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Impairment of Recovery From Incentive Downshift After Lesions of the Anterior Cingulate Cortex: Emotional or Cognitive Deficits?

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The anterior cinculate cortex (ACC) is known to be implicated in pain-fear and reward expectations. Animals were given electrolytic lesions of the ACC and then trained in the consummatory successive negative contrast (cSNC) situation. In cSNC, animals exposed to an incentive downshift from 32% to 4% sucrose exhibit less consummatory behavior than animals always exposed to 4% sucrose. The ACC lesion had no measurable effects on the consummatory performance of animals before the downshift (i.e., the lesion did not affect consumption of 32% vs. 4% sucrose); on the performance of unshifted, 4% sucrose animals; and on the first downshift trial. However, ACC animals exhibited a significant retardation of recovery from cSNC relative to downshifted shams. Within-trial analysis of consummatory behavior indicated that ACC lesions facilitated cSNC during both the initial and last 100 s of postshift trials after the first downshift experience, relative to sham controls. These results suggest that the ACC is part of the neural circuit normally involved in coping with the emotional response induced by the incentive downshift event by inducing learning of the new incentive conditions.

Keywords: anterior cingulate cortex, incentive contrast, psychological pain

An unexpected downshift in the magnitude or quality of an incentive triggers a series of behavioral and physiological changes (Papini & Dudley, 1997). In the consummatory successive negative contrast (cSNC) situation used in the present experiment (see Flaherty, 1996), rats exposed to 32% sucrose solution during several daily trials subsequently consume less of 4% sucrose than rats always exposed to 4% sucrose. Relatively little is known about the neural circuit engaged during an episode of unexpected incentive downshift. cSNC offers the relative advantage that the neural circuits underlying taste processing and the licking response in the rat are relatively well-understood (e.g., Hajnal & Norgren, 2005; Jones, Fontanini, & Katz, 2006; Tabuchi et al., 2002; Travers, Dinardo, & Karimnamazi, 1997). Thus, cSNC can be understood as telencephalic regulation of the taste-licking, brainstem-based circuit (Pecoraro & Dallman, 2005).

Lesion studies suggest some key areas, as well as discard others. For example, from caudal to rostral locations, lesions of the parabrachial nucleus (Grigson, Spector, & Norgren, 1994), gustatory thalamus (Reilly & Trifunovic, 1999), central nucleus of the amygdala (Becker, Jarvis, Wagner, & Flaherty, 1984), and insular cortex (Lin, Roman, & Reilly, 2009) have all been shown to impair the cSNC effect in rats. Although the results of these studies are not identical, they are similar in that the lesion affected both the initial response to the downshift and the subsequent recovery of consummatory behavior. Pecoraro, de Jong, Ginsberg, and Dallman (2008) reported that rats with excitotoxic lesions of the medial prefrontal cortext (mPFC) behave similarly to sham controls in the first downshift trial, but exhibited faster recovery of consummatory behavior in subsequent trials. However, because unshifted controls were not included, it remains to be determined whether this result was specific to the downshift operation or more generally related to consumption of the 4% sucrose solution. The present study involves lesions of yet another cortical area: the anterior cingulate cortex (ACC).

There are at least three reasons to predict that the ACC would be involved in cSNC. First, ACC lesions (by aspiration) reduce instrumental SNC (iSNC) in a runway situation (Gurowitz, Rosen, & Tessel, 1970). In iSNC, the effects of the unexpected incentive downshift are assessed in terms of anticipatory behavior, that is, behavior displayed before the animal consumes the incentive. This result by itself does not allow for an accurate prediction for the cSNC situation because these two contrast paradigms often respond differently to the same lesion (e.g., hippocampus: Flaherty, Coppotelli, Hsu, & Otto, 1998; nucleus accumbens: Leszczuk & Flaherty, 2000; gustatory thalamus: Sastre & Reilly, 2006). For example, lesions of the nucleus accumbens eliminate iSNC in the runway, but spare cSNC.

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Second, Pecoraro and Dallman (2005) reported widespread brain activation during the first downshift trial using a c-Fos-like immunoreactivity assay. The areas activated have also been implicated in cSNC by lesion studies (see above), including the medial prefrontal cortex, insular cortex, lateral amygdala, gustatory thalamus, and parabrachial nucleus. This study also confirmed the role of areas involved in gustatory processing, such as the lateral hypothalamus and the nucleus of the solitary tract (Hajnal & Norgren, 2005; Jones et al., 2006; Tabuchi et al., 2002). However, c-Fos activation does not always coincide with the results of lesion studies. For example, the nucleus accumbens was activated after the first downshift trial (Pecoraro & Dallman, 2005), but lesions studies reported no detectable effects on cSNC (Leszczuk & Flaherty, 2000), and brain dialysis shows an actual reduction in dopamine efflux in neurons from the nucleus accumbens during the first downshift trial (Genn, Ahn, & Phillips, 2004). The c-Fos study also identified the ACC, as well as a host of other cortical regions (including the orbital cortex, various sensory areas, and the claustrum), as significantly active after the first downshift trial.

Third, Gray (1982) proposed that similar neural circuits are involved in conditioned fear (as in avoidance learning) and conditioned frustration (as in the SNC effect), and Papini (2003) suggested that their respective unconditioned states, peripheral pain and primary frustration, could also be linked. These links have suggested a common neural circuit for the type of pain that originates from tissue damage (physical pain) and from an experience of incentive loss (psychological pain) or social exclusion (social pain) (Eisenberger & Lieberman, 2004; Papini, Wood, Daniel, & Norris, 2006). One implication of this hypothesis is that physical pain and frustration should interact, as indeed is the case (Mustaca & Papini, 2005; Ortega, Daniel, Davis, Fuchs, & Papini, 2011). For example, formalin-induced peripheral pain enhances cSNC (Ortega et al., 2011). A second implication of this hypothesis is that the pharmacology of physical and psychological pains should overlap, as it is the case with opioids (Papini, 2009). A third implication of this hypothesis, and the one tested in this experiment, is that physical and psychological pain should engage similar brain structures. Because the ACC is associated with some forms of physical pain, then it was predicted that its damage should affect the development of cSNC. ACC lesions reduce pain responses following formalin administration (Donahue, LaGraize, & Fuchs, 2001) and reduce escape/avoidance learning induced by ligation of the L5 spinal nerve (LaGraize, Labuda, Rutledge, Jackson, & Fuchs, 2004).

Method

Subjects

Forty Long-Evans male rats were used in this experiment. The animals were purchased from Harlan Laboratories (Indianapolis, IN) when they were approximately 60 days old. Rats were housed in wire-bottom cages with water and food freely available, and a rat retreat box that provided enrichment. Surgeries (see below) were carried out when the subjects were about 90 days old. During the week following surgery, animals were weighed and examined daily for signs of disease. The average weight over the last 3 days of recovery from surgery was used as the ad libitum weight. Food (standard laboratory rat chow) was thereafter gradually withheld until the weight of each animal was 81%–84% of its ad libitum weight. Animals were kept at their target weight until the end of behavioral testing by supplementary feeding administered at least 15 min after the daily training trial. A level of deprivation between 80% and 85% of the ad libitum weight is required to induce approach-avoidance conflict (Dachowski & Brazier, 1991; Flaherty, 1991). Water was freely available at the cage throughout the experiment. The vivarium room was lighted from 0700 to 1900 hr, and kept at 22 °C –23 °C temperature and at 50%–65% humidity.

Apparatus

cSNC training was conducted in four conditioning boxes (MED Associates, St. Albans, VT) made of aluminum and Plexiglas (29.3 × 21.3 × 26.8 cm, length × height × width). The floor consisted of steel rods running parallel to the feeder wall. A tray with corncob bedding was placed below the floor to collect feces and urine. In the feeder wall was a hole—1 cm wide, 2 cm long, and 4 cm from the floor—through which a sipper tube, 1 cm in diameter, was inserted. When fully inserted, the sipper tube was flush against the wall. Diffuse light was provided by a house light located in the center of the box's ceiling. A computer located in an adjacent room controlled the presentation and retraction of the sipper tube. When the rats made contact with the sipper tube, a circuit involving the steel rods in the floor was closed and the signal was recorded by the computer. This provided a measure of cumulative contact with the sipper tube, called *goal-tracking time* (measured in 0.05-s bins). Each conditioning box was placed in a sound-attenuating chamber containing a speaker to deliver white noise and a fan for ventilation. Together, the speaker and fan produced noise with an intensity of 80.1 dB (SPL, scale C).

Surgery

Rats received bilateral electrolytic lesions of the ACC. Animals were deeply anesthetized by IP ketamine (50 mg/kg) and xylazine (2.61 mg/kg). Animals were then positioned in a stereotaxic frame with blunt-tipped ear bars. A midline incision was made in the scalp and a burr hole was drilled 0.0 mm posterior to bregma, ±0.9 mm lateral to bregma, and −3.2 mm D/V at a 15-degree angle (coordinates from Paxinos & Watson, 2007). Bilateral electrolytic lesions were performed by passing a 0.5-mA current, during 15 s (lesion-making device, Model 53500, Ugo Basile, Collegeville, PA), using a 0.3-mm electrode, which was insulated except for the tip. Rats were allowed 5–8 days to recover from surgery. Antibiotics were applied as needed. Food and water were continuously available in the cage. After recovery from surgery, animals were deprived of food to 81%–84% of their free-feeding weight. Behavioral training started when the weight of all rats reached the target range.

Behavioral Testing

Rats were randomly assigned to the lesion conditions (ACC vs. sham), and then, within each lesion condition, they were randomly

assigned to the contrast conditions. Four groups of rats ($n = 10$) were formed. In Groups 32/ACC and 32/sham (downshifted groups), rats had access to 32% sucrose solution during Trials 1–10 (preshift), but this solution was replaced by a less sweet 4% sucrose solution during Trials 11–15 (postshift). In Groups 4/ACC and 4/sham (unshifted controls), rats had access to 4% sucrose throughout the 15 trials. Each trial lasted 5 min from the first detected contact with the sipper tube. Solutions were prepared weight/weight, by mixing 32 g (or 4 g) of sucrose for every 68 g (or 96 g) of distilled water. Thus, two types of control conditions were included in this experiment. First, behavioral controls involved unshifted groups not exposed to the reward downshift, always given access to 4% sucrose. Second, sham controls were exposed to the surgery procedures and electrode insertion, but no current was administered.

Histology

When all behavioral testing was finished (after Trial 15), animals were sacrificed using CO_2. The brains were removed and stored in 10% formaldehyde for at least 24 hr. Using a microtome, we sliced 80-μm coronal sections; they were mounted on gelatin-coated glass slides and stained with thionin. The sections were collected for the entire anterior/posterior extent of the lesion, and analysis typically utilized 5–7 sections per animal. An experimenter blinded to behavioral conditions performed the histological analysis under 40× magnification to determine the location and extent to tissue damage relative to plates from the atlas of Paxinos and Watson (2007). The visual analysis of at least 75% bilateral damage to the ACC (Cg1/Cg2) was performed by examining the area outlined from the upper portion of the cingulum bundle to the ventral/medial surface of the cortical tissue and ventral to the border of the corpus callosum. Animals whose lesions were not located in the target ACC were discarded from the analyses.

Results

Histology

One animal (ACC) presented a lesion that extended to the motor cortex of both hemispheres, and its data were not included in the statistical analyses. Nineteen animals had at least 75% bilateral damage to the ACC. Histological analysis (see Figure 1) indicated that the average anterior–posterior extent of the damage for the largest percentage of animals was localized between −0.3 and −0.4 mm relative to bregma. More than 75% of the animals had damage between 0.2 and −0.92 mm relative to bregma. The distribution of damage for animals in the downshifted versus unshifted conditions was similar.

Behavioral Testing

The results of cSNC testing can be seen in Figure 2. During the preshift phase, rats learned to drink the sucrose solutions, with no differences between the experimental groups. Similar preshift performance across groups receiving solutions of different concentration has been reported previously from our lab (e.g., Daniel, Ortega, & Papini, 2009) and from other labs (e.g., Flaherty, 1996, p. 56). A Lesion (ACC, sham) × Contrast (32%, 4%) × Trial (1–10) analysis revealed a significant effect of trial, $F(9, 315) = 116.84$, $p < .01$, but the main effects of lesion, contrast, or their interaction were not significant, Fs < 1.01, ps > 0.37.

Figure 2 also shows the results of the postshift trials. Three points are noteworthy. (1) No lesion effect is observable between the two downshifted groups (Groups 32/ACC and 32/sham) on the first downshift trial (Trial 11). (2) No lesion effect is observable in a comparison between the two unshifted groups (Groups 4/ACC and 4/sham). (3) The ACC lesion retarded recovery from the incentive downshift experience subsequent to Trial 11. These effects yielded a significant triple interaction of Lesion (ACC, sham) × Contrast (32%, 4%) × Trial (11–15), $F(4, 140) = 2.86$, $p < .03$. Also significant were the Trial × Contrast interaction, $F(4, 140) = 6.56$, $p < .01$, the trial effect, $F(4, 140) = 19.16$, $p < .01$, and the contrast main effect, $F(1, 35) = 14.33$, $p < .01$. All other effects were not significant, Fs < 1.54, ps > 0.19.

For further analyses of postshift behavior, LSD pairwise tests were calculated with the error term from the main analysis. Two comparisons for each postshift trial were computed: between the downshifted and unshifted groups for each lesion condition and between lesion and sham groups for each contrast condition. Sham rats showed significant cSNC effects on Trials 11–13, Fs$(1, 35) > 4.85$, ps < 0.04, but not for Trials 14–15, Fs < 1. ACC rats showed a significant cSNC effect on Trials 11–15, Fs$(1, 35) > 6.79$, ps < 0.02. Thus, the ACC lesion extended the cSNC effect for at least two more trials. Further comparisons between Groups 32/ACC and 32/sham for Trials 11–15 yielded a significant difference on Trial 14, $F(1, 35) = 4.51$, $p < .05$; all other trials were not significant, Fs$(1, 35) < 2.65$, ps > 0.11. Similar comparisons between Groups 4/ACC and 4/sham for Trials 10–15 were uniformly negative (Fs < 1).

Figure 3 depicts consummatory behavior during the initial (top) and last (bottom) 100 s of Trials 10–15. For the initial 100 s, a Lesion × Contrast × Trial (11–15) yielded a significant triple interaction, $F(4, 140) = 3.19$, $p < .02$. Also significant were the contrast, $F(1, 35) = 5.20$, $p < .03$, and trial effects, $F(4, 140) = 8.22$, $p < .001$. Other effects were not significant, Fs < 2.27, ps > 0.06. To characterize the triple interaction, LSD pairwise tests were computed using the error term from the main analysis. Four pairs of groups were compared. (1) Group 32/ACC versus Group 4/ACC: significantly different on Trials 12–14, Fs$(1, 35) > 5.66$, ps < 0.03; (2) Group 32/sham versus Group 4/sham: not significantly different on any of the trials, Fs$(1, 35) < 1.83$, ps > 0.18; (3) Group 4/sham versus Group 4/ACC: not significantly different on any of the trials, Fs < 1; and (4) Group 32/ACC versus Group 32/sham: not significantly different on any of the trials, Fs < 3.27, ps > 0.07. Therefore, rats with ACC lesions exhibited cSNC (1) on Trials 12–14, whereas sham-operated animals failed to exhibit cSNC in the initial 100 s of all postshift trials (2). The initial 100 s of postshift trials is a period in which unoperated rats (as the sham animals in this experiment) do not normally exhibit evidence of cSNC (Norris, Daniel, & Papini, 2008). It takes longer than 100 s for rats to detect the disparity between the concentration of the current sucrose solution and the concentration of the preshift sucrose solution, which must be reactivated from mem-

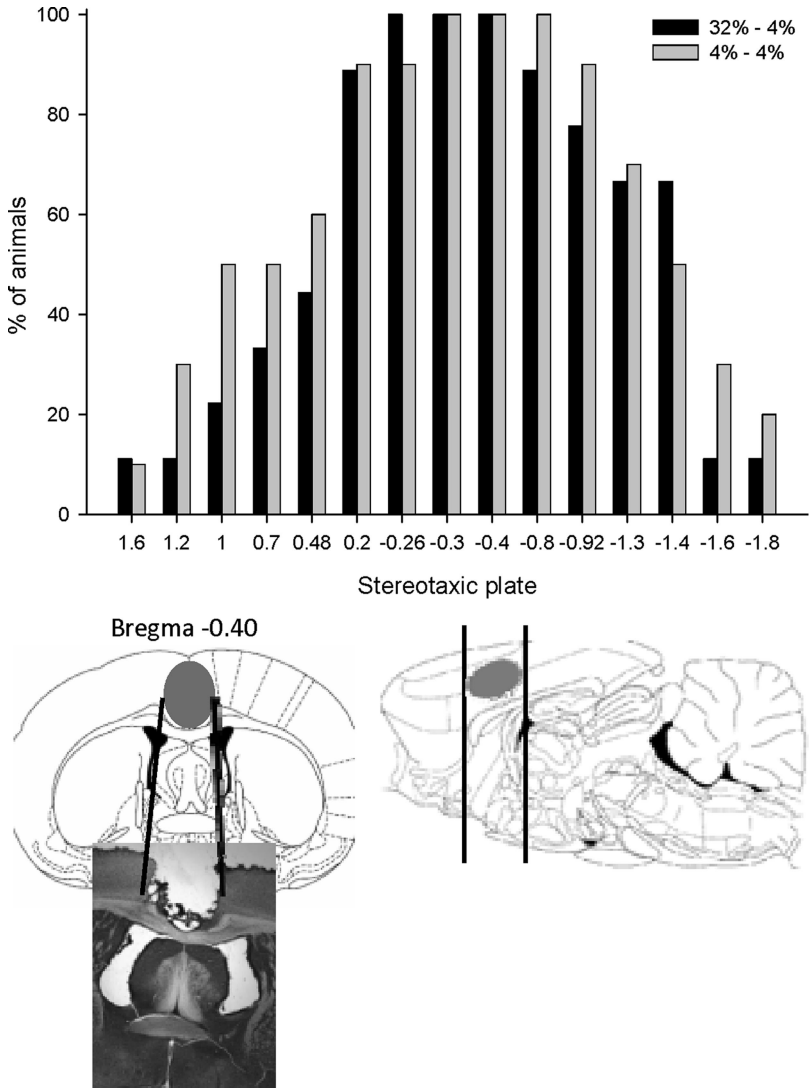

Figure 1. The histogram illustrates the percentage of animals with damage of the ACC based on the stereotaxic plates of Paxinos and Watson (2007) for animals in the 32%-to-4% and 4%-to-4% sucrose downshift conditions. The anterior–posterior extent of the lesion was similar for the two downshift conditions. The bottom portion of the figure illustrates a representative coronal section showing the maximum extent of a bilateral lesion to the ACC centered at Bregma −0.40 mm. Also presented is a midsagittal plate with vertical lines spanning from approximately Bregma 1.6 to Bregma −1.8. The dark areas indicate the location of the lesion. Adapted from *The Rat Brain in Stereotaxic Coordinates* (4th ed., Figures 20 and 80), by G. Paxinos & C. Watson, 1998, New York, NY: Academic Press. Copyright 1998 by Elsevier.

ory. The ACC lesion facilitated the detection of this incentive disparity inducing significant levels of cSNC on Trials 12–14.

For the last 100 s (Figure 3, bottom), there was also a Lesion × Contrast × Trial significant triple interaction for Trials 11–15, $F(4, 140) = 2.90$, $p < .03$. Also significant were the effects of contrast, $F(1, 35) = 19.89$, $p < .001$, and trial, $F(4, 140) = 16.79$, $p < .001$. Other effects were not significant, Fs < 1.97, ps > 0.10. To identify the source of the triple interaction, LSD pairwise tests with the error term from the main analysis were computed. The same four comparisons as before were made. (1) Group 32/ACC versus Group 4/ACC: significantly different on Trials 11–15, Fs(1, 35) > 12.44, ps < 0.003; (2) Group 32/sham versus Group 4/sham: significantly different on Trials 11–13, Fs(1, 17) > 4.82, ps > 0.04; (3) Group 4/sham versus Group 4/ACC: not significantly different on any of the trials, Fs < 1; and (4) Group 32/ACC versus 32/sham: significantly different on Trials 14–15, Fs > 4.22, ps < 0.05. As with the initial 100 s, the ACC lesion retarded recovery from cSNC, from three trials in the sham groups (2) to all five postshift trials in the ACC groups (1).

Discussion

Bilateral ACC lesions retarded the recovery of consummatory behavior after an incentive downshift. The cSNC effect was ex-

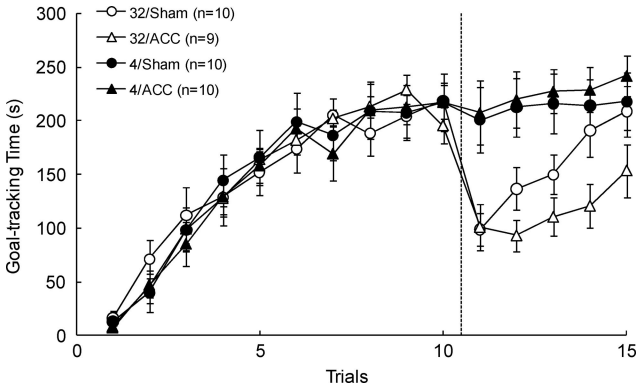

Figure 2. Mean (± SEM) goal-tracking times of groups downshifted from 32% sucrose to 4% sucrose (32) and groups that received 4% sucrose (4) in all trials. ACC groups received bilateral electrolytic lesions of the anterior cingulate cortex, whereas sham groups received a similar surgical treatment, but no current was administered.

tended in ACC-lesioned animals relative to sham-operated animals. Importantly, the effect was specific to the downshifted condition and to postshift trials beyond the first one. Thus, the ACC lesion had no measurable effects on preshift consummatory behavior directed at the 32% and 4% sucrose solutions; on the performance of unshifted, 4% sucrose animals; and on the first downshift trial. In addition, ACC lesions led to significant cSNC effects in the initial 100 s of postshift Trials 12–15, whereas sham groups did not differ in any of the postshift trials during the initial 100 s. The effects of ACC lesions extended to the last 100 s of postshift trials.

To the authors' knowledge, this is the first report of a brain area whose lesion impairs recovery from cSNC, while leaving unimpaired the performance during the first incentive downshift event (Trial 11). Previous studies reported that lesions in several areas associated with the gustatory system impaired cSNC, without affecting the rat's ability to respond differentially to sucrose solutions of different concentration. These areas included the parabrachial nucleus (Grigson et al., 1994), the gustatory thalamus (Reilly & Trifunovic, 1999; Sastre & Reilly, 2006), and the insular cortex (Lin et al., 2009). A common effect of these lesions was to disrupt consummatory behavior from the first downshift trial; thus, rats adjusted to the new solution exhibiting less behavior, but without undershooting the level of the unshifted controls with the same lesion. Amygdala lesions attenuated (lateral nucleus) or eliminated (medial nucleus) the initial response to the incentive downshift (Becker et al., 1984), whereas lesions of the hippocampus and nucleus accumbens had no detectable effect on cSNC (Flaherty et al., 1998; Flaherty, Rowan, Emerich, & Walsh,1989; Leszczuk & Flaherty, 2000). The evaluation of the role played on recovery from cSNC of any area whose irreversible damage impairs the initial response to the incentive downshift is complicated by a potential confound: Does brain damage affect recovery from cSNC directly by affecting memory processes involved in recovery, or indirectly by affecting the initial comparison of obtained and expected sucrose concentrations?

The present results are consistent with a set of pharmacological effects that differentiate between the first and second downshift trials—so-called trial-selective drug effects. For example, benzodiazepine anxiolytics like chlordiazepoxide and midazolam were reported to be effective on the second downshift trial, but not on the first downshift trial (see Flaherty, 1990, Flaherty, 1996). Similarly, the delta opioid receptor agonist D-Pen2,D-Pen5-Enkephalin (DPDPE) and the antagonist naltrindole affected cSNC when administered before the first downshift trial, but had no effect when administered before the second downshift trial (Pellegrini, Wood, Daniel, & Papini, 2005; Wood, Daniel, & Papini, 2005). Conversely, the kappa opioid receptor agonist U50,488H was ineffective when administered before the first downshift trial, but it modulated cSNC in a dose-dependent manner when administered before the second downshift trial (Wood, Norris, Daniel, & Papini, 2008). The present results can also be described in terms of trial selectivity since the ACC lesion had its effects only after the first downshift trial. Because there is evidence of a relatively high density of opioid receptors (especially mu and delta receptors) in the ACC (e.g., Mansour, Fox, Akil, & Watson, 1995; L. J. Vogt, Sim-Selley, Childers, Wiley, & Vogt, 2001; B. A. Vogt, Wiley, & Jensen, 1995), it is hypothesized that the trial selectivity exhibited by opioids in the cSNC situation is at least in part mediated by the ACC.

Similar results were reported with lesions of the medial prefrontal cortex (Pecoraro et al., 2008). In that experiment, rats with such

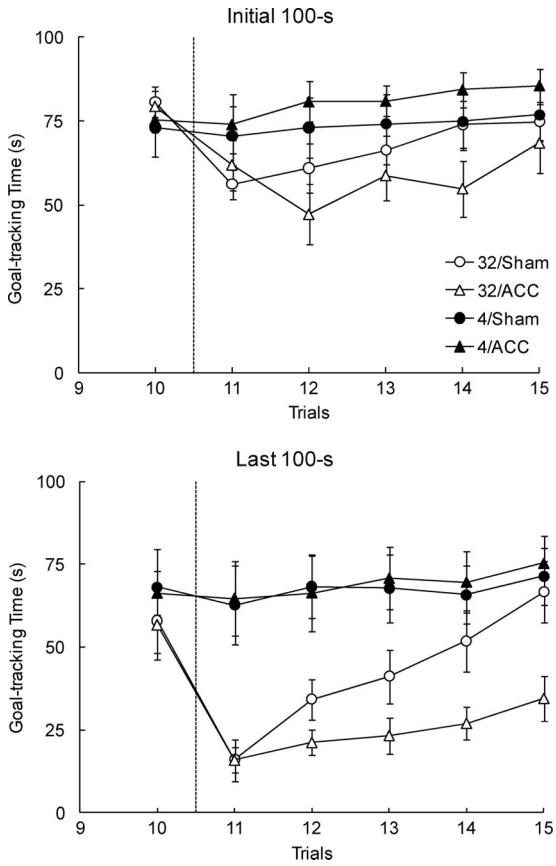

Figure 3. Mean (± SEM) goal-tracking times during the initial 100 s (top) and the last 100 s (bottom) from Trials 10–15. See Figure 2 for further details.

lesions were no different than sham controls during the initial trials following a 32%-to-4% sucrose downshift, but recovered consummatory behavior to a higher asymptotic level than shams. However, two aspects of these results merit caution. First, unshifted, 4%-to-4% sucrose controls were not included, thus making it difficult to determine whether the effects were specific to the downshift event or more generally related to 4% sucrose consumption. Second, rats with medial prefrontal cortex lesions did show higher consumption than shams from the first downshift trial in a second 32%-to-4% sucrose devaluation. Therefore, the present results are unique in that the ACC lesion can be unambiguously interpreted as affecting recovery from cSNC.

The present study also has some limitations. As any research involving electrolytic lesions, the possible functions of the ACC in incentive contrast effects must be weighed against the possible destruction of fibers of passage (e.g., Frey, Morris, & Petrides, 1997). In this case, such fibers refer predominantly to axons interconnecting cortical areas, although some damage to white matter underlying the ACC cannot be discarded. Electrolytic lesions were preferred as a starting point because all tissue is damaged and the region damaged can be clearly delimited, unlike it is the case with chemical lesions. However, chemical lesions targeting different neuronal groups will be required to clarify this issue. Second, the present results also seem inconsistent with research on physical pain and fear conditioning involving ACC lesions. For example, LaGraize, Labuda, Rutledge, Jackson, and Fuchs (2004) rats with spinal nerve ligation (a model of neuropathic pain) show reduced escape/avoidance learning after ACC lesions, an outcome interpreted as reflecting a decrease in the aversiveness of the reinforcer used to induce learning. The inconsistency comes from the claim that situations involving incentive loss (psychological pain) and peripheral tissue damage (physical pain) share an underlying neural circuitry (e.g., Papini et al., 2006). If this were the case, one would expect that ACC lesions would either reduce cSNC (i.e., decreased psychological pain) or enhanced escape/avoidance learning (i.e., increased physical pain). Instead, ACC lesions have what appears to be, at least on the surface, opposite results. The apparent inconsistency between the effects of ACC lesions on incentive contrast and escape/avoidance learning may be resolved in at least three ways: reinterpreting the present results, reinterpreting the escape/avoidance results, or discarding the hypothesis that the brain circuits underlying frustration and pain/fear are the same (Gray, 1982; Papini et al., 2006).

One interpretation of the present results posits that the ACC down-regulates the emotional activation induced by conditioned frustration. Conditioned frustration (Amsel, 1992) develops during the first downshift trial as a result of the unexpected devaluation of the incentive, but only comes to fully control consummatory behavior on subsequent trials (Papini, 2003; Wood et al., 2005). Because conditioned frustration can be described as the animal's ability to anticipate its own emotional reaction, Papini (2003) suggested the name "egocentric learning" to refer to this process. Thus, this egocentric learning hypothesis suggests that the ACC would normally attenuate the emotional intensity of conditioned frustration, perhaps via opioid activation.

An alternative explanation would posit that rats with ACC lesions are impaired in learning about the contingency between behavior and the new incentive, which was called "allocentric learning" since it involves an update of the memory record after environmental change (Papini, 2003). Allocentric learning is necessary to recover normal levels of consummatory behavior. In the cSNC situation, recovery depends on learning to match expectation with the new (downshifted) incentive. Thus, to the extent that the downshift continues to be unexpected (i.e., because of a failure to update memory after the change in incentive), consummatory behavior would continue to be suppressed and recovery from cSNC would be retarded. This allocentric learning hypothesis explains all the results of the present experiment (see summary above). Specifically, the lack of effect on the first downshift is accounted for on the assumption that allocentric learning requires a minimum amount of experience in procuring the new incentive.

The present data cannot distinguish between an effect of the ACC lesion in terms of impairment of egocentric memory or allocentric memory. However, the latter is consistent with available data from other situations. For example, deficits in allocentric learning are consistent with impairments in reversal learning in rats with ACC lesions (Newman & McGaughy, 2011). In that experiment, reversing the validity of olfactory cues increased the number of errors and the number of trials to an acquisition criterion, but significantly more in rats with ibotenic acid lesions of the ACC. Whereas the egocentric learning hypothesis predicts stronger emotional learning resulting from errors during reversal trials and, therefore, improved reversal performance (i.e., the opposite of what happened), the allocentric learning hypothesis suggests that ACC lesions should induce deficits in memory update of the new incentive conditions, thus correctly predicting retardation in reversal learning.

The allocentric memory hypothesis can also account for the deficits in escape/avoidance learning reported by LaGraize et al. (2004), but it suggests a different explanation to that offered by the authors. According to this hypothesis, ACC lesions impair escape/avoidance learning by disrupting the rat's ability to detect behavior-incentive contingencies, rather than by enhancing the aversiveness of the incentive. This is consistent with a number of experiments suggesting that the ACC plays a role in reward expectancies (i.e., expectations about what external events should be contingent on behavior). For example, McKee, Kelley, Moser, and Andrzejewki (2010) reported deficits in the acquisition (but not after asymptotic performance was reached) of instrumental lever pressing following microinfusions of the N-methyl-D-aspartate receptor antagonist AP-5 in the ACC.

The allocentric learning hypothesis has the additional advantage of fitting the more general idea that the neural mechanisms underlying physical pain, fear, and frustration share extensive commonality (Gray, 1982; Papini et al., 2006). Although the ACC would not be playing a role strictly related to these forms of pain, it would still be important as part of a memory mechanisms pertaining to coping with these aversive states.

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