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# Partial reinforcement in rat autoshaping with a long CS: Effects of pramipexole and chlordiazepoxide on sign and goal tracking

Esmeralda Fuentes-Verdugo[1], Ricardo Pellón[1], Mauricio R. Papini[2], Carmen Torres[3] and Patrick Anselme[*4]

[1]*School of Psychology, Universidad Nacional de Educación a Distancia (UNED), 28040 Madrid, Spain*

[2]*Department of Psychology, Texas Christian University, Fort Worth, TX 76129, USA*

[3]*Department of Psychology, Universidad de Jaén, 23071 Jaén, Spain*

[4]*Department of Biopsychology, Ruhr-Universität Bochum,*

*44801 Bochum, Germany*

In Pavlovian autoshaping, sign-tracking responses (lever pressing) to a conditioned stimulus (CS) are usually invigorated under partial reinforcement (PR) compared to continuous reinforcement (CR). This effect, called the PR acquisition effect (PRAE), can be interpreted in terms of increased incentive hope or frustration-induced drive derived from PR training. Incentive hope and frustration have been related to dopaminergic and GABAergic activity, respectively. We examined the within-trial dynamics of sign and goal tracking in rats exposed to 20-s-long lever presentations during autoshaping acquisition under PR vs. CR conditions under the effects of drugs tapping on dopamine and GABA activity. There was no evidence of the PRAE in these results, both groups showing high, stable sign-tracking response rates. However, the pharmacological treatments affected behavior as revealed in within-trial changes. The dopamine D2 receptor agonist pramipexole (0.4

[*]**Corresponding autor**: Patrick Anselme. Department of Biopsychology, Ruhr-Universität Bochum, 44801 Bochum, Germany E-mail: Patrick.Anselme@ruhr-uni-bochum.de.
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mg/kg) suppressed lever pressing and magazine entries relative to saline controls in a within-subject design, but only in PR animals. The allosteric benzodiazepine chlordiazepoxide (5 mg/kg) failed to affect either sign or goal tracking in either CR or PR animals. These results emphasize the roles of dopamine and GABA receptors in autoshaping performance, but remain inconclusive with respect to incentive hope and frustration theories. Some aspects of within-trial changes in sign and goal tracking are consistent with a mixture of reward timing and response competition.

In Pavlovian autoshaping with rats, each trial consists of a brief presentation of a lever acting as a conditioned stimulus (CS) whose termination is automatically followed by an unconditioned stimulus (US; e.g., food delivery; Hearst & Jenkins, 1974). Rats are said to sign track when they interact (press, nibble, and sniff) with the lever during its presentation, while they are said to goal track when they instead approach and inspect the magazine where food is to be delivered after the lever is retracted. In autoshaping with rats, the unpredictable delivery of food after a lever presentation (partial reinforcement, PR) tends to increase sign-tracking responses compared to the predictable delivery of food on each trial (continuous reinforcement, CR; Anselme, Robinson, & Berridge, 2013; Boakes, 1977; Glueck, Torres, & Papini, 2018; Robinson, Anselme, Fischer, & Berridge, 2014; Torres, Glueck, Conrad, Morón, & Papini, 2016). This result resembles the partial reinforcement acquisition effect (PRAE) reported in runways, where rats run faster in the early segment of a runway under PR than under CR (Goodrich, 1959; Haggard, 1959). But the PRAE in a runway also includes a component that is poorly understood in autoshaping with rats. As PR rats approach the goal segment of the runway, their speed becomes slower than that of CR rats (Amsel, MacKinnon, Rashotte, & Surridge, 1964; Chen, Gross, Stanton, & Amsel, 1980; for recent autoshaping studies, see Derman, Schneider, Juarez, & Delamater, 2018; Iliescu, Dwyer, & Honey, in press).

Several models have been proposed to study the CR vs. PR effects. Pearce and Hall (1980) suggested that PR generates an increase in attention that increases orienting responses to the CS (sign tracking) relative to CR training. In another view, the reward prediction error suggested by Schultz (1998) relies on the evidence that PR increases the release of mesolimbic dopamine as a teaching signal that informs the brain that the learning of a task is incomplete. Despite their interest, these models let a number of questions unanswered with respect to the distinction between sign and goal tracking, the dynamics of responses during the CS, and the motivational/emotional dimension that may underpin the orienting response and associative learning. This paper focuses on frustration theory and the

incentive hope hypothesis as possible accounts of the affective components of behavior during PR vs. CR autoshaping training.

To explain the runway effect reported above, frustration theory posits that unexpected reward omissions have associative and motivational effects that generate opposing influences on behavior (Amsel, 1992). Unexpected reward omissions during PR training induce a negative emotion (called primary frustration, an unconditioned response) that can be learned (secondary frustration, a conditioned response). These emotional responses also have the capacity for increasing motivation for responding (e.g., Dudley & Papini, 1995). Thus, far from the goal, the motivational effects of PR training invigorate responding (the PRAE), whereas near the goal, anticipatory frustration promotes goal avoidance tendencies that suppress running speed. Evidence supporting an explanation of the PRAE in terms of frustration comes from pharmacological studies showing attenuating effects of anxiolytics (Gray, 1969; Lewis, 1960; Nelson & Wollen, 1965; Stretch, Houston & Jenkins, 1964; Wagner, 1963). According to frustration theory, this reasoning can indistinguishably be applied to an instrumental (runway) and a Pavlovian (autoshaping) context.

The aim of this report is to determine whether such a within-trial reversal of performance also occurs in Pavlovian autoshaping with rats. Until now, only response invigoration has been shown (i.e., the PRAE). In the rare cases in which within-trial performance was analyzed, the CS presentations were either possibly too short (Gibbon, Farrell, Locurto, Duncan, & Terrace, 1980) or not associated with reward uncertainty (Derman et al., 2018; Iliescu et al., in press; Meltzer & Brahlek, 1970). Pavlov's (1927) inhibition of delay also involves a change in response strength during the presentation of a long CS, but it leads to different predictions. Inhibition of delay would predict suppressed responding during the early portions of a CS, something inconsistent with the PRAE reported in autoshaping, and increase responding as US presentation approaches. Moreover, it is unclear whether inhibition of delay would lead to differential predictions for CR vs. PR training. This experiment was designed to determine whether there is an increase in sign tracking during the early portions of a long CS (the PRAE) and also a decrease in sign tracking toward the end of the long CS. Consistent with frustration theory, such dynamic change is predicted to be stronger following PR than following CR training.

There are reasons to doubt the occurrence of response suppression near the goal event in Pavlovian autoshaping. According to the incentive hope hypothesis, rats exposed to an unreliable CS do not experience frustration, but "hope" for the reliability of its association with food (Anselme, 2018). Indeed, an expectation of nonreward is not assumed to predominate on a trial

when food and the absence of food are equally probable. Incentive hope is related to CS attraction, because of the CS association with a "wanted" food US, but it also has an aversive component, because the food US is not guaranteed. The theory predicts that this aversive component boosts CS attraction in the form of a propensity to invest more time and effort to obtain the food US, through glucocorticoid-induced dopamine release. In autoshaping, the incentive hope hypothesis is supported by the fact that reward uncertainty is associated with a higher mesolimbic dopamine release (Hart, Clark, & Phillips, 2015), a major determinant of incentive motivation (Berridge, 2007), whereas neither the CS alone nor the food US alone induces more responses under uncertainty than certainty in drug-free rats in which a PRAE was shown (Hellberg, Levit, & Robinson, 2018). Like frustration theory, the incentive hope hypothesis predicts behavioral invigoration under PR at the beginning of the lever presentation. Unlike frustration theory, however, no suppression of responding is predicted near the end of the lever presentation.

A pharmacological approach was used to distinguish between these theoretical accounts. Frustration theory rests on the assumption that emotional learning (i.e., anticipatory frustration) is modulated by the same neurochemical systems that regulate conflict. Consistent with this assumption, the administration of benzodiazepine anxiolytics is known to reduce or eliminate several phenomena resulting from unexpected reward omissions. For example, pretrial administration of chlordiazepoxide (CDP) during PR training eliminates the increased resistance to extinction relative to CR training in the runway—the PR extinction effect in the runway situation (PREE; McNaughton, 1984) and attenuates the suppressive effects of unexpected reward downshifts in consummatory behavior (Ortega, Glueck, Daniel, Prado-Rivera, White, & Papini, 2014). Infusion of diazepam in the central amygdala also attenuates the effects of reward downshift in consummatory behavior (Liao & Chang, 2003). In autoshaping with rats, CDP administration before every session retards the emergence of the PREE, although the PRAE was not observed in that experiment (Boughner & Papini, 2008). Frustration theory thus predicts that CDP treatment should reduce both within-trial effects of PR training, namely the early invigoration and the late suppression of behavior. Both effects are explained in terms of the secondary frustration induced by unexpected reward omissions. By contrast, incentive hope theory predicts no within-trial effect for responses trained under CR. As incentive hope is assumed to depend on glucocorticoid-induced dopamine release (Anselme & Güntürkün, 2019) and CDP inhibits the release of glucocorticoids (e.g., McElroy, Miller, & Meyer, 1987), this hypothesis predicts a within-trial uniform reduction in sign tracking during PR training.

In addition, incentive hope assumes a positive motivational factor associated with incentive salience is responsible for the PRAE. In this context, incentive hope predicts that an increase in dopaminergic activity in the brain reward system should enhance incentive salience, a dopamine-dependent brain process responsible for the motivational attraction of rewards and CSs (Berridge, 2007), and therefore contribute to increase the PRAE. Thus, treatment with pramipexole (PPX), a D2 dopamine receptor agonist, is predicted to further increase sign tracking during PR training. Frustration theory is silent on the effects of PPX on autoshaping performance. PPX was selected because it is known to generate pathological gambling in some people treated for a Parkinson disease (e.g., Dodd, Klos, Bower, Geda, Josephs, & Ahlskog, 2005). There is also evidence that this drug (or ropinirole, a pharmacological equivalent) increases the propensity of rats to "gamble" (Johnson, Madden, Brewer, Pinkston, & Fowler, 2011; Tremblay, Silveira, Kaur, Hosking, Adams, Baunez et al., 2017). Furthermore, PPX is known to mimic dopamine in terms of both receptor-binding affinity and efficacy (full agonism) for D2 receptors (Hubble, 2002; Pivonello, Ferone, Lombardi, Colao, Lamerts, & Hofland, 2007).

## METHOD

**Subjects**. Twenty-four naïve male Wistar rats obtained from Charles River Laboratories (Lyon, France) were individually housed in transparent polycarbonate cages (26.7 × 42.7 × 18 cm) with minimal enrichment (one red-tinted polycarbonate tunnel per cage). The room was maintained under a 12-h light/dark cycle (lights on at 08:00 h), with constant temperature (21 ±2 ºC) and relative humidity (55%). Rats were gradually food deprived until reaching 81-84% of their ad libitum bodyweight (342.8 g, ±18 g), measured over 3 days. Rats were weighed daily before the start of experimental sessions and were fed at least 20 min after the end of each session. All animal care procedures were in accordance with the European Union Council Directive 2010/6 and the Spanish Royal Decree 53/2013 for minimizing stress and discomfort in animals, and were approved by UNED bioethics committee.

**Apparatus**. Rats were trained in eight LI-836 (Letica Instruments, Barcelona, Spain) conditioning chambers (29 × 24.5 × 35.5 cm), enclosed in soundproof wooden cabinets equipped with a ventilation system and a small observation window at the front. The left panel of each conditioning chamber was made of aluminum, the front wall and the roof of transparent polycarbonate, and the other two walls of black polycarbonate. The floor was

formed by 12 metal rods located above a removable sawdust tray. A food dispenser allowed the automatic delivery of 45-mg precision pellets (Bio-Serv, Frenchtown, NJ, USA) in an aperture in the front of the chamber wall, located 3.7 cm above the floor level, between the two retractable levers. Only one lever, set at minimum effort, was operational during the experimental sessions. Head entries were measured by means of a photocell beam located at the entrance of the aperture. During experimental sessions, chambers were indirectly lit by a 25-W light bulb placed in the soundproof wooden cabinets. Inside each chamber, a fan produced masking background noise (approximately 60 dB). Lever presses and magazine entries were recorded using MED-PC-IV software in a Windows-7 environment.

**Procedure**. Rats were randomly assigned to two groups (CR and PR; $n$ = 12 per group). Autoshaping training involved 12 sessions, and each session included 12 trials separated by a variable intertrial interval of 180 s (range: 120-240 s). In the CR condition, each trial involved the presentation of a lever for 20 s always followed by the delivery of 5 pellets at a rate of 1 pellet per 0.2 s (100% chance of reward). In the PR condition, the presentation of the 20-s lever was randomly followed by either 5 pellets or nothing (50% chance of reward). Previous research showed that sign-tracking responses develop rapidly and to a high asymptotic level with the reward and ITI parameters used in this experiment (Thomas, Honeycutt, & Papini, 1998). As a result, these parameters have been adopted in a variety of subsequent experiments, including this one.

At the end of acquisition, saline, CDP, and PPX were administered in a within-subject design (drug sequence counterbalanced) in four additional sessions. Saline controls received either an intraperitoneal or subcutaneous injection to match the route of administration of CDP and PPX, respectively. A clearance period of two days between drug tests was included; no training was carried out during these clearance days. CDP hydrochloride (5 mg/kg, ip, at a volume of 1 ml/kg) was dissolved in saline (0.9% sodium chloride) and injected 20 min before the session. PPX dihydrochloride (0.4 mg/kg, sc, equal volume) was dissolved in saline and injected 10 min before the session. All drugs were purchased from Sigma-Aldrich (Madrid, Spain).

Lever presses and magazine entries were registered for the entire session and also in 1-s bins during the 20-s lever presentations for within-trial assessment of performance, assigning responses to the bin where they were initiated. To analyze the stability of performance during the trial, lever presses and magazine entries per 1-s bins were calculated for bins 7-13 and bins 14-20 on sessions 7-9 and 10-12, once animals had reached a stable performance. This selection of bins aimed at comparing time intervals of intermediate length to assess behavioral changes from the middle to the end

of the trial. Moreover, the middle-to-end of trial comparison is where frustration and incentive hope theories make contrasting predictions. A similar statistical approach including within-trial performance (1-s bin) was used for sessions in which saline or drugs were administered either via sc or via ip. The dependent variables were lever presses per trial or bin, and magazine entries per trial or bin. Mixed-model analyses of variance (ANOVAs) and dependent-sample *t*-tests were computed using IBM SPSS v. 26. Pairwise LSD comparisons were derived from the main ANOVAs to identify the source of significant interactions. An alpha level less than 0.05 applied to all tests.

Many analyses of sign and goal tracking focus on individual differences (e.g., Flagel, Clark, Robinson, Mayo, Czui, & Willuhn et al., 2011; Iliescu, Hall, Wilkinson, Dwyer, & Honey, 2018; Lopez, Karlson, & O'Donnell, 2015). Separating the two phenotypes was here not possible given the limited sample size in each group. However, the PR vs. CR effects are typically reported in undifferentiated groups of rats (e.g., Boakes, 1977; Glueck et al., 2018; Robinson, Anselme, Fischer, & Berridge, 2014). We studied sign- and goal-tracking behaviors separately within the same individuals to determine whether competition-induced symmetrical effects in behavioral expression could be observed (Boakes, 1977)

## RESULTS

**Acquisition**. Figure 1 shows the results of the 12 acquisition sessions for each group in terms of lever presses per trial (top) and magazine entries per trial (bottom). There was no evidence of the PRAE in terms of either variable. Schedule (CR, PR) by Session (1-12) ANOVAs uncovered only significant changes across sessions for both dependent variables, $F$s(11, 242) > 2.21, $p$s < 0.02, $\eta^2$s > 0.09. The Schedule and Schedule by Session effects were nonsignificant, $F$s < 1. There was a degree of individual variation in these data. For example, 4/12 animals in Group CR responded to the lever at very low levels. The average lever-presses/magazine entries per trial across all 12 sessions for these animals were 0.06/6.03, 0.08/3.06, 0.03/2.34, and 0.06/12.39, and they had zero lever presses in 10, 6, 9, and 7 sessions, respectively. These animals can be classified as goal trackers according to the criterion traditionally used (Meyer, Lovic, Saunders, Yager, Flagel, Morrow et al., 2012). By contrast, none of the rats in Group PR were goal trackers to the same degree. Only three PR rats produced zero lever presses and only in 1 or 2 sessions.

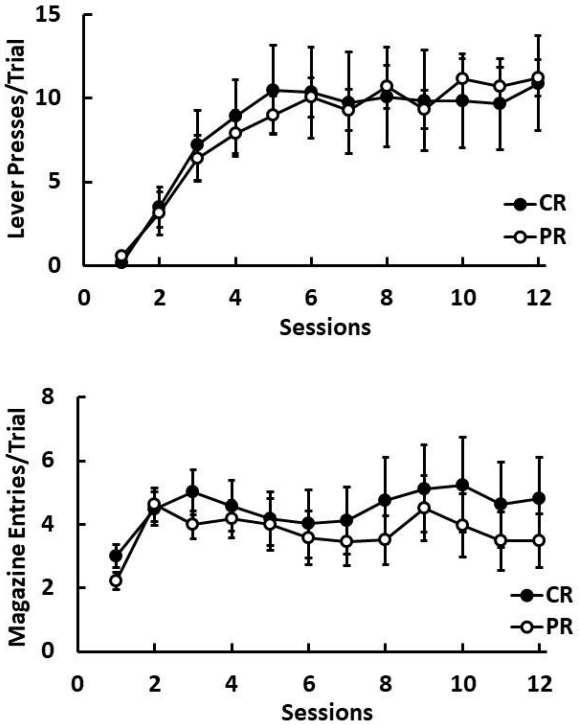


**Figure 1.** Mean (±SEM) lever presses per trial (top) and magazine entries per trial (bottom) in animals trained under continuous reinforcement (CR) or partial reinforcement (PR) across 12 acquisition session in Pavlovian autoshaping.

To determine whether the PRAE would be present in those animals that responded to the lever at the highest level, the six rats with the highest lever-presses per trial over the entire 12 acquisition sessions were selected from each group. Their average performance for lever presses/magazine entries per trial for each dependent variable was 14.72/3.60 and 10.82/3.09 for Groups CR and PR, respectively. Schedule differences for lever pressing and magazine entries were nonsignificant, $F$s < 2.81, $p$s > 0.12, $\eta^2$s < 0.23. The difference in lever pressing came closest to significance, but it was opposite to the PRAE: Lever presses per trial were higher in Group CR than PR.

To assess possible changes within the trial, responses for bins 7-13 and 14-20, for the blocks of sessions 7-9 and 10-12 were computed. The means (±SEMs) are presented in Table 1. Schedule (CR, PR) by Bin (7-13, 14-20) by Block (7-9, 10-12) analyses were computed, with Bin and Block as repeated-measure factors, for lever pressing and magazine entries. For lever pressing, there was a significant Bin by Block interaction, $F(1, 22) = 7.82$, $p < 0.02$, $\eta^2 = 0.26$. All other effects were nonsignificant, $F$s < 3.03, $p$s > 0.09.

Pairwise LSD comparisons revealed that lever pressing decreased across bins during sessions 10-12, $p < 0.02$, but not during sessions 7-9, $p > 0.76$. A similar analysis for magazine entries yielded the following results. In this case, the Bin by Block interaction, $F(1, 22) = 5.43$, $p < 0.03$, $\eta^2 = 0.20$, and the main effect of Bin, $F(1, 22) = 18.95$, $p < 0.001$, $\eta^2 = 0.46$, were both significant. Pairwise LSD comparisons indicated that the within-trial increase in magazine entries was significant in Sessions 7-9 and 10-12, $p$s $< 0.003$. Therefore, as sign tracking decreased toward the end of the CS, goal tracking increased, suggesting a competitive relationship. Importantly, these within-CS changes were similar in CR and PR animals.

**Table 1.** Within-trial analyses during acquisition sessions

| | | Sessions 7-9 | | Sessions 10-12 | |
|---|---|---|---|---|---|
| Group | Behavior | Bins 7-13 | Bins 14-20 | Bins 7-13 | Bins 14-20 |
| CR | Lever pressing | 6.3 (±2.0) | 6.1 (±2.1) | 6.5 (±1.9) | 5.9 (±2.0) |
| PR | Lever pressing | 5.6 (±0.7) | 6.1 (±0.7) | 6.8 (±0.7) | 6.1 (±0.7) |
| CR | Magazine entries | 2.9 (±0.8) | 3.3 (±0.9) | 3.1 (±1.0) | 3.7 (±1.0) |
| PR | Magazine entries | 2.3 (±0.5) | 2.5 (±0.5) | 2.1 (±0.5) | 2.6 (±0.6) |

Note. (±SEMs) are presented in this table. CR: continuous reinforcement. PR: partial reinforcement.

**Saline administration route**. Because the PPX and CDP were administered via different routes (sc and ip, respectively), the performance recorded after saline injections was analyzed with a Schedule (CR, PR) by Via (ip, sc) by Bin (1-20) analysis, with the last two factors as repeated measures. For lever pressing, there was a significant change across bins, $F(19, 418) = 5.95$, $p < 0.001$, $\eta^2 = 0.21$, and a significant Via by Bin interaction, $F(19, 418) = 1.75$, $p < 0.03$, $\eta^2 = 0.07$. Pairwise comparisons indicated a significantly higher lever pressing in subcutaneous than in intraperitoneal injections only on bin 14, $F(1, 22) = 7.06$, $p < 0.02$, $\eta^2 = 0.24$. A similar analysis for magazine entries yielded a significant change across bins, $F(19, 418) = 8.43$, $p < 0.001$, $\eta^2 = 0.28$, and also a significant Via effect,

$F(1, 22) = 9.24$, $p < 0.007$, $\eta^2 = 0.30$. None of the other factors were significant for sign tracking or goal tracking. In view of these differences, saline animals receiving the injection via subcutaneous (control for PPX) and intraperitoneal (control for CDP) were kept separate.

Figure 2 represents within-trial changes in both responses, for both groups, for each via of saline administration, averaged for bins. A Schedule (CR, PR) by Via (sc, ip) by Bin (7-13, 14-20) analysis, with the last two factors as repeated-measure factors, yielded the following results. In terms of lever pressing, there was a significant decline toward the end of the trial detected by a main effect of Bin, $F(1, 22) = 9.71$, $p < 0.006$, $\eta^2 = 0.31$. All other effects were nonsignificant, $F$s < 2.66, $p$s > 0.11, $\eta^2$s < 0.10. A similar analysis computed for magazine entries revealed a significant Bin effect, but in the opposite direction, namely, an increase toward the end of the trial, $F(1, 22) = 11.44$, $p < 0.004$, $\eta^2 = 0.34$. There was also a significantly higher level of magazine entries after ip saline injections than after sc saline injections, $F(1, 22) = 10.89$, $p < 0.004$, $\eta^2 = 0.33$. Importantly, none of the factors and interactions involving Schedule was significant.

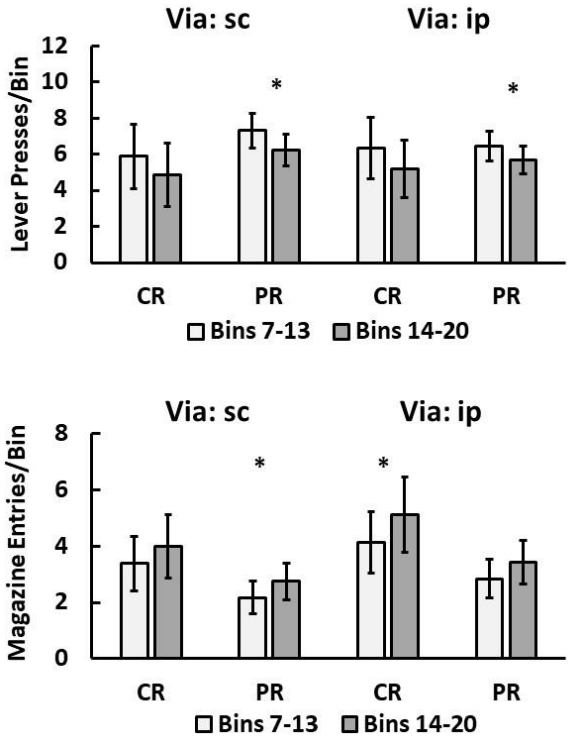


**Figure 2.** Mean (±SEM) lever presses per trial (top) and magazine entries per trial (bottom) in animals trained under continuous reinforcement (CR) or partial

reinforcement (PR), receiving saline administration via subcutaneous (sc) or intraperitoneal (ip). Responses are segregated according to bins 7-13 and 14-20 during the 20-s long lever presentation.

As an additional test of the predictions derived from frustration and incentive hope theories, we compared the performance of each group in the middle vs. end CS period. Frustration theory predicted a reduction in behavior in anticipation of a potential reward omission toward the end of the CS, whereas incentive hope predicted either no effect or even a slight increase in responding close to the goal. In this case, we analyzed the results with dependent-sample *t*-tests (Figure 2). Lever pressing decreased from the middle to the end of the CS presentation, but the reduction was nonsignificant for CR animals, $t$s(11) < 2.16, $p > 0.05$, but significant for PR animals, $t$s(11) > 2.23, $p$s < 0.05. By contrast, magazine entries generally increased from the middle to the ending portion of the CS, but the increase was significant for CR animals receiving ip injections and for PR animals receiving sc injections, $t$s(11) > 2.27, $p$s < 0.05. The increase in magazine entries was not significant for CR animals receiving sc injections and PR animals receiving ip injections, $t$s(11) < 1.82, $p$s > 0.09. The general impression that follows from these results is that sign and goal tracking are in competition for expression, since the reduction in the former is accompanied by an increase in the latter. In addition, it would seem that whereas sign tracking adheres best to frustration theory, goal tracking conforms best to incentive hope.

**Effects of PPX**. Figure 3 shows the results of the sessions involving PPX testing on a within-trial basis. Lever pressing in groups treated with saline showed an early increase that was somewhat higher in the PR condition than in the CR condition, and then responses decreased gradually in both groups. The opposite pattern was observed for saline animals in terms of magazine entries. PPX had a suppressing effect on lever pressing that was apparent in both groups. As for magazine entries, PPX had a more pronounced suppressive effect in Group PR than in Group CR. These results were subjected to a Schedule (CR, PR) by Drug (PPX, Saline) by Bin (1-20) analysis, with repeated measures for the last two factors, that yielded the following results.

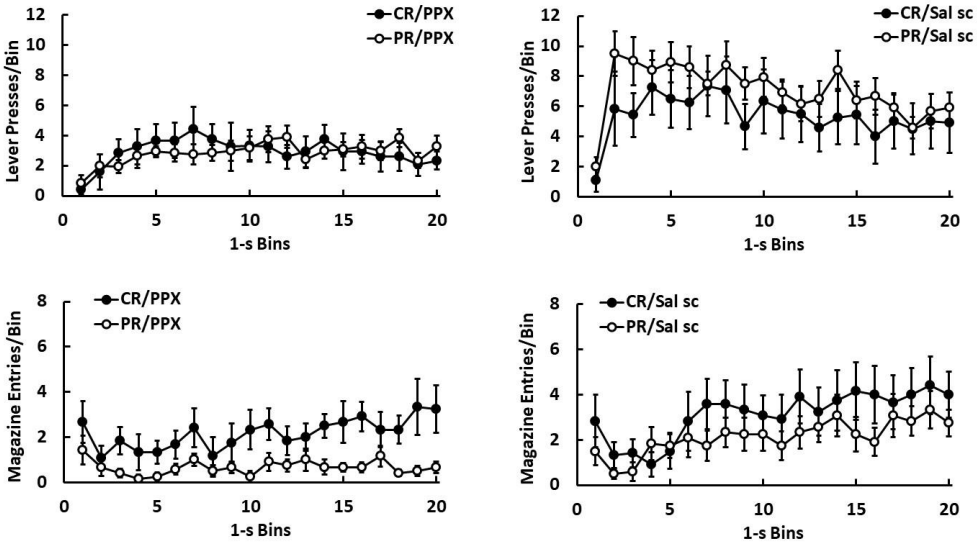


**Figure 3.** Mean (±SEM) lever presses per 1-s bin (top panels) and magazine entries per 1-s bin (bottom panels) in animals trained under continuous reinforcement (CR) or partial reinforcement (PR), after administration of the dopamine D2 agonist PPX or saline (Sal), both via subcutaneous (sc). The abscissa corresponds to 1-s bins of the 20-s long lever presentation.

For lever pressing (Figure 3, top panels), there was a significant Drug by Bin interaction, $F(19, 418) = 3.11$, $p < 0.001$, $\eta^2 = 0.12$, and also significant main effects for Drug and Bin, $F$s > 5.31, $p$s < 0.001, $\eta^2$s > 0.19. The source of the interaction was a higher lever pressing level for saline than PPX animals on all bins except for bins 1 and 18, $p$s < 0.03. To explore the interaction further, separate Drug by Bin ANOVAs were computed for CR and PR conditions. CR animals only displayed a significant change across bins, $F(19, 418) = 3.07$, $p < 0.001$, $\eta^2 = 0.12$, other effects were nonsignificant, $F$s < 2.02, $p$s > 0.17, $\eta^2$s < 0.09. However, PPX significantly affected sign tracking in PR animals. The comparison yielded significantly lower lever pressing in PPX than saline animals, $F(1, 22) = 20.10$, $p < 0.001$, $\eta^2 = 0.48$, a significant change across bins, $F(19, 418) = 4.12$, $p < 0.001$, $\eta^2 = 0.16$ , and also a significant interaction, $F(19, 418) = 3.45$, $p < 0.001$, $\eta^2 = 0.14$. Pairwise LSD comparisons indicated that the source of the interaction was significantly lower lever pressing in PPX compared to saline animals on bins 2-11, 13-17, and 19-20.

Similar results were obtained for magazine entries (Figure 3, bottom panels). The Drug by Bin interaction was significant, $F(19, 418) = 2.38$, $p < 0.002$, $\eta^2 = 0.10$, as well as the main effects for Drug and Bin, $F$s > 4.74, $p$s

< 0.001, $\eta^2$s > 0.18. The interaction effect resulted from a higher level of magazine entries in saline than in PPX animals in bins 5-6, 8-9, and 12-20, *p*s < 0.05. Figure 2 suggests that PPX had a stronger effect on magazine entries in Group PR than in Group CR. Separate Drug by Bin analyses were computed comparing PPX vs. Sal groups for the CR and PR conditions. In both groups, PPX had a suppressive effect on magazine entries, as evidenced by significant Drug effects, *F*s(1, 11) > 6.51, *p*s < 0.03, $\eta^2$s > 0.37. There was also a significant change across bins, *F*s(19, 209) > 2.89, *p*s < 0.001, $\eta^2$s > 0.20. For Group PR there was also a significant Drug by Bin interaction, $F(19, 209) = 2.68$, $p < 0.001$, $\eta^2 = 0.20$, which originated in a higher level of magazine entries in the Sal condition relative to the PPX condition on bins 4-5, 8-10, 12-14, 16, and 18-20, *p*s < 0.04. These analyses indicated that PPX suppressed within-trial sign and goal tracking predominantly in PR animals.

To test whether responding from the middle (bins 7-13) to the end (bins 14-20) portion of the CS changed as differentially predicted by frustration theory and incentive hope theory, we calculated *t*-tests for dependent samples for each group. The results for lever pressing (Figure 4, top) indicated a marginally nonsignificant decrease for CR/Sal animals, $t(11) = 2.16$, $p = 0.054$, and a significant decrease for PR/Sal animals, $t(11) = 2.59$, $p < 0.03$. By contrast, PPX treatment eliminated that within-CS change in performance, *t*s(11) < 1.29, *p*s > 0.22. Similar *t*-tests for magazine entries (Figure 4, bottom) showed no evidence of within-CS change in CR/Sal animals, $t(11) = 1.67$, $p > 0.12$, but a significant increase in PR/Sal animals, $t(1) = 3.21$, $p < 0.009$. The pattern of change was different for groups treated with PPX. Whereas CR/PPX animals showed a significant increase in magazine entries within the CS, $t(11) = 2.47$, $p < 0.04$, there was no evidence of change in PR/PPX animals, $t < 1$. In saline groups the decrease in sign tracking was accompanied by an increase in goal tracking, a pattern suggesting response competition between these two response tendencies. By contrast, PPX eliminated this pattern, both because there was no evidence of a change in sign tracking accompanied by either an increase in goal tracking in CR animals, or no change in goal tracking in PR animals.

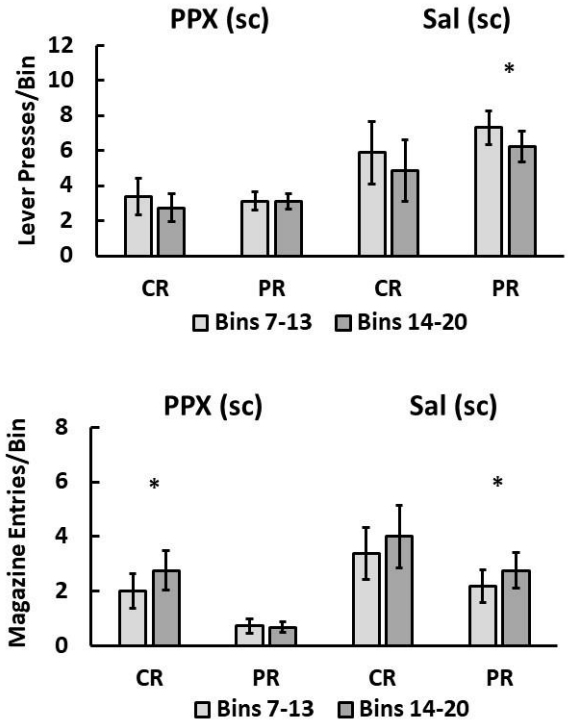


**Figure 4.** Mean (±SEM) lever presses per trial (top) and magazine entries per trial (bottom) in animals trained under continuous reinforcement (CR) or partial reinforcement (PR), receiving either pramipexole (PPX) or saline (Sal) administration via subcutaneous (sc) injection. Responses are segregated according to bins 7-13 and 14-20 during the 20-s long lever presentation

**Effects of CDP**. Figure 5 shows the results of CDP administration on lever pressing and magazine entries. For saline animals, lever pressing was nondifferential in Groups CR and PR, but CR animals tended to perform at a higher level in magazine entries than PR animals. CDP had a suppressive effect on both dependent measures. These results were analyzed with Schedule (CR, PR) by Drug (CDP, Saline) by Bin (1-20) analysis, with repeated measures for the last two factors. The results were the following.

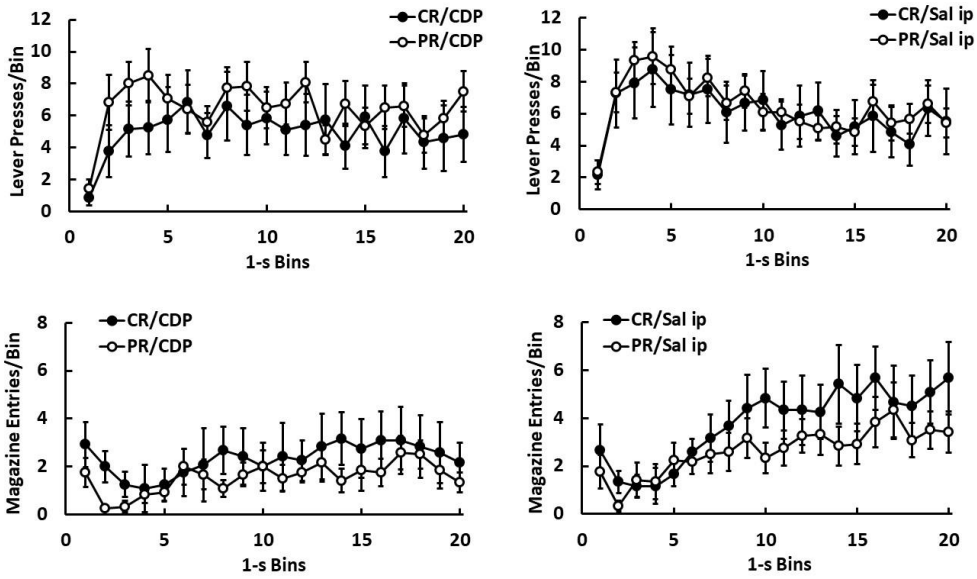


**Figure 5.** Mean (±SEM) lever presses per 1-s bin (top panels) and magazine entries per 1-s bin (bottom panels) in animals trained under continuous reinforcement (CR) or partial reinforcement (PR), after administration of the benzodiazepine chlordiazepoxide (CDP) or saline (Sal), both via intraperitoneal (ip). The abscissa corresponds to 1-s bins of the 20-s long lever presentation.

For lever pressing (Figure 5, top panels), there was a Drug by Bin interaction, $F(19, 418) = 2.65$, $p < 0.001$, $\eta^2 = 0.11$, as well as a significant Bin effect, $F(19, 418) = 5.35$, $p < 0.001$, $\eta^2 = 0.20$. Pairwise LSD tests yielded higher lever pressing performance in Saline than CDP animals on Bins 1 and 7, $p$s $< 0.03$. There was no evidence in these data that the schedule of reinforcement was differentially affected by CDP. Moreover, although there was an increase in performance early in the trial followed by a gradual decline in sign tracking in saline animals, CR and PR animals performed at the same level throughout the trial. To further explore the effects of CDP, separate Drug by Bin analyses were computed for CR and PR conditions. In this case, only changes across bins were significant for both CR and PR conditions, $F$s$(19, 418) > 2.54$, $p$s $< 0.001$, $\eta^2$s $> 0.10$. The drug and drug by bin interactions were nonsignificant for both conditions, $F$s $< 1.38$, $p$s $> 0.12$, $\eta^2$s $> 0.06$.

As for magazine entries (Figure 5, bottom panels), a similar analysis yielded the following results. There was a significant Drug by Bin interaction, $F(19, 418) = 2.78$, $p < 0.001$, $\eta^2 = 0.11$, as well as significant main effects for Drug and Bin, $F$s $> 6.67$, $p$s $< 0.001$, $\eta^2$s $> 0.23$. The source of the interaction was a higher level of magazine entries for saline than CDP

animals on bins 9-17 and 19-20, *p*s < 0.04. The effect of CDP was to flatten within-trial performance for both dependent variables, but there was no indication in these results of differential CR vs. PR performance. As with lever pressing, separate Drug by Bin analyses were computed for CR and PR animals in terms of magazine entries with the same general results. These ANOVAs only uncovered significant changes across bins, Fs(19, 418) > 5.49, ps < 0.001, $\eta^2$s > 0.17. Other factors were nonsignificant, Fs < 2.17, ps > 0.15, $\eta^2$s < 0.09. In light of these results, it would appear that there was no clear evidence that CDP affected sign tracking or goal tracking in either the CR or PR condition.

As an additional test of the predictions based on frustration theory and incentive hope theory, within-trial changes were assessed by dependent-sample *t*-tests for each group. The results for lever pressing (Figure 6, top) indicated a nonsignificant change in CR/Sal animals, $t(11) = 1.18$, $p = 0.26$, but a significant decrease for PR/Sal animals, $t(11) = 2.24$, $p < 0.05$. By contrast, no evidence of change in lever pressing within the trial in animals treated with CDP, *t*s(11) < 1.39, *p*s > 0.19. Similar *t*-tests for magazine entries (Figure 6, bottom) showed no evidence of within CS change in CR/Sal and PR/Sal animals, *t*s(11) < 1.18, *p* > 0.26. The pattern of change was different for groups treated with CDP. Whereas CR/CDP animals showed a significant increase in magazine entries within the CS, $t(11) = 2.28$, $p < 0.05$, a similar increase failed to reach significance for PR/CDP animals, $t(11) = 1.82$, $p > 0.09$. Saline groups again exhibited a correlated change in behavior during the CS: A reduction of sign tracking was accompanied by an increase in goal tracking, a pattern suggesting response competition between these responses. As was the case with PPX, CDP eliminated this pattern, yielding mostly flat response functions from the middle to the ending portions of the CS.

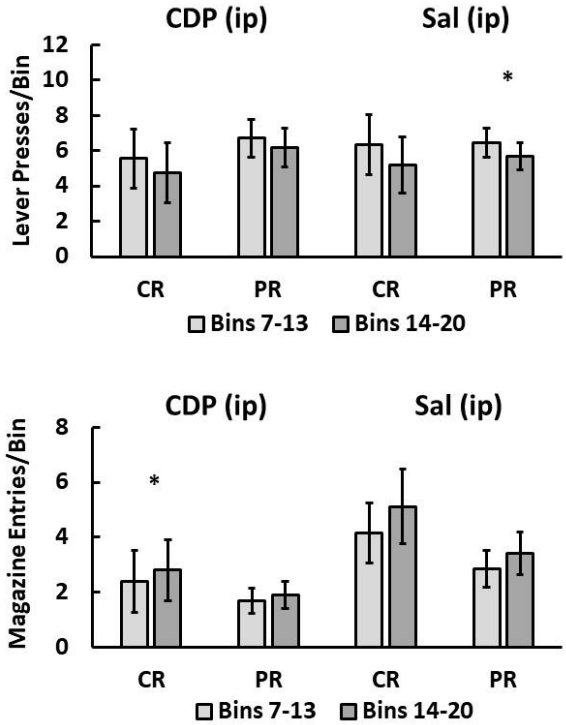


**Figure 6.** Mean (±SEM) lever presses per trial (top) and magazine entries per trial (bottom) in animals trained under continuous reinforcement (CR) or partial reinforcement (PR), receiving either chlordiazepoxide (CDP) or saline (Sal) administration via intraperitoneal (ip) injection. Responses are segregated according to bins 7-13 and 14-20 during the 20-s long lever presentation.

# DISCUSSION

An experiment in which groups of rats received either CR or 50% PR training yielded the following results. First, no evidence of an effect of CR vs. PR training was observed in any of the dependent measures: in lever pressing or magazine entries, across sessions or within trials, and whether saline, PPX, or CDP was administered. Functionally, these two conditions (CR and PR training) operated as if they were a single one since none of the statistical analyses revealed an effect of the schedule of reinforcement. Second, sign-tracking responses were stable during the middle sessions of acquisition (sessions 7-9), although they decreased toward the end of acquisition (sessions 10-12), while magazine entries increased across these session blocks. This applied to both groups. Third, sign-tracking responses declined in both groups during the later portion of the trial relative to the

medial portion of the trial, during the saline sessions. By contrast, goal tracking increased toward the end of the trial in the same sessions. Fourth, the dopamine D2 agonist PPX suppressed sign and goal tracking in PR animals, relative to saline controls, but there was no evidence that it affected CR animals. By contrast, the benzodiazepine anxiolytic CDP did not affect sign tracking or goal tracking in either CR or PR animals.

This experiment was designed to test two competing hypotheses about the PRAE, frustration theory (Amsel, 1992) and incentive hope (Anselme, 2018). Because the PRAE was not observed, we are left in the awkward position of having to postulate an ad-hoc hypothesis that explains the failure. There are at least two possibilities. One explanation for the absence of the PRAE would suggest that one or more training parameters was not optimal to obtain increased lever pressing during PR training relative to CR training. This route does not seem promising for at least two reasons. First, there was a clear acquisition of lever pressing in the present experiment, suggesting that the training parameters were at least sufficiently effective to support learning. Moreover, the level of lever pressing in Group PR in the present experiment was similar to that observed with the same rat strain and similar training parameters in other experiments in which the PRAE was observed. For example, at asymptote, PR animals were responding at a level around 10 lever presses per trial (Figure 1), whereas in Torres et al. (2016) experiment, PR animals were around 8-9 lever presses per trial. Perhaps it was CR animals that were unusually high in the present experiment. The same comparison would suggest 10 lever presses per trial in the present experiment, but only 5-6 lever presses per trial for CR animals in Torres et al.'s (2016) experiment. Second, the PRAE has not been always reported in rat autoshaping (Boughner & Papini, 2008), but it has also been found in several experiments (Boakes, 1977; Anselme et al., 2013; Robinson et al., 2014; Torres et al., 2016; Glueck et al., 2018). This suggests that the PRAE is a replicable phenomenon in autoshaping and that its absence in the present experiment should not reflect the absence of an effect of uncertainty on performance.

A second possibility is that the behavior of CR and PR animals was not different in the present experiment because there was an aspect of the procedure used here that promoted sufficient frustration or uncertainty-induced "hope" in both conditions to render them nondifferential. At least two aspects of the present results are consistent with this possibility. First, lever pressing and magazine entries increased across sessions and, in both cases, they remained stable for at least six of the twelve acquisition sessions (see Figure 1). In analogous experiments, magazine entries tend to peak early in training and then decrease to a low level to remain low for the rest of acquisition and even during a shift to extinction (e.g., Torres et al., 2016;

Glueck et al., 2018). Second, as shown in Figures 2-6, magazine entries tended to increase within the trial. This was especially the case in CR animals, although the schedule effect was nonsignificant (Figures 3 and 5).

One procedural difference that could explain the somewhat peculiar behavioral levels observed in this experiment is the use of a 20-s trial duration. Typically, lever presentations in rat autoshaping last 8-10 s, as in the experiments that provided evidence for the PRAE (Boakes, 1977; Anselme et al., 2013; Robinson et al., 2014; Torres et al., 2016; Glueck et al., 2018). It can be argued that a relatively long CS induces considerable reward uncertainty on two grounds. Temporal delays are frustrating, as shown by experiments involving variable delays of reinforcement that lead to increased resistance to extinction (Crum, Brown, & Bitterman, 1951; Chen, Gross, & Amsel, 1981). Moreover, longer temporal delays increase variability in interval timing, an effect that can be framed in terms of increased reward uncertainty and hope for quicker food delivery (Anselme & Güntürkün, 2019). This scenario suggests that the absence of the PRAE in these data reflects an unintended increase in reward uncertainty in both CR and PR conditions that resulted from the lengthening of CS duration. This was "unintended" since the use of a long CS was introduced to simulate the conditions prevailing in the runway situation in which the PRAE was first described (Goodrich, 1959; Haggard, 1959; Amsel et al., 1964; Chen et al., 1980).

This ad-hoc hypothesis can account for some of the drug effects reported here. Consider first PPX, a dopamine D2 receptor agonist. The effects of PPX were to suppress sign tracking and goal tracking in PR animals, while not affecting either measure in CR animals. As a dopamine D2 receptor agonist and to the extent that reward uncertainty was present in CR and PR conditions, PPX should have increased the motivational impact of incentive hope on behavior, which should have resulted in increased responding, rather than reduced responding and only in PR animals. PPX was shown to stimulate gambling-like behavior in a free-choice task in rats, at increasing doses between 0.03 and 0.3 mg/kg and a time interval of 10 min before testing (Johnson et al., 2011). A reduction in foraging behavior was observed after repeated administration of 0.3 mg/kg of PPX in pigeons (Anselme, Dreher, & Güntürkün, 2018), although extrapolating from pigeons to rats is hazardous. One possibility is that the PPX dose was relatively low, in which case it may have exerted its primary effects on presynaptic dopamine autoreceptors, suppressing the synthesis and synaptic release of dopamine (Dziedzicka-Wasylewska, Ferrari, Johnson, Mireau, Rógoz, Skuza et al., 2001). Another possibility is that the time interval between the PPX injection and the autoshaping test was too short for a single injection. Lagos,

Scorza, Monti, Jantos, Reyes-Parada, Silveira et al. (1998) found that a dose of 500 µg/kg (similar to that used here) decreased dopamine release and locomotion during the first 30 min, but had opposite effects after 2 h. This means that we cannot conclude much from the PPX test, except that it confirms the role of dopamine in rats exposed to uncertainty conditions—possibly shown both in CR and PR individuals here. By contrast, enhancing GABAergic activity and attenuating corticosterone levels by CDP administration should have reduced the intensity of the motivational drive derived from delay-induced frustration and/or incentive hope in both CR and PR animals. Instead, there was no evidence in these results that CDP affected either sign tracking or goal tracking under these conditions.

Overall, these pharmacological effects suggest that different mechanisms support sign and goal tracking under CR and PR conditions of training. Dopamine levels seem to be more important for the behavioral adjustment to PR, but less relevant when animals receive CR training. In turn, GABAergic transmission seems to be less relevant for autoshaping, at least under the present conditions. The fit between these conclusions and the theories tested here is not simple. On the one hand, incentive hope is based on the assumption that sign tracking reflects dopamine levels in the reward pathway (see Introduction for references), and yet a dopamine agonist actually suppressed sign tracking under reward-uncertainty conditions. Special circumstances might be responsible for this effect, as pointed out previously, a possibility that requires further research. On the other hand, frustration theory requires that goal tracking is reduced toward the end of the CS due to anticipatory frustration, but the opposite occurs in saline animals. Such an increase in goal tracking could be accommodated as an example of an increase in motivation for responding induced by anticipatory frustration, but CDP kept goal tracking low across the entire duration of the CS, not just at the end of the CS.

There is also the possibility that the use of a long CS encouraged timing of the 20-s lever presentation, thus resulting in an increase in goal-tracking responses towards the end of the interval and as a consequence a decrease (or stabilization) in sign tracking due to response competition (Papini & Brewer, 1994; Killeen & Pellón, 2013; Pellón & Killeen, 2015), switching rats from sign to goal track (e.g., saline groups in Figures 3 and 5). The temporal control of responding to the CS provides an interpretation of inhibition of delay (e.g., Gallistel & Gibbon, 2000). If magazine entries reflect accuracy of reward timing, the trend toward differential levels of magazine entries could reflect lower timing error when every CS ends in reward (Group CR) than when a random half of the CSs end in reward (Group PR). Consistent with this, albeit nonsignificant, the increase in goal tracking appeared to be

somewhat stronger in Group CR than in Group PR (see Table 1 and Figures 3 and 5). Response competition is almost guaranteed in a long CS autoshaping situation by the mere fact that the rat must approach the magazine to retrieve the food (Pellón, Íbias, & Killeen, 2018). The relatively weaker strength of goal tracking early in the CS would allow for the emergence of sign tracking, a response that is then displaced by a stronger tendency to approach the magazine as CS time advances.

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