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Reward-mediated, model-free reinforcement-learning mechanisms in Pavlovian and instrumental tasks are related

Neema Moin Afshar[1], François Cinotti[2], David A. Martin[3], Mehdi Khamassi[4], Donna J. Calu[3,5], Jane R. Taylor[1,6], and Stephanie M. Groman[1,7,8†]

1. Department of Psychiatry, Yale University
2. Department of Experimental Psychology, University of Oxford
3. Department of Anatomy and Neurobiology, University of Maryland School of Medicine
4. Institute of Intelligent Systems and Robotics, Centre National de la Recherche Scientifique, Sorbonne Université
5. Program in Neuroscience, University of Maryland School of Medicine
6. Department of Psychology, Yale University
7. Department of Neuroscience, University of Minnesota
8. Department of Psychology, University of Minnesota

† Correspondence to be directed to:
Stephanie Groman, Ph.D.; sgroman@umn.edu

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Abstract

Model-free and model-based computations are argued to distinctly update action values that guide decision-making processes. It is not known, however, if these model-free and model-based reinforcement learning mechanisms recruited in operationally based, instrumental tasks parallel those engaged by Pavlovian based behavioral procedures. Recently, computational work has suggested that individual differences in the attribution of incentive salience to reward predictive cues, i.e., sign- and goal-tracking behaviors, are also governed by variations in model-free and model-based value representations that guide behavior. Moreover, it is not appreciated if these systems that are characterized computationally using model-free and model-based algorithms are conserved across tasks for individual animals. In the current study, we used a within-subject design to assess sign-tracking and goal-tracking behaviors using a Pavlovian conditioned approach task, and, then characterized behavior using an instrumental multi-stage decision-making (MSDM) task in male rats. We hypothesized that both Pavlovian and instrumental learning processes may be driven by common reinforcement-learning mechanisms. Our data confirm that sign-tracking behavior was associated with greater reward-mediated, model-free reinforcement learning and that it was also linked to model-free reinforcement learning in the MSDM task. Computational analyses revealed that Pavlovian model-free updating was correlated with model-free reinforcement learning in the MSDM task. These data provide key insights into the computational mechanisms mediating associative learning that could have important implications for normal and abnormal states.

Significance Statement

Model-free and model-based computations that guide instrumental, decision-making processes may also be recruited in Pavlovian based behavioral procedures. Here, we used a within-subject design to test the hypothesis that both Pavlovian and instrumental learning processes were driven by common reinforcement-learning mechanisms. Sign-tracking and goal-tracking behaviors were assessed in rats using a Pavlovian conditioned approach task, and, then instrumental behavior characterized using a multi-stage decision-making (MSDM) task. We report that sign-tracking behavior was associated with greater model-free, but not model-based, learning in the MSDM task. These data suggest that Pavlovian and instrumental behaviors may be driven by conserved reinforcement-learning mechanisms.

Introduction

Cues in the environment that predict rewards can acquire incentive value through Pavlovian mechanisms (Flagel et al., 2009) and are necessary for the survival of an organism by facilitating predictions about biologically relevant events that enable an organism to engage in appropriate preparatory behaviors. Pavlovian incentive learning, however, can imbue cues with strong incentive motivational properties that exert control over behavior, which can lead to maladaptive and detrimental behaviors (Saunders and Robinson, 2013). For example, cues that are associated with drug use can enhance craving in addicts, and, because of their control over behavior, may precipitate relapse to drug-taking behaviors in abstinent individuals (Hammersley, 1992). Understanding the biobehavioral mechanisms underlying associative learning could, therefore, provide critical insights into how stimuli gain incentive salience.

Pavlovian associations have largely been presumed to occur through *model-free*, or stimulus-outcome, learning: cues that are predictive of rewards incrementally accrue value through a temporal-difference signal that is likely to be mediated by mesolimbic dopamine (Huys et al., 2014; Nasser et al., 2017; Saunders et al., 2018). Theoretical work has, however, proposed that Pavlovian associations may also involve learning that is described in the computational field as *model-based* (Dayan and Berridge, 2014; Lesaint et al., 2014a) whereby individuals learn internal models of the statistics of action-outcome contingencies. This hypothesis has been supported by data indicating that Pavlovian associations not only represent accrued value, but also the identity of Pavlovian outcomes (Robinson and Berridge, 2013) and by neuroimaging studies that

identify neural signatures of model-free and model-based learning in humans during a Pavlovian association task (Wang et al., 2020).

Pavlovian autoshaping procedures have been used to quantify the extent to which animals attribute incentive salience to cues predictive of rewards (Flagel et al., 2009, 2011; Nasser et al., 2015). When animals are presented with a cue associated with food reward delivery, the majority of rats – known as sign-trackers (ST) – will approach and interact with the cue, whereas other rats – known as goal-trackers (GT) – will approach the location of the reward delivery (Hearst and Jenkins, 1974; Boakes, 1977). Rats that display sign-tracking behaviors, therefore, attribute incentive salience to the cue, whereas rats that display goal-tracking behaviors do not (Robinson and Flagel, 2009), or at least acquire less incentive to the cue than the goal. Our computational work (Lesaint et al., 2014a; Cinotti et al., 2019) has suggested that these conditioned responses may be linked to individual differences in the extent to which rats use model-free and model-based reinforcement-learning systems to guide their behavior. For example, when using a hybrid reinforcement-learning model to simulate Pavlovian approach behaviors we were able to recapitulate sign-tracking behaviors by increasing the weight of model-free updating and, notably, goal-tracking behaviors by increasing the weight of model-based updating (Cinotti et al., 2019). Variation in Pavlovian approach behaviors in rodents may, therefore, reflect individual differences in model-free and model-based control over behavior (Dayan and Berridge, 2014; Lesaint et al., 2014a).

Use of the multi-stage decision-making (MSDM) task in humans (Daw et al., 2011; Culbreth et al., 2016) and animals (Miller et al., 2017; Groman et al., 2019a;

Akam et al., 2021) has provided empirical evidence that instrumental behavior is influenced by both model-free and model-based reinforcement learning computations. It is not known, however, if the relative contribution of model-free and model-based mechanisms that are recruited in an individual during Pavlovian autoshaping procedures are predictive of their relative contribution during instrumental procedures, such as in the MSDM task (Sebold et al., 2016). If true, this could suggest that the computational mechanisms underlying learning are not unique to Pavlovian or instrumental mechanisms but may represent a common reinforcement-learning framework within the brain that could be useful for restoring the learning mechanisms that are abnormal in disease states (Doñamayor et al., 2021; Groman et al., 2021).

In the current study we sought to test the hypothesis that ST rats would preferentially employ a model-free strategy in an instrumental task, whereas GT rats would preferentially employ a model-based strategy. Pavlovian conditioned approach was assessed in rats (Keefer et al., 2020) before model-free and model-based reinforcement-learning was assessed in a rodent analogue of the MSDM task (Groman et al., 2019a). We report that sign-tracking behavior is correlated with individual differences in reward-mediated model-free, but not model-based, learning in the MSDM task. These data suggest that the model-free reinforcement-learning systems recruited during Pavlovian conditioning parallel those recruited in instrumental learning.

Methods

Subjects

20 Male Long-Evans rats were purchased through Charles River Laboratories at approximately 6 weeks of age. Rats were pair-housed in a climate-controlled vivarium on a 12hr light/dark cycle (lights on at 7 am; lights off at 7 pm). Rats had ad libitum access to water and underwent dietary restriction to 90% of their free-feeding body weight throughout the experiment to maintain the same hunger state in both the Pavlovian and instrumental environments. Experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at Yale University and according to the National Institutes of Health institutional guidelines and Public Health Service Policy on humane care and use of laboratory animals.

Pavlovian conditioned approach

Rats were first trained using a Pavlovian conditioned approach task as previously described (Keefer et al., 2020). During a single trial, a retractable lever (CS) located to the left or right of a food cup was inserted into the chamber for 10s. As the lever retracted, a single sucrose pellet (45 mg; BioServ) was dispensed into the food cup. This CS-US pairing occurred on a variable-interval 60s schedule and each CS-US pairing was present 25 times in each session. Each rat underwent a single, daily session on the Pavlovian conditioned approach task for five consecutive days. The primary dependent measures collected were latency to approach the lever and food cup as well as the number and probability of interactions rats made with the lever and food cup within each session. These dependent measures were used to generate a

Pavlovian score for each session a rat completed (see data analysis). This Pavlovian score is typically referred to as the Pavlovian Conditioned Approach (PCA) score; however, to avoid confusion with the data reduction technique known as principal component analysis (also commonly referred to as a PCA) we refer to this measure as the PavCA score to avoid any confusion.

Deterministic MSDM task

Following the Pavlovian conditioning approach sessions, rats were trained to make operant responses (e.g., nosepokes and lever responses) in order to receive a liquid reward delivery (90 µl of 10% sweetened condensed milk) in different environment than that used for the Pavlovian conditioning approach task. Once operant responding had been established, rats were trained on a deterministic MSDM task using procedures previously described (Groman et al., 2019a). In the deterministic MSDM task, choices in the first stage deterministically led to the second stage state. Second stage choices were probabilistically rewarded. Rats initiated trials by making a response into the illuminated food cup. Two levers located on either side of the food cup were extended into the box and cue lights above the levers illuminated (s_a). A response made on one lever ($s_a a_1$) resulted in the illumination of two noseport apertures (e.g., ports 1 and 2, s_B), whereas a response made on the other lever ($s_a a_2$) would result in the illumination of two other apertures (ports 3 and 4, s_C). Entries into either of the illuminated apertures were probabilistically reinforced using an alternating block schedule.

Each rat was assigned to one specific lever-port configuration (configuration 1: left lever → port 1,2, right lever → port 3,4; configuration 2: left lever → port 3,4, right lever → port 1,2) that was maintained through the study. Reinforcement probabilities assigned to each port, however, were pseudorandomly designated at the beginning of each session (0.90 vs 0.10 or 0.40 vs 0.15; Figure 4A). Sessions terminated when 300 trials had been completed or 90 min had elapsed whichever occurred first. Trial-by-trial data were collected for individual rats and the probability that rats would select the first stage option leading to the highest reinforced second stage option (p(correct|stage1)) was calculated, as well as the probability that rats would select the highest reinforced second stage option (p(correct|stage2)).

Training on the deterministic MSDM task occurred for three primary reasons: (1) to reduce spatial biases that are common in rats, (2) to ensure rats understood the alternating probabilities of reinforcement at the second stage options, and (3) to verify that rats understood the structure of the task and how first stage choices led to different second-stage options. If rats appreciated the reinforcement probabilities assigned to the second state options and how choices in the first stage influence the availability of second-stage options, then the probability that rats choose the first-stage option leading to the second-stage option with the maximum reward probability (e.g., p(correct | stage 1)) should be significantly greater than that predicted by chance. Rats were trained on the deterministic MSDM until they met the criteria of a p(correct|stage1) being significantly greater than chance in four of the five sessions after completing the 35th training session on the deterministic MSDM. If rats did not meet the criterion after

193 completing 43 sessions on the deterministic MSDM (N=3), training was terminated
194 regardless of p(correct|stage1).
195
196 *Probabilistic MSDM task*
197 Choice behavior was then assessed in the probabilistic MSDM task. Initiated
198 trials resulted in the extension of two levers and illumination of cue lights located above
199 each lever. For most trials (70%), first-stage choices led to the illumination of the same
200 second-stage state that were deterministically assigned to that first-stage choice in the
201 deterministic MSDM (referred to as a *common transition*). On a limited number of trials
202 (30%), first-stage choices led to the illumination of the second-stage state most often
203 associated with the other first-stage choice (referred to as a *rare transition*). Second-
204 stage choices were probabilistically reinforced using the same alternating block
205 schedule as that of the deterministic MSDM task. Rats completed 300 trials across five
206 daily sessions on the probabilistic MSDM task.
207 Trial-by-trial data (~1500 trials/rat) were collected to conduct logistic regression
208 analyses of decision making (described below). One rat was excluded from all analyses
209 due to an extreme bias in the first-stage choice (e.g., rat chose one lever on 97% of all
210 trials, regardless of previous trial events).
211
212 *Data analysis*
213 Pavlovian Conditioned Approach
214 To quantify the degree to which individual rats display sign-tracking or goal-
215 tracking behaviors, a PavCA score was calculated for individual rats by averaging three

standardized measures collected, as previously described (Meyer et al., 2012). These three measures were: 1) a latency score which was the average latency to make a food cup response during the CS, minus the latency to lever press during the CS, divided by the duration of the CS (10 s), 2) a probability score which was the probability that the rat would make a lever press minus the probability that the rat would make a food cup response across the session, and 3) a preference score which was the number of lever contacts during the CS, minus the number of food cup contacts during the CS, divided by the sum of these two measures. The PavCA score ranged between -1.0 and 1.0, with values closer to 1.0 reflecting a greater prevalence of ST behaviors and values closed to -1.0 reflecting a greater prevalence of goal-tracking behaviors. Previous studies have calculated the average PavCA score from the last two Pavlovian sessions rats complete to classify rats as either exhibiting high or low ST behaviors (Morrison et al., 2015; Rode et al., 2020), as goal-tracking behaviors are less commonly observed within the population. We refer to this average measure as the summary PavCA score. We conducted a similar median split of the distribution of summary PavCA scores and classified rats as either exhibiting high sign-tracking behaviors (high ST rats; N=10) or low sign-tracking behaviors (low ST rats; N=10). All group-level analyses reported in the current study were conducted using this binary classification.

Additionally, a trial-by-trial Pavlovian score was calculated to serve as the dependent measure used in the computational analyses described below. Latency, probability, and preference scores were calculated on each trial and the average of these measures used to categorize an individual trial as approach to the lever or approach to the magazine. Specifically, the latency score was the average latency to

239 make a food cup response minus the latency to make a lever press during the CS
240 divided by the duration of the CS on that trial. The probability score was the probability
241 that rats would make a lever press (+1) versus make a food cup response (-1) on that
242 trial. The preference score was the number of lever contacts during the CS minus the
243 number of food cup contact during the CS divided by the sum of these measures for
244 that trial. Although rats could vacillate between these responses within a single trial
245 (e.g., approach lever, check magazine, approach lever) characterizing this within-trial
246 variability is difficult and beyond the scope of the current study. The PavCA score and
247 the trial-by-trial Pavlovian score for each of the five Pavlovian sessions was positively
248 correlated (all R^2>0.94; all p<0.001) suggesting that these measures were capturing the
249 same variability in Pavlovian approach behaviors.
250
251 Model-free and model-based learning in the Pavlovian conditioned approach task
252 We have previously reported that individual differences in Pavlovian approach
253 behavior can be recapitulated using a combination of model-free and model-based
254 reinforcement learning algorithms (Lesaint et al., 2014a; Cinotti et al., 2019). We sought
255 to use this hybrid reinforcement-learning model to index the contribution of these
256 reinforcement-learning systems to the Pavlovian conditioned approach behaviors
257 measured in the current study. This model combines the outputs of these two
258 reinforcement-learning systems to determine the likelihood that rats will approach the
259 lever or approach the magazine on each trial. The structure of each trial of the task is
260 represented by a Markovian Decision Process (MDP) consisting of six different states
261 (Figure 1A) defined by the experimental conditions, such as the presence of the lever or

of the food, and the current position of the rat (e.g., close to the magazine or the lever). There are five different actions (explore the environment or goE, approach the lever or goL, approach the magazine or goM, engage the closest stimuli or $eng_{<L>/<M>}$, and eat the reward), and state transitions given a selected action are deterministic. For example, if a rat in state 1 (s_1) chooses the action goL, it will always lead to state 2 (s_2) whereas if a rat in state 1 (s_1) chooses the action goM, it will lead to state 3 (s_3). Action values for all possible actions in the current state are generated by the decision-making model which consists of both a Model-Based (MB) and a Feature Model-Free (FMF) reinforcement-learning algorithm (Figure 1B). The MB and FMF value estimates are combined as a sum into a weighted value determined by the parameter ω. An ω parameter closer to 1 indicates that action values are more influenced by the MB computations, whereas an ω parameter closer to 0 indicates that action values are more influenced by the FMF computations. The weighted values are fed into a softmax function representing the action selection mechanism.

The FMF system, compared to instrumental reinforcement-learning algorithms, assigns value representations to the features associated with each action, rather than to the states of the task, which allows a generalization of values between different states. For example, when the rat goes towards the magazine in state 1 (s_1) or engages the magazine in state 3 (s_3), it does so motivated by the same feature value (e.g., V(M)) in these two different states which means V(M) is updated twice in the course of a single trial. After each action, the value of the corresponding feature is updated according to a standard temporal difference (TD) learning rule by first computing a reward prediction error (δ):

$$\delta = r - V\big(f(s_t, a_t)\big)$$

where r is equal to 1 or 0 if reward delivery occurs or not, respectively. This reward prediction error is integrated in the current estimate of the value of the chosen feature

$$V\big(f(s_t, a_t)\big) \leftarrow V\big(f(s_t, a_t)\big) + \alpha\delta$$

with the learning rate (e.g., α) is bounded between 0 and 1. In contrast to our previous FMF algorithm, the discounting parameter γ was not included here. This was because our model comparisons (described below in Results) indicated that this parameter was not explaining unique variance in approach behavior of this group of rats.

The TD learning rule was only applied to the selected feature (E, environment; L, lever; M, magazine) in each state transition, except in the case of food, which was equal to 1, the value of reward. Because the rat is likely to visit the magazine during inter-trial interval (ITI), the values of the magazine are revised between state 5 and state 0 according to the following equation:

$$V(M) \leftarrow (1 - u_{ITI}) \times V(M)$$

where u_{ITI} determines the rate at which action values for the magazine ($V(M)$) decay during ITI.

The MB system relies on learned transition *T* and reward *R* functions for updating action values. The transition value function aims to determine the probability of going from one state to the next given a certain action. After transitioning from state s_t *to* $s_{t+1}$by performing action a_t, the transition $T(s_t, a_t, s_{t+1})$ is updated according to the following:

$$T(s_t, a_t, s_{t+1}) \leftarrow (1-\alpha)T(s_t, a_t, s_{t+1}) + \alpha$$

with initial values of *T* set to 0 for all possible state and action combinations. The *T* values for unvisited states are decreased according to the following:

$$T(s_t, a_t, s_{t+1}) \leftarrow (1-\alpha)T(s_t, a_t, s_{t+1})$$

Because the environment is deterministic, *T(s,a,s)* should converge perfectly towards values of 1 for all possible state transitions and remain at a value of 0 for all impossible state transitions (e.g., $s_1 \rightarrow s_4$). Similarly, the reward function *R(s,a)* is updated according to the following:

$$R(s_t, a_t) \leftarrow (1-\alpha)R(s_t, a_t) + \alpha r$$

where *r* is set to 1 for (s_5, eat) and 0 otherwise. Initially, *R(s,a)* is equal to 0 for all state-action pairs. Across actions and experience in each state, *R(s,a)* will converge to a value of 1 for (s_5, eat) state-action pair and remain at a value of 0 for all other state-action pairs. The action-value functions for each possible action a_i in the current state s_t are then calculated according to the following:

$$Q(s_t, a_i) = R(s_t, a_i) + \gamma \sum_j T(s_t, a_i, s_j) \max_k Q(s_j, a_k)$$

where γ is the discounting parameter. Once the FMF and MB systems have outputted the feature values and the advantages of the possible actions, these are integrated through a weighted sum:

$$P(s_t, a_i) = \omega Q(s_t, a_i) + (1-\omega)V(f(s,a))$$

with ω bounded between 0 and 1. These integrated values are then entered into a softmax function to compute the probability of selecting each action:

$$p(a_t = a_i) = \frac{e^{\beta P(S_t, a_i)}}{\sum_j e^{\beta P(S_t, a_j)}}$$

where β is the inverse temperature parameter quantifying choice stochasticity.

This model contained five free parameters: the learning rate α, the discounting factor γ, the inverse temperature β, the ITI update factor u_{ITI}, and the integration factor ω. Trial-by-trial behavior was classified as either being a sign-tracking or goal-tracking behavior and fit with five free parameters selected to maximize the likelihood of each rat's sequence of behavior as follows:

$$L = \sum_{trials} ln\big(P(a_t|\alpha, \beta, \gamma, \omega, u)\big)$$

To avoid local maxima, starting values for each free parameter were optimized using a grid search such that each parameter had three possible initial values and all 3^5 possible combinations were tested as the starting point of the gradient descent procedure to maximize the likelihood *L*. Each Pavlovian session only contained 25 trials which proved to be difficult for obtaining reliable parameter estimates from this reinforcement-learning model. To improve accuracy and reliability of parameter estimates and model fit, trial-by-trial data for all five of the Pavlovian sessions were concatenated into a single data set for individual rats and analyzed with the reinforcement-learning model. The parameter estimates that yielded the largest log-likelihood were retained and are reported in Table 1.

Logistic regression of choice data in the MSDM tasks

We have previously shown that the choice behavior of rats in the MSDM task is guided by previous trial events, such as previous trial outcome, choice, and – in the probabilistic MSDM task – state transitions. Trial-by-trial choice data in the deterministic and probabilistic MSDM was analyzed with a logistic regression model using the glmfit function in MATLAB (MathWorks, Inc. v 2017a). These logistic regression models predicted the likelihood that rats would select the same first-stage choice on the current trial (trial *t*) that they had on the previous trial (trial *t-1*), namely the probability of staying or *p(stay)*. The model used to analyze choice data in the deterministic MSDM contained the following predictors:

Intercept: +1 for all trials, which quantifies the tendency for rats to repeat the same first stage option regardless of any other trial events.

Correct: +1 for trials where the rat selects the first stage option with a common transition leads to the highest reinforced stage 2 option.

-1 for trials where the rat selects the first stage option with a common transition leads to the lowest reinforced stage 2 option.

Outcome: +1 if the previous trial resulted in a rewarded outcome

-1 if the previous trial resulted in an unrewarded outcome

The model used to analyze choice data in the probabilistic MSDM contained the same predictors as described above as well as two additional predictors:

Transition: +1 if the previous trial included a common transition

-1 if the previous trial included a rare transition.

Transition-by-Outcome: +1 if the previous trial included a common transition and was

rewarded or if it included a rare transition and was unrewarded.

-1 if the previous trial included a rare transition and was rewarded or included a common transition and was unrewarded.

The "correct" predictor in the logistic regression prevents spurious loading on to the transition-by-outcome interaction predictor (Akam et al., 2015) that can occur when using blocked schedules of reinforcement in the MSDM task. We included the "correct" predictor in all logistic regression models to ensure consistency across analyses and MSDM tasks. Critically, the regression coefficient applied to "outcome" quantifies model-free behavior and the regression coefficient applied to the "transition-by-outcome" interaction quantifies model-based behavior.

Logistic regression of rewarded and unrewarded outcomes

We found that individual differences in the summary PavCA score was related to variation in the outcome regression coefficient (see Results, below). To determine if this relationship was due to differences in the influence of rewarded and/or unrewarded outcomes on choice behavior, we analyzed choice data in the MSDM task using a different logistic regression model that estimated the likelihood that rats would repeat the same first stage choice based on whether the previous trial was rewarded or unrewarded. This logistic regression model, unlike the first, permitted an independent analysis of how each trial outcome (rewarded or unrewarded) influenced first-stage choices. The predictors included in this model were as follows:

Intercept: +1 for all trials. This quantifies the tendency for rats to repeat the same first-stage option regardless of any other trial events.

Rewarded: +1 if the previous trial was rewarded and the rat chose the same lever (first -stage choice) that was selected on the subsequent trial
-1 if the previous trial was rewarded and the rat chose a different lever (first-stage choice) than what was selected on the subsequent trial
0 if the previous trial was unrewarded

Unrewarded: +1 if the previous trial was unrewarded and the rat chose the same lever that was selected on the subsequent trial
-1 if the previous trial was unrewarded and the rat chose a different lever than what was selected on the subsequent trial
0 if the previous trial was rewarded

Positive regression coefficients for the rewarded and unrewarded predictor indicate that rats are more likely to persist with the same first-stage choice, whereas negative regression coefficients indicate that rats are more likely to shift their first-stage choice. The probability that rats would repeat the same first stage choice following rewarded and unrewarded trials was also calculated to examine how this more traditional measure of win-stay and lose-stay behaviors might differ between high and low ST rats.

Statistical analyses

Values presented are mean ± SEM, unless otherwise noted. Statistical analyses were conducted in SPSS (version 26; IBM Corp., Armonk NY), MATLAB (version 2017a; Mathworks) and R (https://www.R-project.org). Generalized linear models (GLM; R glmfit package) were used to analyze the relationship between the summary Pavlovian

score and choice behavior of rats in the MSDM task. The dependent variable was a binary array coding for whether the first stage choice was the same (+1) or different (0) from the previous trial. Predictors in the model could be correct, outcome, transition, the transition-by-outcome interaction, and summary PavCA score or the binary classification of low ST or high ST rats. All higher order (e.g., summary PavCA score x outcome x transition) and lower order (e.g., summary PavCA score x outcome) interactions were included in the model. Significant interactions were tested using progressively lower order analyses. Another GLM was used to examine the relationship between the summary PavCA score and the influence of rewarded and unrewarded outcomes on first-stage choices. The dependent variable was a binary array coding for the first-stage choice (+1 for left lever and 0 for right lever). Predictors in the model were reward, unrewarded, and summary Pavlovian score. All interactions (e.g., summary PavCA score x rewarded) were included in the model and significant interactions tested using lower order analyses.

All other analyses were performed in SPSS. Repeated measures data were entered into a generalized estimating equation (GEE) model using a probability distribution based on the known properties of these data. Specifically, event data (e.g., number of trials in which rats chose the highest reinforced first stage option) were analyzed using a binary logistic distribution. Relationships between dependent variables (e.g., ω and model-free learning) were tested using the Spearman's rank correlation coefficient.

Results

Pavlovian Conditioned Approach

Pavlovian incentive learning was assessed in rats in a Pavlovian conditioned approach task for five days (Figure 2A,B). The summary PavCA score was calculated, and a median split conducted to classify rats as exhibiting either a high (N=10) or low (N=9) sign-tracking behaviors (Figure 2C). As expected, the PavCA score increased across the sessions in the high ST group (Wald $\chi^2 = 91.33$; $p<0.001$) but not in the low ST group (Wald $\chi^2 = 0.23$; $p=0.63$; Figure 2D). We then examined how lever and food-cup directed behaviors changed across the five Pavlovian conditioning sessions in both high and low ST rats (Figure 2E-G). Post-hoc analysis of the group (high vs. low ST) x session interaction (Wald $\chi^2 = 30.37$; $p<0.001$) indicated that the latency score, the probability score, and the preference score increased across the Pavlovian sessions in the high ST group (Wald $\chi^2 = 68.28$; $p<0.001$), but not in the low ST group (all Wald $\chi^2 < 0.99$; $p>0.32$). These session-dependent changes in the high ST rats are similar to observations that we, and others, have reported using Pavlovian conditioned approach tasks (Flagel et al., 2011; Saunders and Robinson, 2011; Keefer et al., 2020).

Computational analysis of Pavlovian approach behavior

Each Pavlovian session consisted of only 25 trials which limited our ability to obtain reliable and accurate reinforcement-learning parameter estimates for each session and each rat. To overcome this, we concatenated the trial-by-trial data from all five Pavlovian sessions into a single 125 trial dataset for individual rats and fitted these data with the hybrid model described above and estimates of the five parameters (e.g.,

457 $\alpha, \beta, \gamma, u_{ITI}, \omega$) are presented in Table 1. We also compared the fits of this hybrid model
458 to other variants of this model in which the ω parameter, which quantifies the degree to
459 which behavior in the Pavlovian approach task is guided by MB and/or FMF learning,
460 was fixed at a value of 1 (e.g., no FMF contribution to the action values) or at a value of
461 0 (e.g., no MB contribution to the action values). The model in which the ω was fixed at
462 a value of 0 had the lowest BIC indicating the FMF-only model best explained the
463 behavior of most rats. This was consistent with the distribution of the Pavlovian scores
464 we observed (see Figure 2C, above) indicating that most rats in the current study
465 exhibited high ST behaviors. The BIC for rats that had the strongest goal-tracking
466 behavior, however, was lowest when the ω was fixed at a value of 1, indicating that the
467 full hybrid model is only required for some individuals. These results suggest that
468 although the FMF-only model (e.g., ω=0) is sufficient in explaining the behavior of most
469 rats in the current study, this is likely an artifact of the large proportion of ST, and few
470 GT, rats in the current cohort and would not be the case with larger samples sizes
471 consisting of more GT rats. Because the current study sought to characterize behavioral
472 variation at an individual level, we believe that the hybrid model in which the ω is a free
473 parameter and can vary for each individual rat is better suited to achieve this goal.
474 We found that some of the parameter estimates were on extreme ends of the
475 distribution and/or boundary, likely because we were trying to optimize five parameters
476 with a limited number of trials (~125 trials/rat). In order to improve model fit, we fixed
477 four of the parameters ($\alpha, \beta, \gamma, u_{ITI}$) to the median value estimate obtained from the
478 hybrid model and optimized only the ω parameter for each individual rat, as we have
479 previously done (Lesaint et al., 2014a). The BIC of this reduced model was lower than

480 the FMF-only model (Table 2) and the ω parameter estimate distribution was found to
481 be less extreme than those observed with the hybrid model (Figure 3A). Moreover, the
482 ω parameter estimate from the full model was correlated with the ω parameter obtained
483 from the restricted model (Spearman's ρ=0.87; p<0.001; Figure 3B) suggesting that the
484 restricted model with only a single free parameter (e.g., ω parameter) was able to
485 capture the individual differences observed with the full hybrid model. Our subsequent
486 analyses involving the ω parameter were those estimates obtained using the restricted
487 model.

488 To ensure that the ω parameter estimate was not being skewed by the dynamics
489 of learning that occurs across the five Pavlovian sessions, we also estimated the ω
490 parameter using the trial-by-trial data collected in the last two Pavlovian sessions (e.g.,
491 50 trials in total). We then compared this estimate that the ω parameter obtained from
492 trial-by-trial data collected in all the Pavlovian sessions (e.g., 125 trials). The ω
493 parameter estimates were positively correlated with one and other (Spearman's ρ=0.41;
494 p=0.08) suggesting that inclusion of earlier sessions when learning was occurring did
495 not bias our estimate of the ω parameter. Subsequent analyses reported below were
496 done using the ω parameter that was estimated from trial-by-trial data from all five
497 Pavlovian sessions.

498 Our previous simulation experiments using this reinforcement-learning model
499 have found that as the ω parameter approaches 0 and the decision-making algorithm
500 favors a FMF system, the prevalence of sign-tracking behaviors increases. We
501 hypothesized, therefore, that the ω parameter would be negatively correlated with the
502 summary Pavlovian scores across rats. Indeed, the ω parameter that was estimated

from the trial-by-trial data collect across the five Pavlovian sessions rats completed was negatively correlated with the summary PavCA score (Spearman's ρ=0.89; p<0.001; Figure 3C). These results, collectively, indicate that the restricted hybrid reinforcement-learning model can capture meaningful variation in Pavlovian approach behavior.

Reward-guided behavior in the deterministic MSDM task is related to ST behaviors

Choice behavior on the deterministic MSDM task was then examined (Figure 4A, B). The probability that rats selected the first-stage choice associated with the most frequently reinforced second-stage option increased across the 35 training sessions (β = 0.012, p<0.001) and was significantly greater than that predicted by chance in the last five sessions that rats completed (binomial test, p<0.001; Figure 4C). Rats were more likely to repeat a first-stage choice that was subsequently rewarded than a first-stage choice that was subsequently unrewarded (Wald χ^2 = 113.57, p<0.001; Figure 4D) indicating that second-stage outcomes were able to influence subsequent first-stage choices. These data, collectively, indicate that rats understood the structure of the deterministic MSDM task and, critically, that their first-stage choices influenced the subsequent availability of second-stage options.

To quantify the influence of previous trial events (e.g., correct, outcome) on first-stage choices, choice data from rats was analyzed with a logistic regression model (Figure 4E; Table 3). The intercept was significantly greater than 0 (z=14.92, *p*<0.001), indicating that rats, similar to humans, were more likely to repeat a first-stage choice regardless of previous trial events. Nevertheless, the effect of outcome was also

525 significantly different from 0 (z=46.56, p<0.001), indicating that rats were using previous
526 trial outcomes (reward and absence of reward) to guide their first-stage choices.
527 We then examined whether individual differences in Pavlovian approach
528 behavior predicted choice behavior of the same rat in the deterministic MSDM task. The
529 summary Pavlovian score was included as a covariate in the logistic regression model
530 and the two-way interaction between outcome and the Pavlovian score examined. The
531 summary Pavlovian score x outcome interaction was a significant predictor in the model
532 (z=7.51; p<0.001; Table 3) and post-hoc analyses indicated that the regression
533 coefficient for outcome was significantly greater in high ST rats compared to the low ST
534 rats (z=9.58; p<0.001; Figure 4F). These data demonstrate that high ST rats were more
535 likely to use previous trial outcomes to guide their choice behavior compared low ST
536 rats.
537 The outcome regression coefficient quantifies the degree to which both rewarded
538 and unrewarded outcomes guide subsequent choice behavior. Differences in the
539 outcome regression coefficient that we observed between high and low ST rats might,
540 therefore, reflect variation in how rats use rewarded or unrewarded outcomes to guide
541 their behavior. To independently assess the impact of rewarded and unrewarded trials
542 on first-stage choices, we conducted a second logistic regression analysis of choice
543 data in the deterministic MSDM task which examined the likelihood that rats would
544 repeat the same first stage choice following a rewarded or unrewarded outcome. The
545 rewarded regression coefficient was positive (β=1.98 ± 0.03; z=71.59; p<0.001)
546 indicating that rats repeated first-stage choices that resulted in reward. The unrewarded
547 regression coefficient was also positive (β=0.33 ± 0.02; z=17.78; p<0.001), but smaller

than that for rewarded regression coefficient (Wald χ^2=106; p<0.001), indicating that rats were more likely to repeat rewarded first-stage choices than unrewarded first-stage choices.

We then examined if the summary Pavlovian score interacted with the rewarded or unrewarded regression coefficients to predict first-stage choices in the deterministic MSDM (Table 4). The interaction between the summary Pavlovian score x rewarded regression coefficient was significant (z=8.93; p<0.001;β=0.51) and post-hoc analyses between the low and high ST groups indicated that the rewarded regression coefficient was greater in high ST rats compared to low ST rats (z=12.89; p=0.001; Figure 4G). The summary Pavlovian score x unrewarded interaction, however, was not significant (z=0.27; p=0.79; β=0.01; Figure 4H). To confirm these differences in outcome-specific behaviors, we compared the probability that rats would repeat a first-stage choice following a rewarded (e.g., win-stay) or unrewarded (e.g., lose-stay) outcome between high and low ST rats. The probability of repeating a first-stage choice following a rewarded outcome was greater in high ST rats compared to low ST rats (Wald χ^2=5.77; p=0.02). No differences were observed for the probability of repeating a first-stage choice following an unrewarded outcome (Wald χ^2=1.50; p=0.22). High ST rats, therefore, used rewarded outcomes to guide their first-stage choices to a greater degree than low ST rats suggesting that these former individual differences in Pavlovian incentive learning are associated with variation in reward-guided instrumental behavior.

Probabilistic MSDM task and relationship to Pavlovian approach behavior

570 To determine if the relationship between the summary Pavlovian score and
571 reward-guided behavior in the above deterministic version of the MSDM task was
572 associated specifically with model-free or model-based reinforcement learning, the
573 choice behavior of rats was assessed in the probabilistic version of the MSDM task
574 (Figure 5A). According to model-free theories of reinforcement learning, the probability
575 of repeating a first-stage choice should be influenced only by the previous trial outcome,
576 regardless of whether the state transition was common or rare (Figure 5B, left). In
577 contrast, model-based theories of reinforcement learning posit that the outcome at the
578 second stage should affect the choice of the first-stage option differently based on the
579 state transition that was experienced (Figure 5B, right). Evidence in humans and in our
580 previous rodent studies, however, indicates that individuals use a mixture of model-free
581 and model-based strategies in the probabilistic MSDM task. Indeed, the probability that
582 rats in the current study would repeat the same first-stage choice according to
583 outcomes received (rewarded or unrewarded) and the state transitions experienced
584 (common or rare) during the immediately preceding trial indicated that rats were using
585 both model-free and model-based learning to guide their choice behavior (Figure 5C).
586 To quantify the influence of model-free and model-based strategies, choice data
587 was analyzed with a logistic regression model (Daw et al., 2011; Akam et al., 2015,
588 2021; Groman et al., 2019b, 2019c). The main effect of outcome, which provides an
589 index of model-free learning, was significantly greater than zero ($z = 22.65$, $p<0.001$;
590 Figure 5D, orange bar) indicating that rats were using second-stage outcomes to guide
591 their first-stage choices. The interaction between the previous trial outcome and state
592 transition, which provides an index of model-based learning, was also significantly

593 greater than zero (z = 15.38, p<0.001; Figure 5D, purple bar). The combination of a
594 significant main effect for outcome and a significant transition-by-outcome interaction
595 suggests that rats were using both model-free and model-based strategies to guide their
596 choice behavior in the probabilistic MSDM task.

597 We then examined whether the summary Pavlovian score interacted with model-
598 free and/or model-based learning to predict the probability of repeating the same first-
599 stage choice in the probabilistic MSDM task (Table 5). The interaction between the
600 summary Pavlovian score and trial outcome significantly predicted choice behavior
601 (z=3.16; p=0.002), but the interaction between the summary Pavlovian score and the
602 outcome-by-transition predictor did not (z=1.60; p=0.11). Post-hoc comparisons
603 between low and high ST rats indicated that the outcome regression coefficient – a
604 measure of model-free learning – was significantly greater in high ST rats compared to
605 low ST rats (z=2.67; p=0.008; β=0.09; Figure 5E), which was a similar effect observed
606 in the deterministic task (see Figure 4F, above). The outcome-by-transition regression
607 coefficient – a measure of model-based learning – did not differ between the low and
608 high ST rats (Figure 5F). These differences in the outcome regression coefficient (e.g.,
609 model-free learning) and lack of differences in the outcome-by-transition coefficient
610 (e.g., model-based learning), collectively, indicate that high ST rats rely to a great
611 degree on model-free learning in the MSDM task compared to low ST rats.

612 Greater model-free learning we observed in high ST rats may be, in part,
613 because high ST rats acquired greater incentive value for the lever used in the
614 Pavlovian conditioning task that then biased responding in the MSDM task. We
615 hypothesized that if this were true, then model-free behavior for the lever used in the

Pavlovian task might be higher than model-free behavior for the lever that was not used in the Pavlovian task. To test this hypothesis, the probability that rats would repeat the same first-stage choice based on the second-stage outcomes (rewarded vs. unrewarded) and state transition (common vs. rare) was calculated for each lever. The difference between the probability of repeating a rewarded first-stage choice and an unrewarded first-stage choice was calculated to obtain an index of model-free learning for each lever. We compared the lever-specific index based on whether the lever in the MSDM task was in the same location as the lever used in the Pavlovian task (referred to as "same") or was in a different location as the lever used in the Pavlovian task (referred to as "different"). We found that the model-free index did not differ between the levers (same lever: 0.21±0.05; different lever: 0.28±0.06; Wald χ^2=0.77; p=0.38). Notably, the model-free index did not differ between the levers in the high ST rats (same lever: 0.26±0.05; different lever: 0.27±0.07; Wald χ^2=0.02; p=0.90) suggesting that prior experience with one of the levers in the Pavlovian conditioning task did not bias high ST rats to use a model-free strategy in the MSDM task.

To determine if the summary Pavlovian score was associated with rewarded or unrewarded outcomes, choice behavior in the probabilistic MSDM task was analyzed with an alternative logistic regression model. Similar to what we had observed in the deterministic MSDM task, the interaction between the summary Pavlovian score and rewarded predictor was significant (z=4.31; p<0.001; β=0.23): high ST rats were more likely to repeat a first-stage choice that led to a rewarded second-stage choice compared to low ST rats (Figure 5G). We also observed a significant interaction between the summary Pavlovian score and the unrewarded predictor (z=-2.69; p=0.007;

639 β=–0.09), but the unrewarded regression coefficient was not statistically different
640 between low and high ST rats (Figure 5H). Moreover, the probability that rats would
641 repeat a first-stage choice following a rewarded, but not unrewarded, outcome was
642 greater in high ST rats compared to low ST rats (rewarded: Wald χ^2=4.39; p=0.04;
643 unrewarded: Wald χ^2=0.30; p=0.58). These results, collectively, indicate that individual
644 differences in Pavlovian approach behavior are associated with variation in reward-
645 mediated, model-free learning.
646
647 *Pavlovian ST behavior is associated with reward-based, model-free updating*
648 We found that Pavlovian conditioned approach behaviors were associated with
649 reward-mediated, model-free learning in both the deterministic and probabilistic MSDM
650 tasks. This suggests that the model-free computations that guide Pavlovian approach
651 behaviors (e.g., FMF learning) may be related to the model-free computations that
652 influence operant choice behavior in the MSDM task. To test this directly, we compared
653 the regression coefficients obtained from the MSDM task in rats who either had a small
654 ω (e.g., more model-free updating in the Pavlovian conditioned approach task) or large
655 ω (e.g., more model-based updating in the Pavlovian conditioned approach task)
656 parameter estimate (Figure 6). We hypothesized that if the Pavlovian FMF mechanisms
657 were related to the operant-based model-free learning then the outcome regression
658 coefficient from the MSDM task would differ in rats with a smaller ω parameter estimate
659 (e.g., greater FMF updating) compared to rats with a large ω parameter estimate (e.g.,
660 greater MB updating). As predicted, the outcome regression coefficient (e.g., model-free
661 learning) was larger in rats with a smaller ω parameter compared to rats with a large ω

parameter (Wald χ^2=6.22; p=0.01; Figure 6A). These differences were specific to model-free learning, as the outcome-by-transition regression coefficient – a measure of model-based learning – did not differ as a function of the ω parameter (Wald χ^2=1.21; p=0.27; Figure 6B). Furthermore, when we compared the rewarded and unrewarded regression coefficients between rats with either a high or low ω parameter, only the rewarded regression coefficient differed between the groups (rewarded: Wald χ^2=6.51, p=0.01, Figure 6C; unrewarded: Wald χ^2=1.42, p=0.23, Figure 6D). These data suggest that the model-free reinforcement-learning systems recruited during Pavlovian conditioning parallel those recruited in the instrumental MSDM task.

673 **Discussion**

674 The current study provides new evidence that the model-free mechanisms that
675 are utilized during the Pavlovian conditioned approach task are related to the model-
676 free mechanisms that guide instrumental decision-making behaviors. We report that a
677 greater prevalence of sign-tracking behaviors in the Pavlovian approach task is
678 associated with greater model-free, but not model-based, learning in the MSDM task.
679 Differences in model-free updating observed in high and low ST rats were associated
680 specifically with reward-guided behaviors: rats with higher sign-tracking behaviors were
681 more likely to repeat a rewarded choice than rats with lower sign-tracking behaviors. No
682 differences in choice behavior following an unrewarded outcome were observed
683 between low and high ST rats. Our data, collectively, provide direct evidence indicating
684 that individual differences in sign-tracking behaviors are associated with reward-based,
685 model-free computations. These results suggest that the model-free mechanisms
686 mediating Pavlovian approach behaviors might be controlled by the same model-free
687 computations that guide instrumental behaviors and utilize conserved learning systems
688 that are known to be altered in psychiatric disorders.

689

690 *Individual differences in model-free computations are conserved across instrumental*
691 *and Pavlovian tasks*

692 Rats with higher sign-tracking behaviors in the Pavlovian approach task were
693 found to have greater model-free reinforcement-learning in both the deterministic and
694 probabilistic MSDM tasks. These data suggest that the mechanisms that assign and
695 update incentive value to cues predictive of rewards might be the same as those that

696 update representations following rewarded actions. We propose, therefore, that
697 Pavlovian and instrumental behaviors are controlled by overlapping model-free,
698 reinforcement-learning mechanisms. Alternatively, the related model-free measures that
699 we quantified in the Pavlovian and MSDM tasks may be driven by unique model-free
700 mechanisms that rely on the same behavioral output. There is evidence that the neural
701 mechanisms governing Pavlovian and instrumental learning differ from one and other
702 (Bouton et al., 2021), but how these neural systems are involved in model-free
703 computations that govern both Pavlovian and instrumental learning is not fully
704 understood. Future studies comparing how reward-mediated, model-free computations
705 are encoded within these discrete circuits across Pavlovian and instrumental
706 environments could provide mechanistic insights into the behavioral correlations
707 observed here.

708 The logistic regression analyses of choice behavior in the MSDM task indicated
709 that rats with higher sign-tracking behaviors were more likely to repeat rewarded actions
710 compared to rats with lower sign-tracking behaviors. This suggests that the degree of
711 action value updating following rewards was greater in rats with higher sign-tracking
712 behaviors and may explain why rats with greater sign-tracking behaviors are more
713 resistant to outcome devaluation and slower to extinguish to reward-predictive cues
714 compared to GT, or lower ST, rats (Morrison et al., 2015; Nasser et al., 2015; Ahrens et
715 al., 2016; Smedley and Smith, 2018; Fitzpatrick et al., 2019; Amaya et al., 2020; Keefer
716 et al., 2020). For example, cached representations of cues predictive of rewards may be
717 exaggerated in individuals with greater sign-tracking behaviors and, consequently, lead
718 to slower adjustments in behavior when the value of the outcome changes. This is not a

general impairment in extinction learning as rates of extinction of operant responses are similar between ST and GT rats (Ahrens et al., 2016; Fitzpatrick et al., 2019). Rather, previous work has proposed that strong attribution of incentive salience to reward-predictive cues may bias attention and lead to inflexible patterns of responding (Nasser et al., 2015; Ahrens et al., 2016; Keefer et al., 2020). Indeed, this may explain why sign-tracking behaviors in rats are associated with suboptimal choice behavior in a gambling task (Swintosky et al., 2021).

We did not, however, observe a relationship between Pavlovian approach behaviors and model-based updating in the MSDM task. This was surprising given our previous theoretical work and the experimental work of others (Lesaint et al., 2014b; Cinotti et al., 2019). The lack of association between the Pavlovian summary score and model-based learning in the MSDM task is likely because we only observed a limited number of GT rats in the current sample. Specifically, only three rats in the current cohort of twenty would have been classified as GT rats (see Figure 2, above). This was not because the distribution of Pavlovian approach behaviors in the current study was abnormal – previous studies using larger sample sizes than the current study (e.g., N=560 vs. N=20) have observed similarly skewed distributions (Fitzpatrick et al., 2013) in food restricted rats (Fraser and Janak, 2017). It is possible that our food restriction procedure biased rats towards a more model-free strategy in both Pavlovian and instrumental environments. Future studies that employ large sample sizes and manipulate hunger states to obtain behavioral measures which span the distribution of Pavlovian approach behaviors may, therefore, find a relationship between goal-directed behaviors and model-based learning.

742 Prior experience with a particular lever in the Pavlovian conditioning task did not
743 appear to bias the behavior of rats in the MSDM task. It is possible, however, that the
744 use of levers in both the Pavlovian and operant environments had a more general
745 influence on behavior in the MSDM task and this influence was greater in high ST rats
746 who attributed greater incentive salience to the lever. Although the testing environments
747 and outcomes (e.g., sucrose pellet vs. sweetened condensed milk solution) used for the
748 Pavlovian and MSDM tasks were different from one another, randomizing the order in
749 which animals proceeded through each of the tasks would have reduced any potential
750 order effects that may be confounding our results. We did consider implementing a
751 cross-over design to reduce any potential order effects but believed that extensive
752 training in the MSDM task first – compared to the limited exposure in the Pavlovian
753 conditioning task – was more likely to impact behavior in the Pavlovian task. A more
754 optimal design would have used different manipulandum in the Pavlovian and
755 instrumental tasks. Nevertheless, this is a limitation of the current study design that we
756 will address in future experiments.
757 The current study was only conducted in male rats which limits our
758 understanding of how these Pavlovian and instrumental reward-based, model-free
759 systems interact in females. Previous studies have not reported robust differences in
760 the prevalence of sign-tracking and/or goal-tracking behaviors between male and
761 female rats (Pitchers et al., 2015) or model-free and model-based learning in male and
762 female humans (Gillan et al., 2015). We would not anticipate observing different results
763 in female rats from those reported here in male rats. Nevertheless, it is possible that the
764 model-free mechanisms mediating Pavlovian approach behaviors in females are not the

765 same model-free computations that guide instrumental behavior. This might explain the
766 divergent learning strategies that have been observed between male and female mice
767 (Chen et al., 2020).
768
769 *Neurobiological mechanisms*
770 Although the neurobiological mechanisms underlying Pavlovian and instrumental
771 learning are not fully understood, dopamine neurotransmission is likely to be a point of
772 convergence between sign-tracking behaviors and reward-guided, model-free updating.
773 Midbrain dopamine neurons are known to encode reward-prediction errors (RPEs),
774 which is a fundamental computation in model-free learning (Hollerman and Schultz,
775 1998). The results of studies using voltammetry to quantifying changes in dopamine
776 concentration in the nucleus accumbens – a main output of midbrain dopamine neurons
777 – have proposed that phasic dopamine signals in ST rats is how incentive salience is
778 transferred from the outcome to cue(s) predictive of reward (e.g., lever extension; Flagel
779 et al., 2011). These dopaminergic RPEs were not observed in goal-tracking rats
780 suggesting that variation in attribution of incentive salience may reflect underlying
781 differences in dopaminergic RPEs (Derman et al., 2018; Lee et al., 2018). Indeed,
782 antagonism of dopamine signaling in the nucleus accumbens attenuates the expression
783 of sign-tracking behaviors (Saunders and Robinson, 2012).
784 Dopamine, however, has also been implicated in model-based reinforcement
785 learning. Individual differences in [^{18}F]DOPA accumulation and dopamine tone in the
786 nucleus accumbens of humans and rats, respectively, are associated with variation in
787 model-based learning in the MSDM task (Deserno et al., 2015; Groman et al., 2019a).

Dopamine may play a role in both reinforcement-learning systems. Indeed, recent studies have reported that both model-free and model-based calculations are encoded in the activity of midbrain dopamine neurons (Sadacca et al., 2017; Sharpe et al., 2017; Keiflin et al., 2019), but the influence of these dopaminergic neurons over behavior – and likely learning systems – is mediated by functionally heterogeneous circuits (Keiflin and Janak, 2015; Saunders et al., 2018). For example, mesocortical dopaminergic projections may encode model-based computations whereas mesostriatal/mesopallidal dopaminergic projections may encode model-free computations (Chang et al., 2015). Studies that integrate circuit-based imaging approaches with biosensor technology (e.g., DLIGHT) to measure circuit-specific dopamine transients in behaving animals could help resolve these critical questions regarding the functional role of dopamine circuits in these learning mechanisms (Kuhn et al., 2018).

Implications for addiction

Differences in the degree to which individuals attribute incentive salience to cues predictive of reward have been hypothesized to confer vulnerability to addiction. Indeed, there is evidence that ST rats will work hard to obtain cocaine (Saunders and Robinson, 2011), show greater cue-induced reinstatement (Saunders and Robinson, 2010; Saunders et al., 2013; Everett et al., 2020), are resistant to punished drug use (Saunders et al., 2013; Pohořalá et al., 2021), have a greater propensity for psychomotor sensitization (Flagel et al., 2008), and, also display a higher preference for cocaine over food (Tunstall and Kearns, 2015) compared to GT rats. Drug self-administration in short access sessions, however, does not differ between ST and GT

811 rats (Saunders and Robinson, 2011; Pohořalá et al., 2021). These data suggest that
812 drug reinforcement may be similar between ST and GT rats, but that ST rats may be
813 more susceptible or prone to developing compulsive-like behaviors following initiation of
814 drug use.

815 Only a few studies have used the MSDM task to examine the role of model-free
816 and model-based learning in addiction susceptibility. In a recent study we reported that
817 individual differences in model-free learning in the MSDM task were predictive of
818 methamphetamine self-administration in long-access sessions (Groman et al., 2019c).
819 This relationship, however, was negative: rats with lower model-free learning in the
820 MSDM task took more methamphetamine than rats with higher model-free learning.
821 Although additional addiction-relevant behaviors were not assessed in this previous
822 study (e.g., progressive ratio, extinction, or reinstatement), the negative relationship
823 between model-free learning and methamphetamine self-administration is surprising
824 given the positive relationship between model-free learning and sign-tracking behaviors
825 we observed here. These data might suggest a dynamic role of model-free learning in
826 the different stages of addiction susceptibility (Kawa et al., 2016). For example, greater
827 model-free learning prior to drug use may protect against drug intake but render
828 individuals more vulnerable to the detrimental effects of the drug when ingested.
829 Indeed, ST rats are less sensitive to the acute locomotor effects of cocaine but have a
830 greater propensity for psychomotor sensitization (Flagel et al., 2008). Future studies
831 that assess Pavlovian conditioned approach behaviors and instrumental reinforcement-
832 learning mechanisms in the same individual prior to evaluating drug-taking and -seeking

behaviors may provide a greater understand of the biobehavioral mechanisms underlying addiction susceptibility.

Summary

The current manuscript provides direct evidence linking incentive salience processes with reward-guided, instrumental behaviors in adult male rats. Our data suggest that Pavlovian approach behaviors and choice behavior of rats in a multi-stage decision-making task are driven by conserved model-free reinforcement-learning mechanisms that are known to be altered in individuals with mental illness, such as addiction (Groman et al., 2022). Future studies integrating systems-level approaches with the sophisticated behavioral and computational approaches used here will provide new insights into the biobehavioral mechanisms that are altered in individuals with mental illness.

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Table 1: Parameter estimates from the full hybrid model. Values presented are those from the 25th, median, and 75th percentile.

	α	γ	β	u_{ITI}	ω
25th	0.88	1	36.05	0.33	0.90
Median	0.26	0.90	5.11	0.12	0.72
75th	0.17	0.56	4.16	0.04	0.20

Table 2: Goodness-of-fit measures for the full hybrid model and other variants. BIC – Bayesian Information Criterion. NA – not applicable.

	Hybrid model	FMF only ($\omega = 0$)	MB only ($\omega = 1$)	Reduced model
Free parameters	$\alpha, \beta, \gamma, \omega, u_{ITI}$	α, β, u_{ITI}	$\alpha, \beta, \gamma, u_{ITI}$	ω
Fixed parameters	NA	ω	ω	$\alpha, \beta, \gamma, u_{ITI}$
BIC	2019	1891	2147	1792

Table 3: Logistic regression for the deterministic MSDM task.

Independent variable	**Beta**	**Z value**	**p value**
Intercept	1.12	14.16	<0.001
Correct	0.17	11.89	<0.001
Outcome	0.73	46.48	<0.001
Summary PavCA score	0.31	1.90	0.06
Outcome x Summary PavCA score	0.27	8.54	<0.001

Table 4: Simple logistic regression for the deterministic MSDM task.

Independent variable	Beta	Z value	p value
Intercept	-0.02	-0.26	0.795
Correct	-0.05	-3.88	<0.001
Rewarded trial	1.91	75.13	<0.001
Unrewarded Trial	0.33	18.78	<0.001
Summary PavCA score	-0.06	-0.30	0.76
Rewarded x Summary PavCA score	0.54	10.47	<0.001
Unrewarded x Summary PavCA score	0.001	0.03	0.98

Table 5: Logistic regression for the probabilistic MSDM task.

Independent variable	Beta	Z value	p value
Intercept	0.87	15.20	<0.001
Correct	0.09	6.60	<0.001
Outcome	0.37	19.77	<0.001
Transition	0.16	8.77	<0.001
Outcome x transition	0.26	13.80	<0.001
Summary Pavlovian score	0.09	0.80	0.42
Outcome x Summary PavCA score	0.13	3.49	<0.001
Transition x Summary PavCA score	0.07	1.88	0.06
Outcome x Transition x Summary PavCA score	0.05	1.41	0.16

Table 6: Simple logistic regression for the probabilistic MSDM task.

Independent variable	Beta	Z value	p value
Intercept	0.05	0.36	0.72
Correct	-0.03	-2.46	0.01
Rewarded Trial	1.45	56.55	<0.001
Unrewarded Trial	0.36	20.35	<0.001
Summary Pavlovian score	0.11	0.44	0.66
Rewarded Trial x Summary PavCA score	0.22	4.40	<0.001
Unrewarded Trial x Summary PavCA score	-0.09	-2.42	0.02

Figure legends:

Figure 1: The FMF-MB decision-making model. (A) The Markov decision process of a single trial from the Pavlovian approach task. There are five possible actions leading deterministically from one state to the next: exploring the environment (goE), approaching the lever (goL), approaching the magazine (goM), engaging with the closest stimulus (eng), and eating the reward (eat). Each of these actions focuses on a specific feature indicated in brackets: the environment (E), the lever (L), the magazine (M), and the food (F). These are the features used by the FMF learning component. The red path corresponds to sign-tracking behavior and the blue path to goal-tracking behavior. (B) Schematic of the FMF-MB decision-making model adapted from Lesaint et al. (2014) and Cinotti et al. (2019). The model combines a MB learning system which learns the structure of the MDP and then calculates the relative advantage of each action in a given state, with a FMF system which attributes a value to different features of the environment which is generalized across states (e.g., the same value of the magazine is used in states 1 and 4). The advantage function and value function are weighted by ω, their relative importance determining the sign- vs goal-tracking tendency of the individual and then passed to the action selection mechanism modelled by a softmax function.

Figure 2: Pavlovian approach task. (A) Schematic of the experimental design. Rats (N=20) underwent five sessions on the Pavlovian approach task before being trained in the deterministic MSDM task (35-43 days) and tested in the probabilistic MSDM tasks (5-7 days). (B) The PavCA score for individual rats across the five Pavlovian sessions.

(C) Distribution of the summary PavCA score obtained from Pavlovian sessions 4 and 5. Rats were divided into two groups based on a median split (red line) of the summary PavCA score – low sign-tracking (ST) rats (N=9) and high ST rat (N=10); (D) The PavCA score for low ST and high ST rats across the five Pavlovian sessions. (E) The latency score increased in high ST rats across the Pavlovian sessions but did not change in the low ST rats. (F) The probability score increased in the high ST rats across the Pavlovian sessions but did not change in the low ST rats. (G) Preference score increased in the high ST rats across the Pavlovian sessions but did not change in the low ST rats.

Figure 3: The hybrid reinforcement model for assessing model-based and model-free mechanisms of Pavlovian learning. (A) The ω parameter estimate in the full (left) and restricted (right) hybrid model. (B) The relationship between the ω parameter in the full hybrid model and the ω parameter from the restricted hybrid model. (C) The relationship between the ω parameter from the restricted hybrid model – estimated from trial-by-trial data for all five Pavlovian sessions - and the summary PavCA score – measured in the last two Pavlovian sessions.

Figure 4: Decision-making in the deterministic MSDM task. (A, top) Rats were trained on the MSDM task in which state transitions were deterministic. (A, below) Stage 2 choices were reinforced according to an alternating block schedule of reinforcement. (B) Schematic of single-trial events. Rats initiated trials by entering an illuminated magazine. Two levers (stage 1) located on either side of the magazine were extended

into the operant box and a single lever response led to the illumination of two port apertures (stage 2) located on the panel opposite to the levers. Entries into the illuminate apertures resulted in probabilistic delivery of reward. (C) Probability of selecting the stage 1 option associated with the highest reinforced stage 2 options (p(correct|stage1)) during the first 35 days of training. The probability that choices were at chance level is represented by the dashed line. (D) The probability that individual rats would choose the same first-stage option following a rewarded or unrewarded second-stage choice. (E) Regression coefficients for the explanatory variables (e.g., correct, outcome) in the logistic regression model predicting the likelihood that rats would make the same first-stage choice on the current trial as they had on the previous trial in the deterministic MSDM task. Positive regression coefficients indicate a greater likelihood that the rat will repeat the same first-stage choice. (F) The outcome regression coefficient was higher in high ST rats compared to low ST rats indicating that second stage outcomes were guiding first-stage choices to a greater degree in high ST rats. (G) The likelihood that rats would repeat the same first-stage choice following a rewarded outcome was greater in high ST rats compared to low ST rats as evidence by differences in the rewarded regression coefficient. (H) The likelihood that rats would repeat the same first-stage choice following an unrewarded outcome did not differ between high and low ST rats. *** $p<0.001$

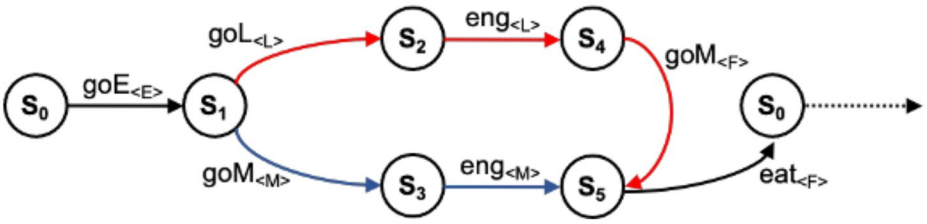
Figure 5: Decision-making in the probabilistic MSDM task. (A) Choice behavior was assessed in the probabilistic MSDM task, which was similar in structure to the reduced MSDM, but the transition between stage 1 and stage 2 was probabilistic. (B)

Hypothetical data for a pure model-free agent (left) and a pure model-free agent (right). The probability of repeating the same first-stage option based on the previous trial outcome (rewarded vs. unrewarded) and the state transition (common vs. rare) .(C) The probability that rats would repeat the same first-stage option based on the previous trial outcome (rewarded vs. unrewarded) and the state transition (common vs. rare). (D) Regression coefficients for explanatory variables (e.g., correct, outcome, transition, and transition-by-outcome) in the logistic regression model predicting the likelihood that rats will choose the same first-stage choice as they had on the previous trial. The outcome regression coefficient (orange bar) represents the strength of model-free learning, whereas the transition-by-outcome regression coefficient (purple bar) represents the strength of model-based learning. (E) The outcome regression coefficient, a measure of model-free learning, was greater in high ST rats compared to low ST rats. (F) The transition-by-outcome regression coefficient did not differ between low ST and high ST rats. (G) The rewarded regression coefficient was greater in high ST rats compared to low ST rats. (H) The unrewarded regression coefficient did not differ between low and high ST rats. ** $p<0.01$; *** $p<0.001$.

Figure 6: Model-free learning in the MSDM is related to model-free learning in the Pavlovian approach task. Trial-by-trial data in the Pavlovian approach task was quantified with the hybrid reinforcement learning model and the degree to which rats used model-based (MB) and/or feature model-free (FMF) learning to guide their behavior quantified with the ω parameter. A median split of the ω parameter distribution was conducted and rats classified as having a low ω parameter estimate (e.g., greater

1199 FMF updating and sign-tracking behaviors) or a high ω parameter estimate (e.g.,
1200 greater MB updating and goal-tracking behaviors). (A) The outcome regression
1201 coefficient – a measure of model-free learning in the probabilistic MSDM task – was
1202 greater in rats with a low ω parameter estimate compared to rats with a high ω
1203 parameter estimate. (B) The transition-by-outcome regression coefficient – a measure
1204 of model-based learning in the probabilistic MSDM task – did not differ between the low
1205 and high ω parameter rats. (C) The rewarded regression coefficient from the MSDM
1206 task was greater in rats with a low ω parameter compared to rats with a high ω
1207 parameter. (D) The unrewarded regression coefficient from the MSDM task in rats with
1208 a low ω parameter did not differ from rats with a high ω parameter. * $p<0.05$
1209

A



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