Social Learning in Rats: The Effects of Orienting Phenotype, Sex, and Social Training

Miriam E. Ortega

Honors Thesis

Department of Psychology, The University of Texas at Austin

Faculty Advisor: Marie-H. Monfils, Ph.D.

Secondary Faculty Advisor: Hongjoo Joanne Lee, Ph.D.

Graduate Student Advisor: Laura A. Agee, Ph.D.

December 2021

Abstract

Rats, like humans, are social animals with the ability to learn through observation, interaction with conspecifics, and direct experience. Animal social learning models provide insight into mechanisms of fear and reward-mediated learning, though individual differences in social learning remains an under-investigated area. Previous studies suggest that an animal's attentional response style to stimuli may represent a difference in information processing. As opposed to those with reward-directed styles ("non-orienters"), rats with cue-directed response styles ("orienters") may express higher reward-seeking, impulsivity, and risk-taking. Research also indicates that females may be more susceptible to the effects of rewarding stimuli. The current study tested whether the orienter phenotype, sex, and social training may explain individual variability in social learning of cue-reward associations. Rats were categorized as orienters or non-orienters based on their cue-directed responses during appetitive Pavlovian conditioning. To investigate the effect of social training on subsequent cue-reward learning, observer rats were paired with a trained demonstrator who they observed perform the association. The results indicated that non-orienters showed significantly higher reward contact, but only at certain sessions. No significant effects between social training and sex on learning cue-reward associations emerged. Future studies should account for dominance and familiarity/kinship between demonstrator-observer rats in social training, as this may allow for a more robust analysis of how the orienter phenotype and sex influence reward learning among peers.

Keywords: Pavlovian conditioning, social learning, individual differences, appetitive learning

Social learning, the act of learning about the environment via observation or interaction with another individual, is an essential adaptive process for social animals such as humans. Reward-mediated or appetitive learning is a hallmark of addiction and reward-seeking behaviors, while fear-mediated learning is characteristic of phobias and learned fears (Monfils & Agee, 2019). The prevalence of such disorders in the United States merits investigation into the neural and behavioral mechanisms of appetitive and aversive learning (Centers for Disease Control [CDC], 2021); however, the role of social learning in fear and appetitive learning is not yet fully understood. Individual differences such as sex, phenotype, such as an animal's response style in cue-reward paradigms, and social influence may influence the success of social learning (Saunders & Robinson, 2013). The focus of this study is to examine variation in learning of a cue-reward association by the orienter phenotype, which is thought to serve as a model of impulsivity. Additionally, social learning, a primary source of obtaining knowledge, may vary as a result of the orienting phenotype. Orienter rats, as compared to non-orienters, may relate to some human conditions involving gambling, drug addiction, and impulsivity (Lee et al., 2014; Robinson & Anselme, 2020). Peer interventions and treatments for fear and reward-mediated clinical disorders may be informed from research using rodent models of social learning with populations of different information processing. Next, I review the primary literature on orienting and social learning as it relates to sex and reward-seeking.

Social Transmission of Food Preference

The sharing of information regarding valued resources, such as food, is evolutionarily adaptive when sharing promotes survival. In rats, social learning has been studied through paradigms like social transmission of food preference (STFP) and fear conditioning by proxy (FCbP) (Monfils & Agee, 2019; Galef & Wigmore, 1983; Bruchey, Jones, & Monfils, 2010),

which provides insight into the broad mechanisms of reward and fear mediated learning. Social mammals, like rats and humans, can benefit from exchanging information with conspecifics at a central site (the burrow, for rats) concerning food availability in the larger environment (Galef & Wigmore, 1983). In rats, social transmission of food preference provides an animal model of social learning related to appetitive (or reward-driven) conditioning. Rats exhibit neophobic responses and are wary of consuming unknown food. When rats smell a novel food on another rat's breath, this olfactory cue allows them to conclude that the food is safe to eat (see Monfils & Agee, 2019 for a review). When presented with two novel food choices, rats are more likely to choose the food they observed a conspecific "demonstrator" ingest (Galef & Wigmore, 1983; Monfils & Agee, 2019). Therefore, when important to survival, rats engage in the social transmission of reward information.

By testing the boundaries of social learning in rats using such a common demonstrator and observer paradigm, one in which an “observer” rat watches a “demonstrator” rat, Galef and Wigmore (1983) laid the groundwork for later social learning research in the field which relies on the STFP paradigm (Wang et al., 2020; Agee & Monfils, 2018; Van der Jeugd & D'Hooge, 2018). The STFP paradigm is particularly useful for studying how environmental and social factors influence the strength of social learning. Results of Galef and Wigmore's (1983) series of lab experiments suggest that olfactory cues drive social learning of food preference in rats. The STFP design separates the animals by a wire screen, prohibiting free interaction but not the transmission of olfactory cues (Galef & Wigmore, 1983). Factors identified as influential in STFP are instability of the environment, observer health, and level of uncertainty (Galef et al., 2009). Notably, an observer’s response tendency to stimuli may influence social learning, though

this has not been widely studied. STFP demonstrates the abilities of rats to engage in social learning behaviors in appetitive or reward-mediated contexts.

In a 2018 study, the effect of faulty or unreliable information on the reliance of social information was tested in STFP (Agee & Monfils, 2018). Though animals were made mildly ill by socially transmitted food preference provided by specific demonstrators, observer rats did not alter their reliance on socially transmitted information. The results of this experiment suggest that, in situations that are unstable, the recency of a demonstrator-observer interaction is the most powerful factor in determining whether social learning occurs instead of the success of previous learning (Agee & Monfils, 2018). The impact of an animal's orienter status or behavioral response phenotype in appetitive conditioning, which involves learning a cue-reward association, has not been thoroughly investigated in the context of social learning. The major focus of the present study is to fill this gap by examining if orienters learn differently socially than non-orienters.

Fear Conditioning by Proxy (FCbP)

Fear learning is most often studied via Pavlovian conditioning, a type of classical conditioning in which an unconditioned stimulus (US) is naturally aversive or rewarding and is temporally paired with a predictive conditioned stimulus (CS) which is inherently neutral. Fear is learned through a CS-US pairing where the CS predicts an aversive US, leading to increased fear responses to the CS even without the US. In animal research, a tone (CS) might co-terminate with a foot shock (US), where repeated presentations cause an animal to fear the predictive CS. In humans, public speaking (CS) might induce a feeling of nausea (US). In addition to individual learning, fear can also be acquired indirectly through social context (Bruchey, Jones, & Monfils, 2010). Direct experience is not necessarily required for the development of fear, as indirect

experiences occur in phobias and anxieties (Monfils & Agee, 2019). Often, fear and other forms of social learning are evolutionarily adaptive, but phobias are not always. Investigating social learning mechanisms in fear and appetitive learning is a first step in developing strategies for fear attenuation and blocking reward-seeking behavior (Monfils & Agee, 2019; Bruchey, Jones & Monfils, 2010).

In FCbP, experiments attempt to discern which factors drive fear learning. FCbP is designed to allow for the investigation of how the observation of a conspecifics fear conditioning influences an animal's fear response (Bruchey, Jones & Monfils, 2010). For example, an otherwise naïve observer rat displays a fear expression when a demonstrator rat expressed fear in the presence of a conditioned stimulus (CS), such as a tone without the US (foot shock). Though the observer rat has no direct experience with the CS, learning through conspecifics may occur. This effect varies with familiarity, dominance order, sex, and kinship (Mikosz, Nowak, Werka & Knapska, 2015; Jones & Monfils, 2016; Agee, Jones & Monfils, 2019; Bruchey, Jones & Monfils, 2010). The value of the FCbP paradigm is the clearance it provides for testing social learning in a fear-mediated setting. Though the focus of the current study is on the behavioral phenotype of orienting and social learning in an appetitive context, the results should be broadly applicable to social learning. Future studies may show a role of orienting phenotype in fear learning, as the mechanisms of social learning, whether aversive or reward-driven, may overlap.

FCbP and STFP provide insight into mechanisms of social learning. While both paradigms showcase rats' ability to engage in social learning, results vary due to individual differences, potentially due to phenotype, such as orienter classification. Given the importance of peer familiarity in learning within appetitive contexts such as STFP, the broader question of how social influence impacts learning of appetitive associations arises. Appetitive paradigms, which

have broad implications for other rewarding contexts (drug use, as an extreme example) provide a window into reward-seeking behaviors. Both FCbP and STFP allow for the examination of social influence as a factor across both reward and fear-mediated contexts, ultimately providing insight into the interaction between social learning and stimuli. An appetitive context with social influence incorporated as a key factor has the potential to be a valuable model of distinguishing a subject susceptible to reward-seeking in the context of a social group.

Peers as Conditioned Stimuli

Substance use disorders are most successfully treated when the individual avoids drug-using peers (Weiss et al., 2018; Smith, Zhang & Robinson, 2016). Smith and colleagues (2015) were the first to test the impact of social cues on drug-seeking reinstatement experimentally in rats, finding that the acquisition of drug self-administration was enhanced in rats that were tested alongside a drug-experienced partner. However, social contact did not always facilitate drug use. At times, social contact inhibited drug-seeking, specifically when the peer was not drug-experienced. Smith and colleagues (2018) later tested social context and drug-seeking, with their data affirming that social partners can serve as stimuli to influence drug-seeking responses. Research from the field of social learning and substance use indicates that peers and social context influence both addiction and recovery (Saunders & Robinson, 2013).

Recent research suggests that social context, such as the presence of drug-using peers, can act as a cue for drug availability (Hofford et al., 2020; Weiss et al., 2018; Smith, Zhang, & Robinson, 2016). In humans, peer groups influence substance use in a myriad of ways. Descriptive self-report measures indicate that peer affiliation among recovering drug users impacts relapse and recovery. Weiss and colleagues (2018) found evidence indicating that a social peer can act as a reinforcing stimulus to signal drug availability. Following the extinction

of drug-seeking behavior, the presence of a peer previously paired with a drug was found to induce relapse or reinstatement. The findings of Weiss et al. (2018) and Smith et al. (2016) provide support for social peers' role in addictive behavior and relapse.

Other recent research has further demonstrated the importance of social context as a critical factor in relapse. Hofford et al. (2020) found that the presence of a social peer enhanced drug intake during acquisition. Similarly, when given a choice between two levers to self-administer the drug Remifentanil, a highly addictive narcotic, rats chose the lever closest to the peer. Sampedro-Piquero et al. (2019) showed that, when mice were given a choice to choose between a cocaine-paired compartment in a conditioned place preference task and a compartment with a novel mouse, they spent more time in the latter interacting with the novel mouse. These results confirm that rats and mice find interaction with conspecifics rewarding regardless of familiarity, suggesting a possible role for peers in relapse and recovery.

The results of the few notable studies on social influence and relapse indicate that a peer can serve as a conditioned stimulus and may carry incentive salience, a theorized psychological process that gives rise to "wanting" (Robinson et al., 2013). Incentive salience results in long-lasting brain changes in which dopamine, the primary neurotransmitter implicated in drug abuse, related systems such as the ventral tegmental area (VTA), nucleus accumbens (NAc), amygdala, prefrontal cortex, and other reward areas become sensitized due to drug use. Consequently, cue-triggered "wanting" is sensitized and increased through addiction (Robinson et al., 2013). Peers and other stimuli, both unconditioned and conditioned, may have the capacity to obtain incentive salience.

Cue-Directed Behaviors

Within Pavlovian appetitive conditioning, two classes of cue-association conditioned responses may emerge (Olshavsky et al., 2014). One conditioned response is exhibited via cue-directed behaviors in which some animals, known as sign-trackers, orient and attend to a conditioned stimulus (CS) itself. Sign-trackers direct their behavior towards the CS, which acts as a "motivational magnet" (Colaizzi et al., 2020). For example, a CS lever may gain both predictive and incentive value for sign-tracker animals (Colaizzi et al., 2020; Flagel et al., 2009; Robinson & Flagel, 2009). Other animals, known as goal-trackers, direct their behavior towards the reward delivery site, associated with an unconditioned stimulus (US). In contrast to sign-trackers, goal-trackers instead spend increased time near the reward delivery site. Sign-trackers and goal-trackers show stability in their response tendencies over time, suggesting that these are enduring phenotypes. These phenotypes suggest differential information processing in goal-tracking and sign-tracking animals, as divergent behavioral patterns between the two phenotypes exist.

Conditioned orienting, a variation of sign-tracking, is specific to light cue-food pellet paradigms (Olshavsky et al., 2014). In this paradigm, the CS is a light cue, where the US are food pellets. Rather than lever-directed, conditioned orienting is cue-directed behavior towards a light cue CS. Conditioned orienting usually occurs within the first 5 seconds of a 10 second light CS, while food approach behavior is more often observed during the last half of the light cue (Olshavsky et al., 2014). Two resulting phenotypes, orienters and non-orienters, can be assigned based upon the tendency to orient to a light CS or approach the reward/food delivery site. As in sign-tracking, these phenotypes reflect differences in impulsivity and other externalizing behaviors (Olshavsky et al., 2014 ;Papachristou et al., 2013; Lovic et al., 2011).

Sign-tracker and orienter animals reflect attentional bias towards conditioned stimuli, which gains both predictive and incentive value. In addition to attentional bias, sign-trackers and orienters show higher-reward seeking and higher impulsivity. When a CS gains incentive value because of its association with a reward US it biases attention, becomes desirable, and increases reward-seeking behaviors (Robinson et al., 2013; M. Robinson, T. Robinson, & Berridge, 2013). These factors suggest higher vulnerability to addiction in rats of the orienter or sign-tracker phenotype.

Reward circuits in the brain are highly active during cue-reward learning. Heightened dopamine function and other neural differences in animals with cue-directed behavior strengthen the link between cue-directed phenotypes and higher reward-seeking (Cooper et al., 2017). The reward circuit mechanism begins in the ventral tegmental area and projects neurons into nucleus accumbens, which mediates reward behavior. The VTA also projects to areas such as the amygdala, prefrontal cortex, and hippocampus. Regions important to emotion, executive function, and memory are therefore subject to the effects of reward-seeking and addiction on the brain (Cooper et al., 2017; Hilz et al., 2019).

Sign-tracking, similar to conditioned orienting with the CS being a lever rather than a light, is characterized by distinct profiles of dopamine release in the nucleus accumbens (NAc) relative to goal-tracking (Gillis & Morrison, 2019). Sign-trackers also show increasing dopamine release in response to a cue and decreasing release in response to the reward throughout training (Flagel et al., 2011). Activation in the nucleus accumbens is uniquely linked to association acquisition in sign-tracker animals, but the same is not observed in goal-tracker animals. However, both sign-tracker and goal-tracker animals show activation in the nucleus accumbens after acquisition or learning. Therefore, the sign-tracking and goal-tracking phenotypes are

characterized by divergent but related neural regions. Evident neural differences support differential information processing between sign-trackers and goal-trackers during and after learning.

Orienters and non-orienters show differing responses under post-consolidation memory attenuation manipulations. One approach, extinction, similar to exposure therapy, is not effective for all (Maren, Phan & Liberzon, 2013). In addition to the return of fear memory through renewal, reinstatement, and spontaneous recovery mechanisms, extinction is less effective for some than others, suggesting that some individuals might be better candidates for other approaches (e.g., retrieval+extinction) (Monfils et al., 2019; Monfils et al., 2009). According to reconsolidation theory, upon retrieval, consolidated memories enter a labile phase that renders them susceptible to updating and requires the synthesis of new proteins to be stable again (Nader et al., 2000). Developed by Monfils and colleagues, retrieval-extinction is a procedure used to persistently attenuate both fear and reward associations through updating the original memory (Monfils et al., 2009). This is made possible by interfering with memory reconsolidation during the labile phase in which memories are sensitive to disruption following retrieval. Studies have shown that retrieval-extinction attenuates drug-seeking in humans and rats (Xue et al., 2012). Lee, Monfils, and colleagues found that orienter and non-orienters respond differently to retrieval-extinction, with orienters responding significantly better to retrieval-extinction than non-orienters, who responded better to standard extinction (Olshavsky et al., 2013). Taken together, studies suggest differential information processing in orienter and non-orienter animals, though the exact mechanism is still to be uncovered.

Sex Differences in Addiction

Females demonstrate increased susceptibility to the rewarding effects of drugs, though female rats are less studied due to variability and technicalities attributed to the estrous cycle (Becker et al., 2017; Anker et al., 2011; Becker & Hu, 2008; Lynch et al., 2002). Animal studies point to sex differences in addiction during initiation, maintenance, and relapse (Becker et al., 2017). Across most drugs, females show more rapid self-administration and higher effort for drug rewards (Becker et al., 2017). The extent of sex differences in acquisition of less extreme appetitive associations using more mild rewards is unknown.

Hilz and colleagues (2019) propose that the orienting phenotype is a predictor of females' drug proclivity. In support of the hypothesis that orienting relates to drug-seeking behavior, Hilz and colleagues found that female orienter rats show a stronger preference for a drug-associated context. As expected, female orienters were resistant to the extinction of this preference compared to non-orienters (Hilz et al., 2019). Externalizing behaviors, such as impulsivity and aggression, are generally thought of as male-dominated behaviors. Conversely, females might be more susceptible to accelerated addiction compared to males (Becker et al., 2017). Disentangling the effects of sex and orienting/sign-tracking phenotype may reveal factors leading to reward-seeking and eventually, the development of addictive behaviors.

Conclusions

The mechanisms of social learning are not fully understood. Furthermore, the relationship between externalizing behavior, such as impulsivity and sign-tracking/orienting, and vulnerability to addiction, has not been studied in the context of social learning. This study's primary goal is to assess social influence in the context of appetitive conditioning, with a specific focus on orienters. It stands to reason that it would prove adaptive, though not required for survival, for conspecifics to share information regarding rewards with one another. The orienter/non-orienter model applied to social learning holds the potential to identify individuals susceptible to appetitive stimuli' rewarding effects, from food to drugs. Through this paradigm, individuals at risk for reward-seeking and impulsivity may be discerned, and implications for reward-driven behaviors may be discovered (Meyer et al., 2012; Lovic et al., 2011).

In this study, I hypothesize that orienter rats will show increased learning of the cue-reward association when provided social training. Furthermore, these effects will be amplified in females. Orienters, characterized by high impulsivity, risk-taking, and attentional bias, are of increased susceptibility to addiction and reward-seeking. In social contexts, when peers may be observed consuming rewards, observational learning may facilitate speed and intensity association acquisition in individuals. Additionally, females demonstrate increased vulnerability to the rewarding effects of drugs and might learn cue-reward associations more effectively than males.

By examining the orienting phenotype, a model of impulsivity and high reward-seeking, I hope to understand how reward-seeking behaviors manifest in social contexts as a result of appetitive associative learning and social training. I plan to examine the relationship between those with externalizing behaviors, orienters, and propensity towards reward learning. By

including social peers in this experiment, translational implications for humans, who often exhibit high reward-seeking behaviors (such as drug consumption) in social contexts, may be identified.

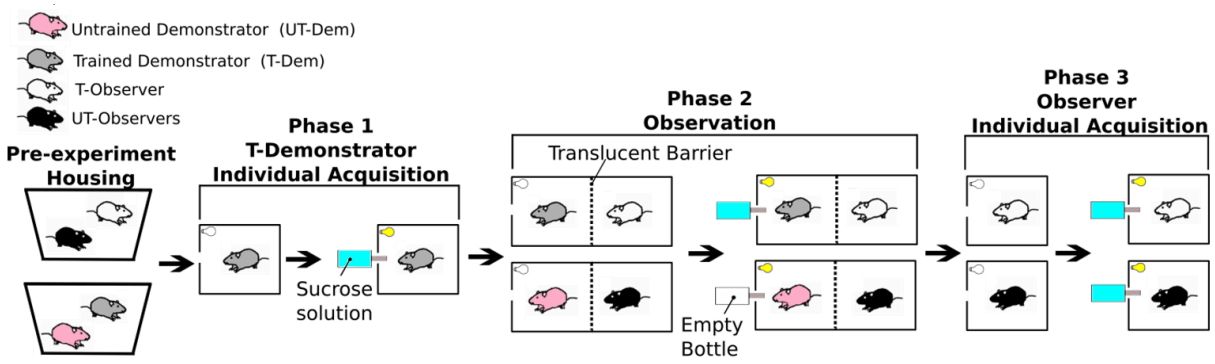
Materials and Methods

Experimental Design Overview

This study aimed to test the hypothesis that rats of the orienter phenotype, compared to non-orienters, would show enhanced acquisition of a cue-reward association when provided social training. Furthermore, it was expected that these effects would be amplified in females. To test the effects of the orienter phenotype and social training on the learning of a cue-reward association, data from rats trained in an observer-demonstrator cue-reward learning paradigm in 2 experiments was utilized (see Figures 1 and 2). Orienter phenotype and social training were analyzed as primary independent variables. The primary dependent variable, reward contact duration during each CS-US timepoint, was measured across experimental sessions. To examine the effects of sex in addition to social training and phenotype, data from two experiments were combined to allow for a more robust analysis. In experiment 1, rats were trained to associate a 10 second light cue (CS) with a sucrose solution reward (US), which became available halfway through the CS presentation, as depicted in Figure 1. In experiment 2, rats were trained to associate a 10 second light cue (CS) with food pellet rewards (US), which became available 7 seconds into the presentation of the CS. All measures are based on the observer training phase (Phase 3) in each experiment which occurred over 14 days in experiment 1 and 7 days in experiment 2.

Figure 1

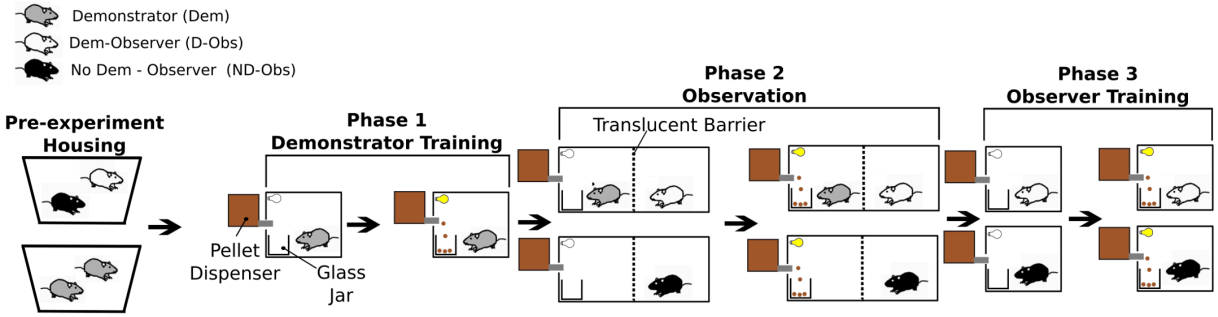
Experiment 1 design overview



Note. In this experiment, the CS was a light cue while the US was a sucrose solution. There were four possible assignments: trained demonstrator (T-Dem), untrained demonstrator (UT-Dem), trained observer (T-Observer), and untrained observer (UT-Observer). Figure courtesy of Laura Agee.

Figure 2

Experiment 2 design overview



Note. In this experiment, the CS was a light cue while the US were feed pellets dispensed into a glass jar. There were three possible assignments: demonstrator (Dem), observer with demonstrator (D-Obs), and observer without demonstrator (ND-Obs). Figure courtesy of Laura Agee.

Subjects

Forty-eight Long-Evans rats, 24 males and 24 females, (Harlan, Houston, TX, USA) of approximately 65 days old were used. Rats were housed in same-sex dyads. Experiments were conducted in accordance with the *National Institutes of Health's Guide for the Care and Use of Laboratory Animals*. Experimental protocols were approved by the Institutional Animal Care and Use Committee at the University of Texas at Austin.

Twenty-four rats, 12 males and 12 females, were used in experiment 1. In each observer condition there were 12 rats, 6 males and 6 females. In experiment 1, there were four possible assignments: trained demonstrator (T-Dem), untrained demonstrator (UT-Dem), trained observer (T-Observer), and untrained observer (UT-Observer). Cages were randomly assigned to observer or demonstrator conditions and were then paired with a cage of the opposite condition. Within each cage, one rat was assigned to the trained condition and the other rat to the untrained condition. A single demonstrator cage was allowed to be paired with multiple observer cages.

Twenty-four rats, 12 males and 12 females, were used in experiment 2. In each observer condition there were 12 rats, 6 males and 6 females. In experiment 2, there were three possible assignments: demonstrator (Dem), observer with demonstrator (D-Obs), and observer without demonstrator (ND-Obs). The demonstrator rats in this experiment were used as observer rats in experiment 1 and were reconditioned with the new US. All animals were experimentally naïve otherwise.

In both experiments, following random assignment, rats were left undisturbed for 5 days to allow for habituation to the colony. Rats in experiment 1 were allowed *ad libitum* food access and were not food-restricted at any point. In experiment 2, rats were food-restricted following habituation to the colony. Food deprivation began approximately 7 days before training for

demonstrators (or before observation for observers). Females were initially allowed 9g/day/rat, and males were allowed 12g/day/rat. Once rats were brought down to 90% of their original body weight, food portions were increased to maintain this weight (typically 12g/day/rat for females and 15g/day/rat for males).

Apparatus

Experimental phases took place in conditioning chambers of two designs, depending on whether rats were in experiment 1 or 2. The conditioning chamber in experiment 1 was obtained from Med Associates, Inc. (Fairfax, VT) (interior dimensions: 30.5cm L x 24.1 cm W x 29.2 cm H). Chambers were placed within sound-attenuating cubicles. Cubicles were supplied with an exhaust fan and a video camera (KT&C USA, Fairfield, NJ). Each chamber was outfitted with a houselight and a retractable bottle assembly. The houselight was installed facing downward at the top center panel of the right chamber wall. The retractable bottle assembly was on the front wall's right panel, resulting in the metal sipper positioned approximately 8.5 cm above the grid floor. The sipper hole was approximately 8.5 cm to the right and 16 cm lower than the houselight.

In experiment 2, Habitest conditioning chambers obtained from Coulbourn Instruments (Whitehall, PA) (interior dimensions: 61 cm L x 58.4 cm W x 46 cm H) were used. These chambers contained a food pellet dispenser rather than a retractable bottle assembly. Another critical difference was the placement of the light cue, which was significantly higher than in the chambers used in experiment 1. A small clear glass jar was placed in front of the pellet receptacle (to increase incentive value). At the top of the cage above where pellets were dispensed, a light cue served as the CS while food pellets served as the US. In phase 3 of the

experiment, a cage separator made of 40-gauge transparent vinyl cloth with aluminum siding was secured to either side of the cage via velcro strips to divide the conditioning chamber.

Procedure: Experiment 1

Phase 1: Demonstrator training. Following 5 days of habituation and group assignment, demonstrators were allowed an hour to habituate to the conditioning chamber, in which they were also provided free access to the sucrose/water solution to overcome any possible neophobia. The next day, the experiment moved into phase 1. In experiment 1, once daily for 14 days, rats assigned to the trained demonstrator (T-Dem) condition were moved to a conditioning chamber outfitted with a retractable bottle assembly holding a bottle containing a 0.5 M sucrose/water solution which served as the reward US. During a 60-minute training session, 30 presentations of a 10 second light cue served as the CS. Halfway through the light cue, the bottle's nozzle was inserted into the chamber and was available for 5 seconds. Trials were separated by a variable interval averaging 90 seconds (60-120 second range). Each 5-second interval was binned into 1.25 seconds and was scored for approach behavior depending on whether the rat displayed an active interest in the sipper site (such as pawing, actively examining, or sticking their snout into it). The number of approaches determined the training's success to the sipper site during the CS presentation.

Phase 2: Observation. Training sessions occurred once daily for 7 days in both experiments 1. In experiment 1, the trained demonstrator (T-Dem) and the observer assigned to the trained condition (T-Obs) were placed in the conditioning chamber with a translucent barrier separating them. Untrained demonstrators (UT-Dem) and the remaining untrained observer rats (UT-Obs) were placed in similar conditions, the only difference being an empty bottle rather than a sucrose bottle. The observation sessions were approximately 30 minutes long and

consisted of 15 cue-sipper presentations. During piloting, the experimenters varied the number of observation sessions to determine the minimum number needed to produce a difference in performance during the next phase.

Phase 3: Observer training. In experiment 1, all observers underwent the same training procedure as in Phase 1 of experiment 1 once daily for 14 days. No cage separator was present during observer training.

Procedure: Experiment 2

Phase 1: Demonstrator Training. Following 5 days of habituation and group assignment, demonstrator rats (Dem) underwent magazine-style training during which they were permitted a single 30-minute session in the conditioning chamber while feed pellets (45 mg, TestDiet, Richmond, IN, USA) were dispensed as a US reward every 2 minutes. The next day, the experiment moved into phase 1. Demonstrator rats were brought to the conditioning chamber for a 30-40 minute training session once daily for 7 days. On each CS-US pairing trial, the light cue was presented for 10 seconds. 7 seconds into each presentation, food pellets began to be dispensed, with 3 total pellets (US) dispensed for every light (CS) presentation. In each training session, demonstrators received 15 CS-US pairings separated by 60, 120, or 180 seconds. On the final day of training, a vinyl cage separator (as used in experiment 1) was placed within each demonstrator's chamber to ensure habituation to the separator before phase 2.

Phase 2: Observation: In experiment 2, demonstrators (Dem) and observers (D-Obs) were placed together in the conditioning chambers and were trained on the exact procedure used for demonstrator training. Observers and demonstrators were kept from coming into contact with each other using a separator, made of 40-gauge transparent vinyl cloth with aluminum siding, secured to either side of the cage via Velcro strips. Demonstrators were placed on the side with

the food cup while observers were placed on the opposite side of the chamber, so they did not have access to the food cup. Observers in the no demonstrator condition (ND-Obs) were placed in the same environment as their yes demonstrator (D-Obs) counterparts, with the only difference being that no demonstrator was present.

Phase 3: Observer training. In experiment 2, all observers underwent the same training procedure as in Phase 1 of experiment 2 once daily for 7 days. No cage separator was present during observer training.

Measures

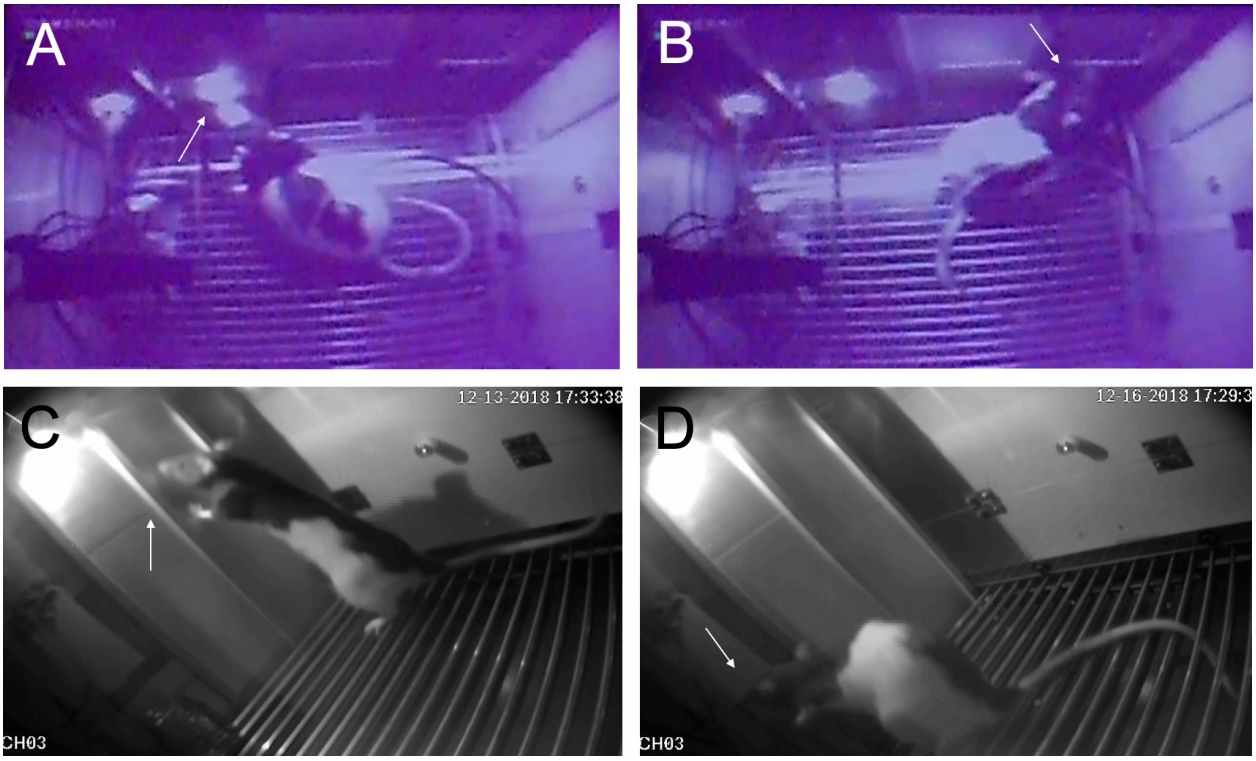
Orienting: In all behavioral scoring, each CS-US trial was divided into three timepoints: (1) pre-CS, the 5 seconds before the light turned on, (2) CS1, the first 5 seconds of the light CS turned on, and (2) CS2, the second 5 seconds of the light CS turned on, paired with the US sucrose sipper or feed pellet rewards. Orienting was contingent upon a rat's close proximity to the light itself, meaning that the rat must have been in the corner with the light cue (see Figure 3). The light cue was significantly lower to the ground in experiment 1 than in experiment 2. In experiment 1, orienting was defined as cue-directed behavior noted by head direction and aim or direct contact with the light cue CS. In experiment 2, orienting was scored for when a rat "reared" (a rat's front paws lift while standing on their hind legs) towards the light cue CS. Rearing was not a criterion for orienting in experiment 1 because the light cue was so low that the light was not in a rat's field of vision when rearing. Orienting was measured as the percentage of time a rat spent orienting in a given US-CS presentation. This calculation was based on each animal's total duration orienting per CS timepoint and was divided by the total amount of time responding possible. Orienting duration was calculated so that each animal's total duration orienting per session was binned into pre-CS, CS1, and CS2 timepoints. After

conversion to a percentage, pre-CS percentage orienting was subtracted from the CS1 and CS2 to account for baseline responding.

Unconditioned Stimulus/Reward Contact: Food cup/sucrose sipper reward or US contact was defined by contact with the sucrose sipper faceplate or the food cup via paw or face (see Figure 3). Orienting and faceplate contact could not co-occur by definition. For example, if a rat maintained contact with the sucrose sipper using only a paw but had their head directed towards the light, it was considered sucrose sipper or food cup contact. The primary measure of learning, reward contact, was measured as the percentage of time a rat maintained sucrose sipper/faceplate contact in a given trial. Duration of time in contact with the reward site was calculated for the pre-CS period, CS1, and CS2 (reward entry) and was transformed into an easily interpretable percentage based on CS presentation duration. This calculation was based on each animal's total duration at or in contact with the reward site per CS-US presentation and was divided by the total amount of time responding possible. In experiment 1, the maximum responding during each CS timepoint per session was 150 seconds because there were 30 CS-US trials per session, each consisting of 15 seconds each. In experiment 2, each session consisted of 15 CS-US trials comprised of 15 seconds each, so 75 seconds was the maximum amount of time a rat could attend to the US per CS time point. Finally, to account for each animal's baseline responding, the percentage of US contact during the pre-CS time period was subtracted from each animal's CS1 and CS2 percentages to account for the change in responding due to the CS.

Figure 3

Video Examples of Learning and Orienting Measures



Note. An example of the cue-directed orienting response in experiments 1 and 2 is shown (A and C, respectively), noted by close attention to light cue (see arrows). The reward-directed response in experiments 1 and 2 is also shown (B and D, respectively), noted by contact to the reward delivery site (see arrows).

Orienter Categorization: In order to classify rats as orienters or non-orienters, a median split method was utilized. The median split was based on the CS1 timepoint, when conditioned orienting was highest. Furthermore, session 7 was used for all splits based on stability in orienting levels by this session. Animals who had CS1, session 7 orienting levels higher than the median were defined as orienters, and those who had orienting levels below were defined as non-orienters.

Statistical Analysis

All statistical analyses were conducted using R-Studio Version 1.4.1106 (RStudio Team, 2021). To analyze the validity of the orienter categorization on time spent orienting, two-way mixed ANOVAS were conducted for experiments 1 and 2 for each CS timepoint. To analyze the effects of social training and phenotype on reward acquisition, two-way mixed ANOVAS were conducted for experiment 1 at each CS timepoint. The same was done for experiment 2. To investigate broad statistical trends, data from experiments 1 and 2 were combined to create a dataset pooled across the two studies. To analyze the validity of the orienter categorization on time spent orienting across pooled studies, three-way mixed ANOVAS were conducted for each CS timepoint. A three-way mixed ANOVA was conducted to analyze the effects of sex, phenotype, and social training on reward contact as each CS timepoint in experiments 1 and 2 combined and pooled. Significant interaction effects were followed up with one-way ANOVAS or pairwise comparisons with Bonferroni corrections when appropriate.

Results

Orienting Analyses

Median Split

Consistent with previous studies, conditioned orienting was consistently highest during the CS1 timepoint in both experiments, when the light cue was on but the reward was not yet available. In experiment 1, in which rats underwent 14 sessions of individual acquisition, conditioned orienting stabilized and reached asymptote by session 7. In experiment 2, the final individual acquisition session, session 7, was showed similar stability. Rat's orienting levels during the CS1 timepoint of their 7th session in both experiments were used to determine their phenotype based on a median split. Orienting levels differed across experiments. In experiment 1, the orienting percentage during the CS1 timepoint at session 7 was low, M = 1.59, SD = 5.99. In experiment 2 at the same session and timepoint orienting was somewhat higher with greater variability, M = 3.33, SD = 13.02. In both experiments, animals scoring above the median in CS1 of session 7 were categorized as orienters, and those below the median as non-orienters.

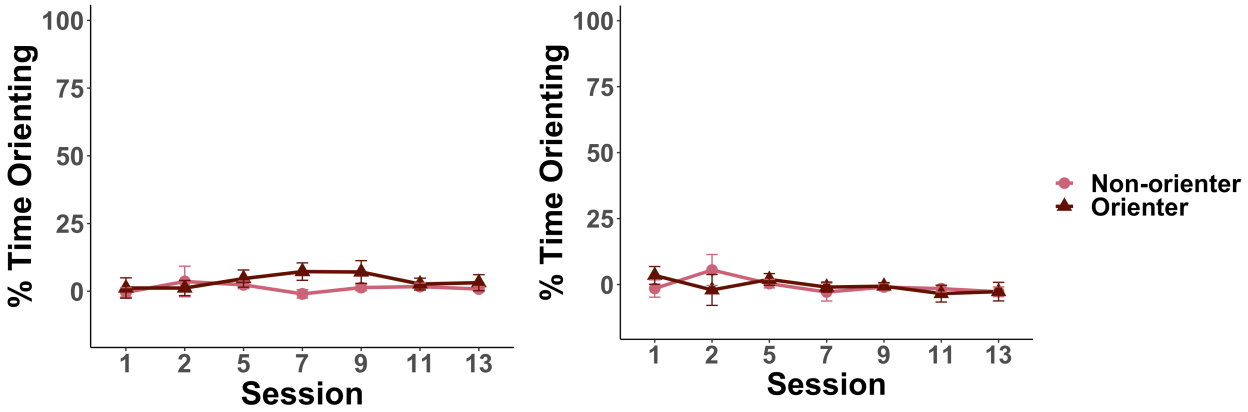
Orienters and non-orienters were defined in the pooled dataset according to a new median split based on the two experiments together. As in experiments 1 and 2, the orienter categorization was completed based on orienting levels during the CS1 timepoint. Consistent with the methods of experiments 1 and 2, session 7 was used to split rats into orienters and non-orienters, M = 2.65, SD = 10.22. Across the two experiments pooled, animals scoring above the median in CS1 of session 7 were categorized as orienters and those below the median as non-orienters.

Orienting in Experiment 1

To confirm the validity of the orienter split in experiment 1, a three-way mixed measures ANOVA was conducted for the percentage of orienting during the CS1 timepoint with condition, phenotype, and session as independent variables. There was not a significant main effect of phenotype on time spent orienting during the CS1 timepoint, $F(1, 8) = 3.07$, $p > .05$. A second three-way mixed measures ANOVA was conducted for the percentage of orienting during the CS2 timepoint with condition, phenotype, and session as independent variables. Again, there was not a significant main effect of phenotype on levels of orienting during the CS2 timepoint, $F(1, 8) = 0.76$, $p > .05$. These results indicate that orienters and non-orienters did not differ in levels of orienting during either the CS1 or CS2 timepoints (see Figure 4), rendering the validity of orienter split in experiment 1 low. Consequently, alternative analyses will be explored and results relating to phenotype in experiment 1 will be taken skeptically.

Figure 4

Experiment 1: Duration Orienting by Phenotype, CS1 and CS2



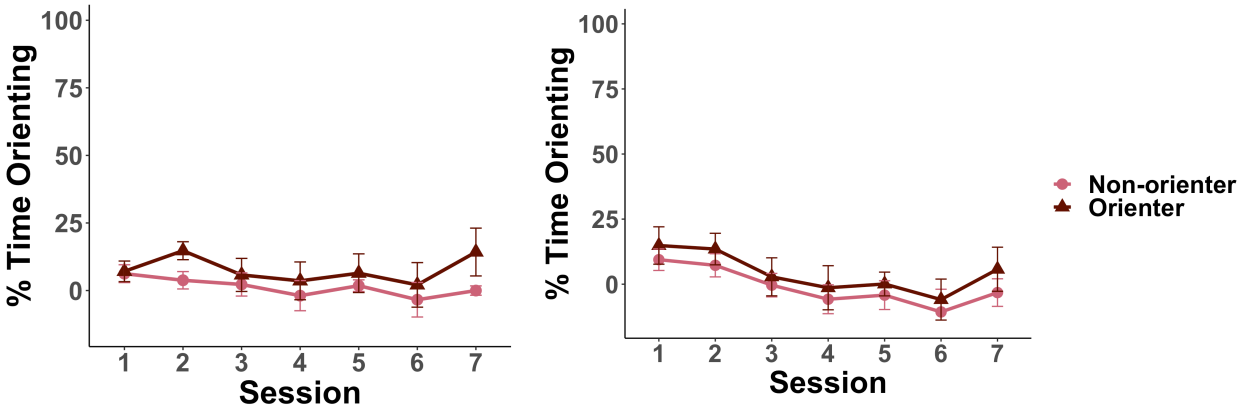
Note. Mean ± SE orienting during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Assignment of the orienter phenotype was not significantly related to duration orienting during either time point, indicating a weak relationship of phenotype to orienting levels (CS1 $p > .05$, CS2 $p > .05$).

Orienting in Experiment 2

To confirm the validity of the orienter split in experiment 2, a three-way mixed measures ANOVA was conducted for the percentage of orienting during the CS1 timepoint, with condition, phenotype, and session as independent variables. A significant main effect of phenotype on time spent orienting emerged, $F(1, 20) = 11.29$, $p < .005$. This same analysis was conducted for the CS2 timepoint, which also showed a significant main effect of phenotype on time spent orienting, $F(1, 20) = 4.73$, $p < .05$. These results indicate that orienters and non-orienters overall showed differing levels of orienting during both the CS1 and CS2 timepoints, with orienters showing higher levels of orienting (see Figure 5). The validity of the orienter split in experiment 2 is high.

Figure 5

Experiment 2: Duration Orienting by Phenotype, CS1 and CS2



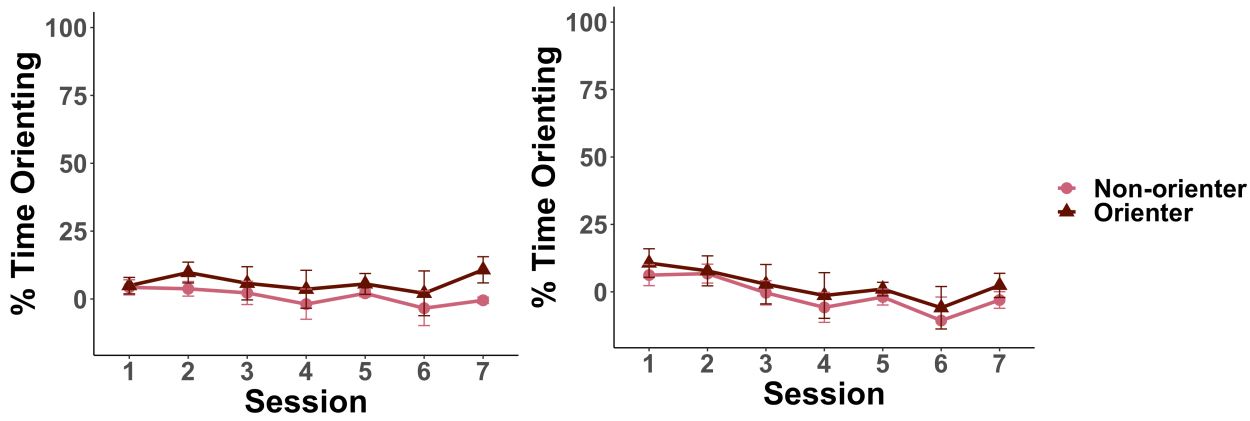
Note. Mean ± SE orienting during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Assignment of the orienter phenotype was significantly related to duration orienting during either time point, indicating a strong relationship of phenotype to orienting levels (CS1 *p < .005, CS2 *p < .05).

Orienting in Pooled Studies

To confirm the validity of the orienter split in the pooled data, a factorial mixed measures ANOVA was conducted for the percentage of orienting during the CS1 period with phenotype, sex, condition, and session as independent variables. A significant main effect of phenotype on time spent orienting during the CS1 timepoint emerged, $F(1, 16) = 17.47$, $p < .005$. The same analysis was conducted for the CS2 timepoint, which also showed a significant main effect of phenotype on time spent orienting, $F(1, 16) = 9.27$, $p < .05$. Pooled across both studies, the orienter phenotype was associated with higher levels of orienting at both the CS1 and CS2 timepoints (see Figure 6). The validity of the orienter split in the pooled data is high.

Figure 6

Pooled Studies: Duration Orienting by Phenotype, CS1 and CS2



Note. Mean ± SE orienting during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Assignment of the orienter phenotype was significantly related to duration orienting during either time point, indicating a strong relationship of phenotype to orienting levels (CS1 *p < .005, CS2 *p < .05).

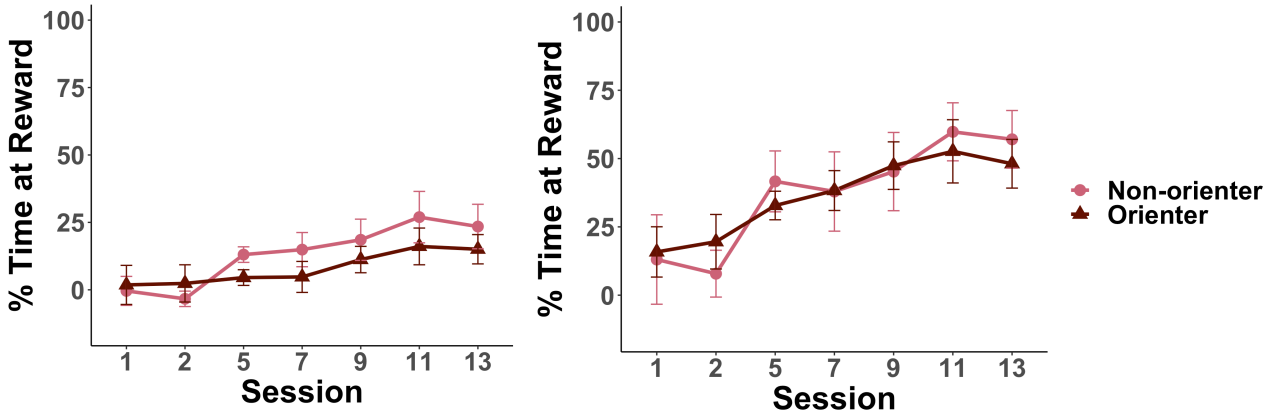
Reward Analyses

Reward Contact in Experiment 1

A three-way mixed measures ANOVA was conducted for the percentage of reward contact during the CS1 period with condition, phenotype, and session as independent variables. During the CS1 period, only a main effect of session emerged, $F(6, 42) = 6.241$, $p < .001$. No effects or interactions of phenotype or condition were found. Another three-way mixed measures ANOVA was conducted for the percentage of reward contact during the CS2 period, with condition, phenotype, and session as independent variables. Results indicate a significant main effect of session, $F(6, 48) = 19.31$, $p < .001$. Results do not support any significant main effects or interactions of phenotype or condition on reward contact at the CS1 or CS2 timepoints (see Figures 7 and 8).

Figure 7

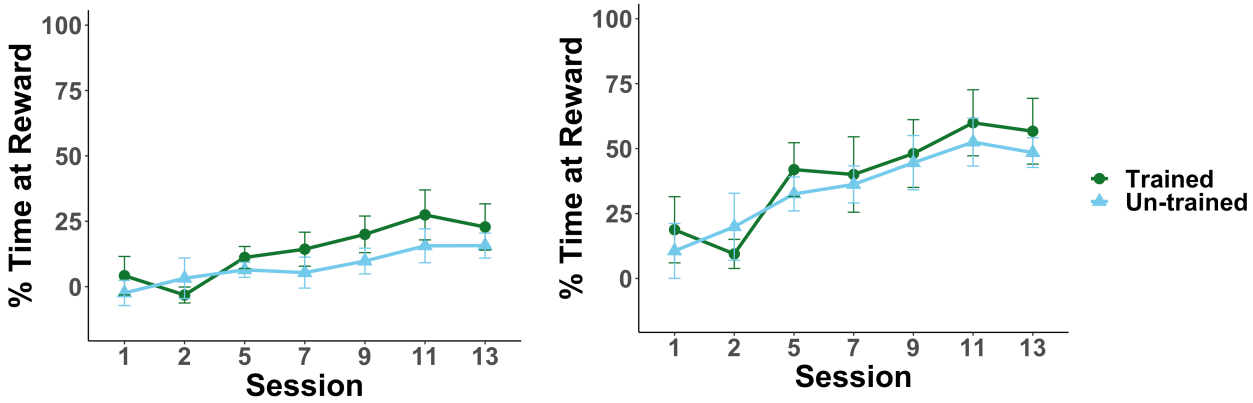
Experiment 1: Reward Contact by Phenotype, CS1 and CS2



Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Assignment of the orienter phenotype was not significantly related to reward contact during either time point, indicating no difference in cue-reward association learning between orienters and non-orienters (CS1 $p > .05$, CS2 $p > .05$).

Figure 8

Experiment 1: Reward Contact by Social Training, CS1 and CS2

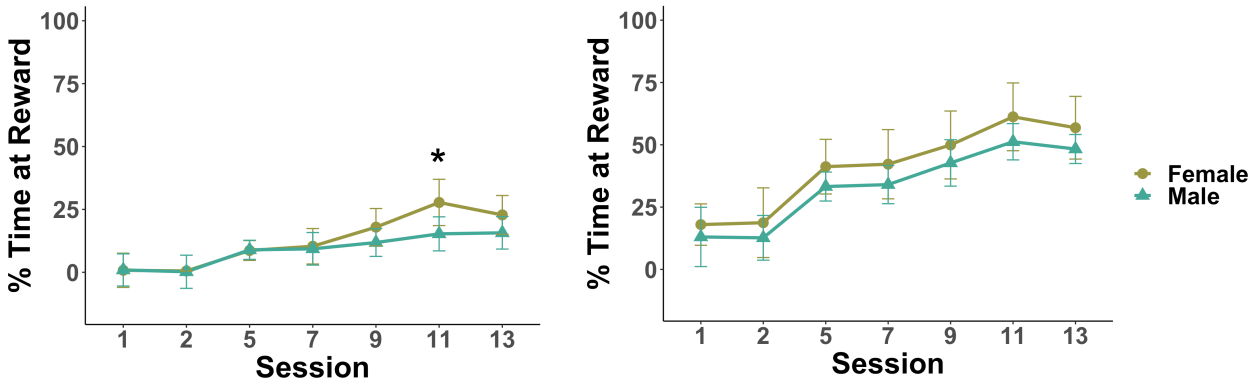


Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Rats who received social training and those who did not showed no difference in their learning on a cue-reward association (CS1 $p > .05$, CS2 $p > .05$).

An exploratory three-way mixed ANOVA of reward contact based on phenotype, sex, and session was conducted for the CS1 timepoint. A statistically significant interaction of sex and session emerged, $F(6, 42) = 3.69$, $p < .005$. To investigate the meaning of this interaction, a follow-up ANOVA was conducted to examine the effect of sex across sessions, in which only session 11 was shown to be significant, $F(1, 22) = 4.78$, $p < .05$. A pairwise comparison confirmed that males and females differed at session 11, $p < .05$ (Bonferroni adjusted). Visual inspection showed this effect to be only in females. Another three-way mixed ANOVA was conducted to examine the effects of sex, condition, and session on reward contact for the CS2 timepoint. No significant main effects or interactions of sex and condition emerged on reward contact (see Figure 9). There was a significant main effect of session, $F(4, 48) = 25.39$, $p < .0001$.

Figure 9

Experiment 1: Reward Contact by Sex, CS1 and CS2



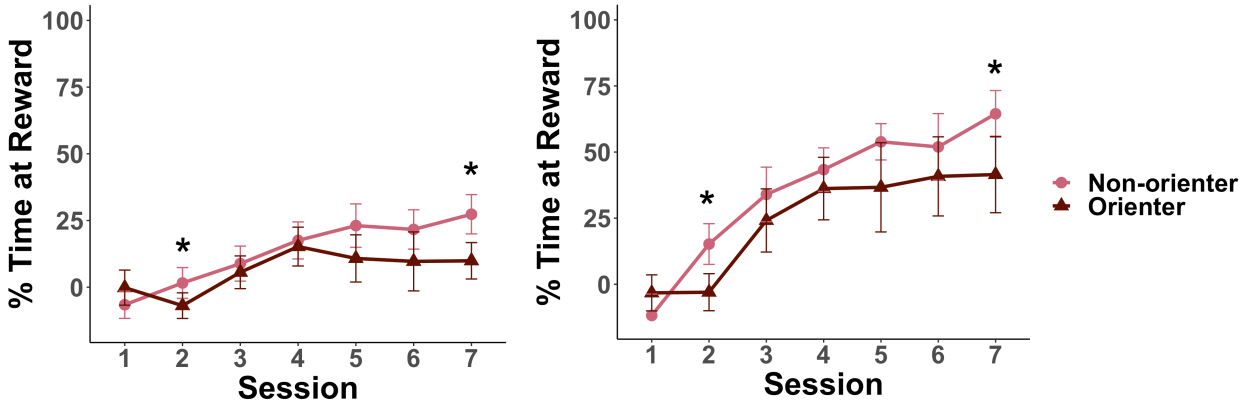
Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Male and female rats differed on their learning of the cue-reward association only during session 11 of the CS1 timepoint (*$p < .05$), but not during the CS2 timepoint ($p > .05$).

Reward Contact in Experiment 2

A three-way mixed measures ANOVA was conducted for the percentage of reward contact during the CS1 period with condition, phenotype, and session as independent variables. Results showed a significant interaction between session and phenotype, $F(6, 120) = 3.54$, $p < .01$. A post-hoc analysis revealed that at sessions 2 and 7, non-orienters spent significantly more time at the reward site than orienters, $F(1, 22) = 5.12$, $p < .05$ and $F(1, 22) = 12.1$, $p < .01$, respectively. Another three-way mixed measures ANOVA was conducted for the percentage of reward contact during the CS2 period, with session, condition, and phenotype as independent variables. Results showed a significant interaction between session and phenotype, $F(3.57, 71.49) = 2.87$, $p < .05$. As found during the CS1 period, a post-hoc analysis revealed that at sessions 2 and 7, non-orienters spent significantly more time at the reward site than orienters, $F(1, 22) = 12.3$, $p < .05$ and $F(1, 22) = 7.39$, $p < .05$, respectively. No main effects or interactions of social training emerged during either CS1 or CS2 timepoints (see Figures 10 and 11).

Figure 10

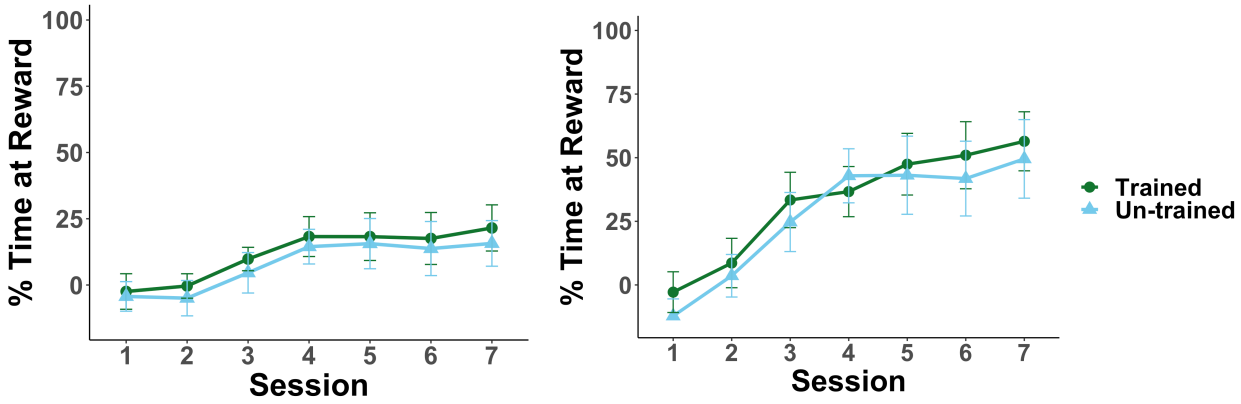
Experiment 2: Reward Contact by Phenotype, CS1 and CS2



Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Non-orienters show higher reward contact during sessions 2 and 7 of the CS1 timepoint (session 2 *$p < .05$, session 7 *$p < .01$), as well as sessions 2 and of the CS2 timepoint (session 2 *$p < .05$, session 7 *$p < .05$).

Figure 11

Experiment 2: Reward Contact by Social Training, CS1 and CS2



Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. Rats who received social training and those who did not showed no difference in their learning on a cue-reward association (CS1 $p > .05$, CS2 $p > .05$).

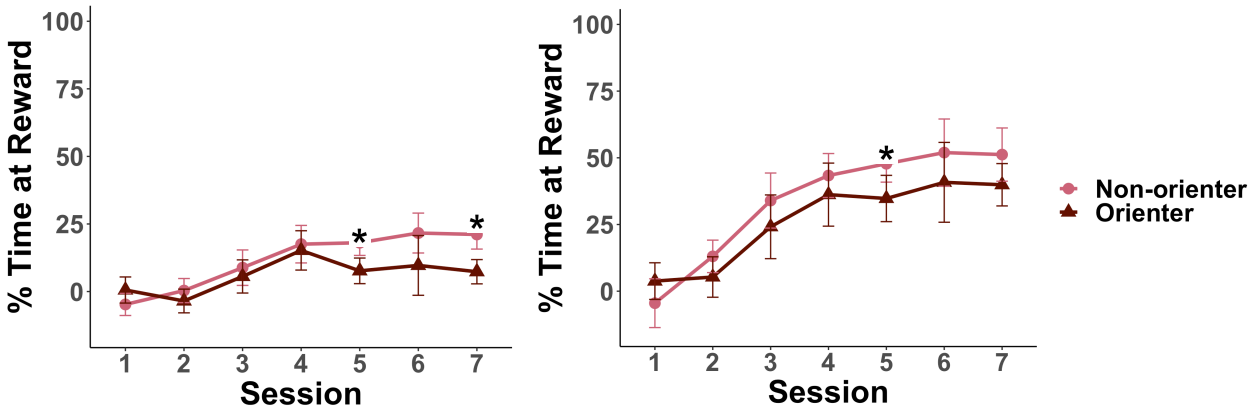
Reward Contact in Pooled Studies

The analyses in experiments 1 and 2 did not examine sex, thus a pooled dataset across both experiments was created to examine the effect of sex across both experiments, in addition to social training, phenotype, and session. Experiment 1 had 14 sessions and experiment 2 had only 7, hence only the first 7 sessions of both experiments were used in the pooled analyses.

A factorial mixed measures ANOVA was conducted for the percentage of reward contact during the CS1 period, with sex, condition, and phenotype, and session as independent variables. A phenotype by session interaction emerged, $F(6, 96) = 3.44$, $p < .005$. Post-hoc tests showed session 5, $F(1, 46) = 9.71$, $p < .005$, and session 7, $F(1, 46) = 15.4$, $p < .001$ as significant, with non-orienters spending significantly more time at the reward site than orienters. A second factorial mixed measures ANOVA was conducted for the percentage of reward contact during the CS2 period, with session, sex, condition, and phenotype as independent variables. A phenotype by session interaction emerged, $F(6, 96) = 2.47$, $p < .05$. Post-hoc tests showed only day 5 as significant, with non-orienters spending significantly more time at the reward site than orienters, $F(1, 46) = 5.52$, $p < .05$. No main effects or interactions of sex or social training emerged (see Figures 12, 13, and 14).

Figure 12

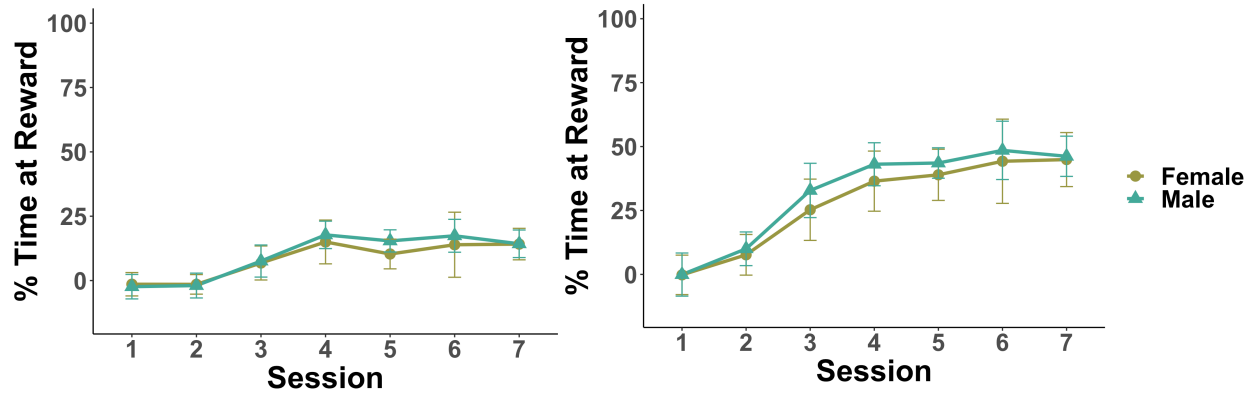
Pooled Studies: Reward Contact by Phenotype, CS1 and CS2



Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. During the CS1 timepoint, non-orienters show higher reward contact during sessions 5 and 7 (session 5 *$p < .005$, session 7 *$p < .001$). During the CS2 timepoint, non-orienters show higher reward contact at session 5 only (*$p < .05$).

Figure 13

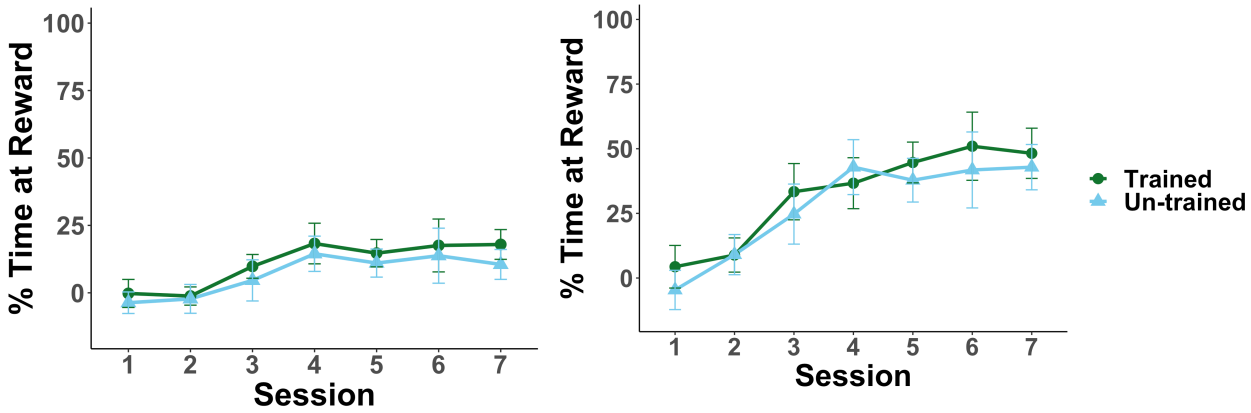
Pooled Studies: Reward Contact by Sex, CS1 and CS2



Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. At either timepoint, rats did not differ on their learning of the cue-reward association by sex (CS1 $p > .05$, CS2 $p > .05$).

Figure 14

Pooled Studies: Reward Contact by Social Training, CS1 and CS2



Note. Mean ± SE reward contact during the CS1 timepoint is shown on the left, and the CS2 timepoint on the right. At either timepoint, rats did not differ on their learning of the cue-reward association by social training (CS1 $p > .05$, CS2 $p > .05$).

Discussion

In this study, I hypothesized that orienter rats would show increased learning of the cue-reward association when provided with social training. Furthermore, I expected that these effects would be amplified in females. Contrary to expectations, non-orienter rats showed highest cue-reward association learning, though this effect was only found in experiment 2 at certain sessions. Furthermore, these effects were not related to social training or sex. The results of experiment 1 suggest no effects of the orienter phenotype or social training on the learning of a cue-reward association. When data was combined across experiments 1 and 2, non-orienters were again shown to learn better only at certain sessions, with no significant effects between social training or sex on the learning of cue-reward association. The present study suggests that non-orienters may acquire cue-reward associations with greater success than their orienter counterparts, though these effects were not consistently observed.

It is unclear why the effect of non-orienters' increased reward-contact did not sustain across all sessions, or more importantly, across both experiments. It is likely that the success of categorization of rats into orienters and non-orienters was dependent upon which experiment the rat was in. In experiment 1, orienting levels were very low, possibly as a result of the low light cue placement. In experiment 2, orienting was higher, likely related to the higher light cue placement. Furthermore, the categorization of orienters was statistically valid in experiment 2, providing confidence that the results of experiment 2 can be trusted in regard to phenotype. However, in experiment 1, this same analysis showed that the categorization of rats in orienters and non-orienters did significantly differ in their orienting levels.

The cause for a difference in the efficacy of categorizing rats into orienters and non-orienters between the two experiments likely results from differing chambers and scoring of

orienting. As previously mentioned, the light cue was very low to the ground in experiment 1, meaning that rats were considered orienting only if closely inspecting the light or in direct contact with it. In experiment 2, because the chambers differed and the light cue was much higher, the primary measure of orienting was rearing, in which rats stood on their hind legs to attend to the light cue. In the primary literature, orienting is defined almost exclusively by rearing to the cue. Thus, the differing methods between experiments challenged the categorization of rats based on cue-directed responses.

Given the intertwined nature of reward association and learning in this study, it is impossible to address whether the present results extend to either learning or reward-seeking alone. It's possible that non-orienters may learn better in general, or they may learn reward associations better. Future studies should seek to directly compare learning of both appetitive and aversive reward learning using in orienter and non-orienter animals.

Orienters, implicated in the literature as having poorer attentional control and higher impulsivity, show higher cue-directed behavior than their non-orienter peers, who only show reward-directed behavior. This cue-directed behavior is thought to manifest as higher reward-seeking and vulnerability to addiction in orienters because the incentive value of reward cues is increased, resulting in attentional bias to conditioned stimuli. Considering that non-orienters occasionally showed the highest learning in this study, the attentional bias characteristic of orienters may result in faulty learning. Orienters were expected to learn best based on the appetitive nature of the study, meaning that they were expected to show higher reward-seeking and thus, learning of the cue-reward association. However, the motivational properties gained by a CS in orienters apparently overpower the value of sucrose sipper and food pellet rewards. Even

in experiment 2 with a reward of increased salience and incentive by being made visible, orienters continued to show poorer learning compared to their non-orienter counterparts.

As a consequence of being underpowered to robustly examine sex differences in either experiment 1 or experiment 2, a pooled dataset was created using data from both experiments. There were some methodological differences between the experiments which limit robust comparability. These primarily included differences in chambers, reward stimuli, light cue placement, number of observational sessions, and number of testing sessions. Despite these differences, these studies were analyzed together to broadly examine the effects of sex, phenotype, and social training on the learning of the cue-reward association. Results from this analysis again point to non-orienters as the best learners of the cue-reward association, though this effect only reached significance at certain sessions.

Social training did not impact the learning of a cue-reward association. Rats, highly social animals, learn from others largely through interaction. Thus, because rats were only allowed observation and not direct interaction in this study, it could be that contact or interaction between demonstrator and observer rats is required for any benefit of social training to be observed. Other factors also impact the success of social learning and interactions between rats, such as dominance. Future studies seeking to utilize the present social learning paradigm should account for dominance status in demonstrator and observer rats.

In future social training studies, demonstrator phenotype should be examined and accounted for. In the present study, data from demonstrator learning sessions was unavailable and we were unable to categorize demonstrators into orienters and non-orienters. Consequently, we could not assess the effect of demonstrator phenotype on the learning of their observer peers. A rat who observed a demonstrator of the orienter phenotype perform a cue-reward association

may learn differently than a rat who observed a non-orienter perform the same association. Orienters, who attend highly to the light cue, may have inadvertently trained their observer peers to also attend to the light cue. Given that the results of the present study point to a role orienter phenotype in determining learning success, it is conceivable that demonstrator orienters are less effective in training their peers. Future social training studies should first determine a whether a demonstrator is an orienter or non-orienter, then should proceed to include only non-orienters as demonstrators.

This study shows that males and females do not differ in their learning of a cue-reward association, though it was hypothesized that females would show higher learning, especially if orienters or if they received social training. Sex differences are shown during all stages of drug use, with females generally showing higher susceptibility to drug addiction. Females were expected to show higher learning of the cue-reward association because though not drugs, sucrose sipper and feed pellets are rewarding. However, the rewards in this study were too mild for any sex differences in reward acquisition to emerge. Sex differences may emerge in an experiment of similar design which utilizes a drug or alcohol reward stimulus.

In conclusion, I *a priori* hypothesized that rats of the orienter phenotype would learn better, specifically when provided social training, but my findings did not support this hypothesis. Rather, non-orienters selectively showed increased learning of a cue-reward association. Sex and social training did not influence cue-reward association learning. Future studies should seek to improve or expand upon this study's methods for social training. Furthermore, I believe that more robust differences in orienters and non-orienters, as well as between males and females might emerge with a more rewarding stimulus, such as drugs or alcohol.

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