effects (Fs < 1). The extinction performance is presented in Figure 4 as a function of 1-min bins, for each extinction session. On Trial 6, before the posttrial corticosterone treatment, the performance of both groups was very similar. A Drug × Bin analysis indicated a significant within-trial decrease in goal-tracking times, $F(4, 68) = 6.75$, $p < .001$, but nonsignificant drug or interaction effects (Fs < 1). Thus, groups were behaviorally matched before the posttrial treatment.

A Drug × Trial (7–9) × Bin analysis of the last three trials indicated a significant drug by bin interaction, $F(4, 136) = 4.01$, $p < .007$. None of the other effects reached a significant level (Fs < 2.58, ps > 0.06; the closest to a significant level was the within-trial effect, $p < .062$). One-way analyses for each bin, on Trials 7–9, indicated significantly lower extinction performance in the corticosterone group than in the vehicle group on the second bin of Trial 7 and the fourth bin of Trial 9. Although this effect was relatively small, it was in the expected direction.

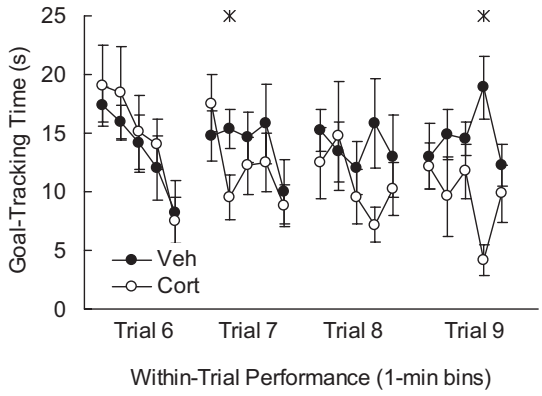

Figure 4. Results of Experiment 4. Within-trial goal-tracking times during consummatory extinction trials with an empty tube after training with 4% sucrose. The critical treatment involved the administration of corticosterone (cort; 3 mg/kg, sc) or the vehicle (veh; equal volume) immediately after the end of the first extinction trial. (Asterisks: $p < .05$; see text for details.)

General Discussion

Previous research had shown that the administration of corticosterone immediately after the first downshift event facilitated the cSNC effect, retarding the recovery of consummatory behavior to normal levels (Bentosela et al., 2006). That report also showed that this effect failed to occur when corticosterone was administered 3 hr after the end of the first downshift trial. The present series of experiments extended the conditions of this effect of posttrial corticosterone on cSNC, providing insights into its boundaries. This effect failed to occur when the incentive discrepancy was relatively small (Experiment 1); when the incentive downshift occurred in an anticipatory, rather than successive, incentive contrast situation (Experiment 2); and when rats were exposed to the sucrose solution in the absence of a downshift experience (Experiment 3). Furthermore, albeit relatively weak, there was also evidence that posttrial corticosterone enhanced the extinction of consummatory behavior, an effect analogous to that observed in the cSNC situation (Experiment 4). Together, the effects reported here and in a previous report (Bentosela et al., 2006) suggest several working hypotheses.

The first hypothesis strengthened by these results is that posttrial corticosterone facilitates the consolidation of an egocentric emotional memory of the downshift event experienced for the first time on the initial postshift trial. This conclusion is consistent with a large literature on the effects of posttrial glucocorticoid administration on memory consolidation in both aversive and appetitive tasks (McGaugh, 2000; Roozendaal, 2000). For example, intracerebroventricular pretrial administration of RU38486, a corticosteroid-receptor antagonist, impaired 24-hr retention of fear conditioning, whereas systemic posttrial administration of corticosterone (5 mg/kg, ip) enhanced retention of the same task at both 2- and 7-day retention intervals (Cordero & Sandi, 1998). In the present Experiment 1, the enhancing effects of posttrial corticosterone on cSNC were observed up to 4 days after the single injection. It remains to be determined whether a similar corticosterone treatment would enhance cSNC after a retention interval interpolated between Trials 11 and 12, a procedure that would be analogous to that used by Cordero and Sandi (1998) in fear conditioning. Such a result would strengthen the hypothesis that an egocentric memory of the downshift experience is indeed established during Trial 11.

The second hypothesis consistent with the present results maintains that the facilitatory effect of glucocorticoids on memory consolidation requires a minimum amount of emotional arousal. Okuda et al. (2004) tested this hypothesis in an object-recognition task with rats. Levels of emotional arousal were manipulated by differential preexposure to the to-be training context. Thus, rats habituated to the training context (and thus theoretically experiencing lower levels of novelty-induced emotional arousal) did not benefit from a posttrial corticosterone (0.3–3.0 mg/kg, sc) administration treatment, whereas nonhabituated rats exhibited enhanced retention of object recognition. Experiment 1 provided results that parallel these findings. In the present experiment, posttrial corticosterone facilitated cSNC when rats were exposed to a 32–4 discrepancy, but not when exposed to an 8–4 discrepancy between pre- and postshift sucrose concentrations. The level of consummatory suppression after an incentive downshift operation is known to depend on the ratio of the postshift-to-preshift sucrose concentrations (Papini & Pellegrini, 2006): The smaller the ratio, the stronger the consummatory suppression. In Experiment 1, the two ratios in question were 0.125 (for the 32–4 downshift) and 0.5 (for the 8–4 downshift). Assuming that the reduction in consummatory suppression resulting from a fourfold increase in the size of this ratio reflects a reduction in the aversiveness of the downshift, then the present results are consistent with the hypothesis that posttrial corticosterone acts predominantly when the situation induces a minimum amount of emotional arousal.

This conclusion is also consistent with the lack of effect of posttrial corticosterone on cANC, as studied in Experiment 2. As is mentioned above, there is no evidence that cANC is vulnerable to anxiolytic treatments that have been effective in reducing cSNC (Flaherty & Rowan, 1988). Additionally, posttrial drug administration in appetitive tasks is open to the potential development of taste aversion to the incentive. In a typical conditioned taste aversion experiment, access to a sweet solution (e.g., sucrose, or saccharin) is paired with drug-induced aversive posteffects (e.g., lithium-chloride-induced gastrointestinal sickness). Clinical observations in humans suggest that corticosterone can lead to aversive posteffects, including increased irritability and depression, but experimental research with rats does not support this conclusion (see Dietz, Wang, & Kabbaj, 2007). Still, it is possible that failures to produce aversive effects, such as conditioned place preferences, may depend on the use of relatively insensitive dependent variables or tasks. Experiment 3 tested this possibility by replicating the conditions of the first postshift trial in the absence of a downshift event to determine whether the increased consummatory suppression observed in the cSNC situation could be attributed to the development of an aversion for the consumption of sucrose. The data failed to confirm such a result. The results also failed to find an enhancement of sucrose consumption, a result that might be expected on the basis of reports showing the incentive properties of corticosterone self-administration (Deroche, Piazza, Deminiere, Le Moal, & Simon, 1993).

Together, the results of the present and previous experiments on the effects of posttrial administration on cSNC suggest that corticosterone enhances the consolidation or retrieval of an egocentric memory of the downshift experience in the cSNC situation. The next task is to determine what additional systems participate in the encoding of such a memory. As is mentioned at the beginning of this article, iSNC is enhanced by administration of oxotremorine, a muscarinic receptor agonist, into the amygdala immediately after the first downshift session (Salinas et al., 1997). Findings such as these (see the beginning of this article for further references) suggest that stress hormones may strengthen the egocentric memory of the incentive downshift in the iSNC situation. Furthermore, the amygdala appears to be a critical brain location mediating the effects of glucocorticoids on memory. Noradrenergic activation of the basolateral nucleus of the amygdala enhances the effects of systemic adrenaline and glucocorticoids on aversive memory. For example, intraamygdala administration of atenolol, a β_1-adrenoreceptor antagonist, had no effect on the retention of fear conditioning, but it blocked the facilitatory effect of corticosterone on memory consolidation for that task (Roozendaal, Hui, Hui, Berlau, McGaugh, & Weinberger, 2006). Because the basolateral nucleus of the amygdala has also been shown to be important for cSNC (Becker, Jarvis, Wagner, & Flaherty, 1984), it seems plausible that the effects of corticosterone reported here and previously (Bentosela et al., 2006) may be mediated by noradrenergic activity in the amygdala.

References

Becker, H. C., Jarvis, M. F., Wagner, G. C., & Flaherty, C. F. (1984). Medial and lateral amygdalectomy differentially influences consummatory negative contrast. *Physiology & Behavior, 33,* 707–712.

Bentosela, M., Ruetti, E., Muzio, R. N., Mustaca, A. E., & Papini, M. R. (2006). Administration of corticosterone after the first downshift trial enhances consummatory successive negative contrast. *Behavioral Neuroscience, 120,* 371–376.

Bialik, R. J., Pappas, B. A., & Pusztay, W. (1982). Chlordiazepoxide-induced released responding in extinction and punishment-conflict procedures is not altered by neonatal forebrain norepinephrine depletion. *Pharmacology, Biochemistry & Behavior, 16,* 279–283.

Buchanan, T., & Lovallo, L. (2001). Enhanced memory for emotional material following stress-level cortisol treatment in humans. *Psychoneuroendocrinology, 26,* 207–217.

Cahill, L., & Alkire, M. (2003). Epinephrine enhancement of human memory consolidation: Interaction with arousal at encoding. *Neurobiology of Learning and Memory, 79,* 194–198.

Cahill, L., Gorski, L., & Le, K. (2003). Enhanced human memory consolidation with post-learning stress: Interaction with the degree of arousal at encoding. *Learning & Memory, 10,* 270–274.

Cahill, L., Prins, B., Weber, M., & McGaugh, J. L. (1994). B-Adrenergic activation and memory for emotional events. *Nature, 371,* 702–704.

Cannon, D. S., Best, M. R., & Batson, J. D. (1983). Taste familiarity and apomorphine-induced taste aversion. *Behavior Research & Therapy, 21,* 669–673.

Cordero, M. I., & Sandi, C. (1998). A role for brain glucocorticoid receptors in contextual fear conditioning: Dependence upon training intensity. *Brain Research, 786,* 11–17.

Crespi, L. (1942). Quantitative variation in incentive contrast studies involving discrete-trial procedures. *American Journal of Psychology, 55,* 467–517.

Daniel, A. M., Ortega, L. A., & Papini, M. R. (2008). *Naloxone fails to support conditioned taste aversion in rats (with methodological implications for demonstrations of conditioned taste aversion).* Manuscript submitted for publication.

Davis, H., Memmott, J., MacFadden, L., & Levine, S. (1976). Pituitary-adrenal activity under different appetitive extinction procedures. *Physiological Behavior, 17,* 687–690.

Deroche, V., Piazza, P. V., Deminiere, J.-M., Le Moal, M., & Simon, H. (1993). Rats orally self-administer corticosterone. *Brain Research, 622,* 315–320.

Dietz, D., Wang, H., & Kabbaj, M. (2007). Corticosterone fails to produce conditioned place preference or conditioned place aversion in rats. *Behavioural Brain Research, 181,* 287–291.

Elliott, M. (1928). The effect of change of reward on the maze performance of rats. *University of California Publications in Psychology, 4,* 19–30.

Flaherty, C. F. (1990). Effect of anxiolytics and antidepressants on extinction and negative contrast. *Pharmacology & Therapeutics, 46,* 309–320.

Flaherty, C. F. (1996). *Incentive relativity.* Cambridge, U. K.: Cambridge University Press.

Flaherty, C. F., Becker, H. C., & Pohorecky, L. (1985). Correlation of corticosterone elevation and negative contrast varies as a function of postshift day. *Animal Learning & Behavior, 13,* 309–314.

Flaherty, C. F., Grigson, P. S., & Rowan, G. A. (1986). Chlordiazepoxide and the determinants of negative contrast. *Animal Learning & Behavior, 14,* 315–321.

Flaherty, C. F., & Rowan, G. A. (1988). Effect of intersolution interval, chlordiazepoxide, and amphetamine on anticipatory contrast. *Animal Learning & Behavior, 16,* 47–52.

Iwamoto, E. T., & Williamson, E. C. (1984). Nicotine-induced taste aversion: Characterization and preexposure effects in rats. *Pharmacology Biochemistry & Behavior, 21,* 527–532.

Lubow, R. E. (1989). *Latent inhibition and conditioned attention theory.* Cambridge, U. K.: Cambridge University Press.

Lyons, D., Fong, K., Schrieken, N., & Levine, S. (2000). Frustative nonreward and pituitary-adrenal activity in squirrel monkeys. *Physiology & Behavior, 71,* 559–563.

McGaugh, J. L. (2000). Memory—A century of consolidation. *Science, 287,* 248–251.

Miczek, A., & Lau, P. (1975). Effects of scopolamine, physostigmine and chlordiazepoxide on punished and extinguished water consumption in rats. *Psychopharmacology, 42,* 263–269.

Mitchell, C., & Flaherty, C. F. (1998). Temporal dynamics of corticosterone elevation in successive negative contrast. *Physiology & Behavior, 64,* 287–292.

Mustaca, A. E., Bentosela, M., & Papini, M. R. (2000). Consummatory successive negative contrast in mice. *Learning and Motivation, 31,* 272–282.

Mustaca, A. E., Freidin, E., & Papini, M. R. (2002). Extinction of consummatory behavior in rats. *International Journal of Comparative Psychology, 1,* 1–10.

Mustaca, A. E., & Martínez, C. (2000). Respuestas agonísticas en ratas sometidas a frustración. *Revista Latinoamericana de Psicología, 32,* 485–504.

Mustaca, A. E., Martínez, C., & Papini, M. R. (2000). Surprising nonreward reduces aggressive behavior in rats. *International Journal of Comparative Psychology, 13,* 91–100.

Norris, J. N., Daniel, A. M., & Papini, M. R. (in press). Spontaneous recovery of consummatory behavior, but not of consummatory successive negative contrast. *Learning & Motivation.*

Okuda, S., Roozendaal, B., & McGaugh, J. L. (2004). Glucocorticoid effects on object recognition memory require training-associated emotional arousal. *Proceedings of the National Academy of Sciences, USA, 101,* 853–858.

Papini, M. R. (2003). Comparative psychology of surprising nonreward. *Brain, Behavior and Evolution, 62,* 83–95.

Papini, M. R., & Dudley, R. T. (1997). Consequences of surprising reward omissions. *Review of General Psychology, 3,* 275–285.

Papini, M. R., & Pellegrini, S. (2006). Scaling relative incentive value in consummatory behavior. *Learning and Motivation, 37,* 357–378.

Papini, M. R., Wood, M., Daniel, A. M., & Norris, J. N. (2006). Reward loss as psychological pain. *International Journal of Psychology and Psychological Therapy, 6,* 189–213.

Pellegrini, S., Wood, M., Daniel, A. M., & Papini, M. R. (2005). Opioid receptors modulate recovery from consummatory successive negative contrast. *Behavioural Brain Research, 164,* 239–249.

Romero, L. M. (2002). Seasonal changes in plasma glucocorticoid concentrations in free-living vertebrates. *General and Comparative Endocrinology, 128,* 1–24.

Roozendaal, B. (2000). Glucocorticoids and the regulation of memory consolidation. *Psychoneuroendocrinology, 25,* 213–238.

Roozendaal, B., Hui, G. K., Hui, I. R., Berlau, D. J., McGaugh, J. L., & Weinberger, N. M. (2006). Basolateral amygdala noradrenergic activity mediates corticosterone-induced enhancement of auditory fear conditioning. *Neurobiology of Learning and Memory, 86,* 249–255.

Salinas, J., Introini-Collison, I., Dalmaz, C., & McGaugh, J. L. (1997). Posttraining intraamygdala infusions of oxotremorine and propanolol modulate storage of memory for reductions in reward magnitude. *Neurobiology of Learning and Memory, 68,* 51–59.

Salinas, J., & McGaugh, J. L. (1995). Muscimol induces retrograde amnesia for changes in reward magnitude. *Neurobiology of Learning and Memory, 63,* 277–285.

Salinas, J., Williams, C., & McGaugh, J. L. (1996). Peripheral post-training administration of 4-OH amphetamine enhances retention of a reduction in reward magnitude. *Neurobiology of Learning and Memory, 65,* 192–195.

Soubrie, P., Thiebot, P., Simon, P., & Boissier, J. R. (1978). Benzodiazepines and behavioral effects of reward (water) omission in the rat. *Psychopharmacology, 59,* 95–100.

St. Andre, J., Albanos, K., & Reilly, S. (2007). c-Fos expression in the rat brain following lithium chloride-induced illness. *Brain Research, 1135,* 122–128.

Tomie, A., Tirado, A., Yu, L., & Pohorecky, L. (2004). Pavlovian autoshaping procedures increase plasma corticosterone and levels of norepinephrine and serotonin in prefrontal cortex in rats. *Behavioral Brain Research, 153,* 97–105.

Wood, M., Daniel, A. M., & Papini, M. R. (2005). Selective effects of the δ-opioid receptor agonist DPDPE on consummatory successive negative contrast. *Behavioral Neuroscience, 119,* 446–454.

Wood, M., Norris, J. N., Daniel, A. M., & Papini, M. R. (2008). Trial-selective effects of U50,488H, a κ-opioid receptor agonist, on consummatory successive negative contrast. *Behavioural Brain Research, 193,* 28–36.

Received April 8, 2008
Revision received July 21, 2008
Accepted July 24, 2008 ■