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Role of the opioid system in incentive downshift situations

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ABSTRACT

Previous research has shown that opioid blockage enhances consummatory successive negative contrast (cSNC)—a suppression of consummatory behavior following a downshift from 32% to 4% sucrose solution. In Experiment 1, administration of the nonselective opioid receptor antagonist naloxone (2 mg/kg, ip) distorted the comparison between expected and received incentives. The results of Experiment 2 discarded the alternative that naloxone enhances cSNC by inducing a conditioned taste aversion. The results of Experiments 3a–3c provided no evidence that opioid administration after the first downshift trial modulated subsequent consummatory performance. The opioids tested included naloxone (2 mg/kg, ip), the δ-opioid receptor selective antagonist naltrindole (1 mg/kg, ip), and the δ-opioid receptor selective agonist DPDPE (24 μg/kg, ip). The selected doses have proven in earlier experiments to be effective when administered before training. Experiments 4–5 failed to uncover any effects of posttraining opioid blockage with naloxone in an appetitive extinction task (autoshaping with lever-food pairings). These results add to our previous understanding of opioid function in situations involving incentive downshifts, suggesting a role in the comparison process that triggers cSNC, but no apparent function in memory consolidation related to the downshift event.

1. Introduction

Vogel, Mikulka, and Spear (1968) reported that rats given access to 32% sucrose solution for 5 min daily for 11 trials exhibited consummatory suppression after a downshift to 4% sucrose, relative to an unshifted control group only exposed to the 4% sucrose. Consummatory behavior recovered over the subsequent six postshift trials to the level of the unshifted controls. This phenomenon is called consummatory successive negative contrast (cSNC). Flaherty (1996) characterized cSNC in terms of a multistage hypothesis consisting of two distinct stages. The first stage involves the detection of the downshift, the rejection of the downshifted incentive, and the searching for the missing reward. Failure to locate the missing reward initiates a second stage, called recovery, during which conflict and stress are involved. Based primarily upon pharmacological data, Flaherty (1996) described the first stage in the multistage hypothesis as purely cognitive, while the second stage involved an emotional reaction of frustration.

The multistage hypothesis has since been adapted to Amsel's (1992) frustration theory, which has the advantage of making some of the components more explicit (Papini, Wood, Daniel, & Norris, 2006; Wood, Daniel, & Papini, 2005). Amsel's (1992) theory of frustration attributes the emotional reaction resulting from surprising reward loss to the violation of an incentive expectancy by the presentation of a smaller reward than expected. The main differences between Flaherty's sequential hypothesis and Amsel's frustration theory are the following. In the first stage, frustration theory interprets "rejection" as resulting from the elicitation of primary frustration, an internal aversive state induced by surprising reward loss. Thus, the initial stage is not purely cognitive, but it also contains an emotional unconditioned response to the downshift. In the second stage, frustration theory suggests that the avoidance component of the approach-avoidance conflict reflects secondary frustration, that is, a conditioned anticipatory version of primary frustration. Frustration theory also suggests two additional conditioning processes that contribute to recovery from cSNC. One involves the counterconditioning of secondary frustration by its pairing with the downshifted incentive and the other is the update of the incentive expectation to match the postshift incentive value. The counterconditioning of secondary frustration leads to a reduction in competing responses that interfere with drinking behavior, whereas the memory updating process reduces the discrepancy between expected and obtained incentives, thus weakening primary frustration and, consequently, promoting consummatory behavior.

The modified multistage model of cSNC suggests a sequence of stages that can be characterized as involving detection, rejection, search, approach-avoidance conflict, counterconditioning, and memory update. Although these stages occur in rapid succession, the pharmacological evidence alluded to below suggests that the

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effects of conflict peak after at least 5 min after the initial downshift experience. Because each trial lasts 5 min, this implies that pharmacological manipulations acting on the conflict (e.g., administration of benzodiazepine anxiolytics such as chlordiazepoxide) tend to be more effective on the second postshift trial (usually trial 12) than on the first (e.g., Becker, 1986; Flaherty et al., 1990; Flaherty & Rowan, 1989). However, anxiolytics can be effective on the first postshift trial provided that the trial is lengthened beyond the typical 5 min (Flaherty, Grigson, & Rowan, 1986; Mustaca, Bentosela, & Papini, 2000) or when the animal is downshifted repeatedly (Flaherty, Clarke, & Coppotelli, 1996). Anxiolytics attenuate cSNC only after some experience with the downgraded solution.

Based on the characterization of cSNC provided by the modified multistage model, it could be argued that this phenomenon is based on three fundamental processes: detection (a perceptual–cognitive process), rejection (a motivational–emotional process), and learning (acquiring information about the new incentive conditions, called allocentric learning, and about the aversive experience of the downshift, called egocentric learning; Papini, 2003). Previous research shows that the opioid system is involved in both the rejection and the recovery process in a surprisingly selective manner. For example, the δ-opioid receptor subsystem is selectively involved in modulating the initial reaction to the downshift. Thus, the agonist DPDPE ([D-Pen2,D-Pen5]-Enkephalin) attenuates cSNC when administered before the first downshift trial, but has no effect when administered before the second downshift trial (Wood et al., 2005). Conversely, the antagonist naltrindole enhances cSNC when administered before the first downshift trial, but has no effect on the second downshift trial (Pellegrini, Wood, Daniel, & Papini, 2005). A second set of experiments suggest that the κ-opioid receptor agonist U-50,488H (*trans*-(±)-3,4-dichloro-*N*-methyl-*N*-[2-(1-pyrrolidinyl)cyclo-hexyl]-benzeneacetamide) attenuates cSNC when administered before the second downshift trial, but has no effect when administered before the first downshift trial—just the opposite trial selectivity as that exhibited by δ-opioid receptor modulators (Wood, Norris, Daniel, & Papini, 2008). Interestingly, the nonselective opioid receptor antagonist naloxone administered before the first and second downshift trials enhances cSNC, suggesting that the downshift experience naturally induces the release of endogenous opioids (Pellegrini et al., 2005). Consistent with the effects of naloxone, the nonselective opioid receptor agonist morphine attenuates cSNC when administered before the first and second downshift trials (Rowan & Flaherty, 1987).

Opioid modulation of cSNC can be understood in terms of effects on detection, rejection, and/or learning. The available evidence does not distinguish between these potential effects, providing only evidence of trial and receptor selectivity. Notice that the effects of opioid peptides on cSNC cannot be accounted for in terms of altered sucrose palatability because these drugs had no effect on consummatory behavior in unshifted control groups. Therefore, although opioids can modulate sucrose palatability under some conditions (e.g., Kelley et al., 2002), such modulation does not appear to be a factor in the cSNC situation. Similarly, whereas opioids may be less effective in modulating feeding when animals are food deprived (Lowy, Maickel, & Yim, 1980), this was not a factor in cSNC experiments given the lack of opioid effects in unshifted controls and the trial-selective effects of some opioids such as DPDPE and U50,488H described above. The experiments reported here were designed to test the role of the opioid system on detection of the incentive downshift (Experiment 1), on rejection based not on frustration, but on conditioned taste aversion (Experiment 2), and on the modulation of egocentric memory consolidation (Experiment 3). In addition, Experiments 4–5 explored the role of the opioid system on appetitive extinction, a training situation that shares with cSNC the incentive downshift operation.

2. Experiment 1

Papini and Pellegrini (2006) reported that incentive downshifts of different magnitudes but with the same ratio of discrepancy between solutions resulted in similar amounts of consummatory suppression. Based on this evidence (see also Pellegrini, Lopez Seal, & Papini, 2008; Pellegrini & Papini, 2007), it was argued that the detection of an incentive downshift operates under constraints similar to those described by Weber's law for sensory systems. If opioids influence the comparison between the solutions, then administration of naloxone will distort this scaling property. For example, if opioid receptor blockage enhances the disparity between the preshift and postshift incentives, then naloxone administration should cause the groups with greater absolute disparity between solutions to show enhanced consummatory suppression compared to groups with the same ratio but smaller disparity.

2.1. Method

2.1.1. Subjects

The subjects were 66 male, experimentally naive Long–Evans rats, 90 days old at the start of the experiment. Rats were bred in the TCU vivarium from parents purchased at Harlan (Indianapolis, IN) and maintained under a 12:12 h light:dark cycle (lights on at 07:00 h). The vivarium temperature (18–23 °C) and humidity (40–70%) were monitored daily. Animals were deprived of food to 81–84% of their free-food weight. Free-food weights were defined as the average of each animal's weight during three successive days before deprivation started. Water was continuously available in each individual wire-mesh cage. Animals were trained during the light phase of the daily cycle.

2.1.2. Apparatus

Training was conducted in four conditioning boxes (MED Associates, Fairfax, VT) constructed of aluminum and Plexiglas (29.3 × 21.3 × 26.8 cm, $L \times H \times W$). The floors were made of steel rods, 0.4 cm in diameter and 1.6 cm apart, running parallel to the feeder wall. A bedding tray filled with corncob bedding was placed below the floor to collect fecal pellets and urine. Against the feeder wall was an elliptical opening 1 cm wide, 2 cm high, 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 of the box. A house light (GE 1820) located in the center of the box's ceiling provided diffuse light. A computer located in an adjacent room controlled the presentation and retraction of the sipper tube. When rats contacted the sipper tube, a circuit involving the steel rods in the floor and the sipper tube was closed and the signal was recorded by the computer. Each conditioning box was placed in a sound-attenuating chamber that contained 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).

2.1.3. Procedure

Training lasted 15 daily trials. All trials lasted 5 min starting from the first contact with the sipper tube. The first 10 were the preshift trials and the last 5 were postshift trials. For all the groups, each preshift trial consisted of access to either 32% or 16% sucrose solution (w/w; e.g., 32% was prepared by mixing 32 g of commercial sugar for every 68 g of distilled water). At the end of the preshift, groups given either 32% or 16% sucrose were each divided into two subgroups matched for preshift responding. The 5 postshift trials were exactly like preshift trials, except for the concentration of the sucrose solution. The rats originally trained with 32% sucrose were assigned to either the 32-6 or 32-12 conditions,