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Research article

A novel operant task to assess social reward and motivation in rodents

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HIGHLIGHTS

- A simple task for quantifying social and non-social reward.
- A novel approach to measure social reward without a memory component.
- Uses a simple apparatus that is easy to construct and inexpensive.
- Ideal for investigating the neural mechanisms controlling reward.

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ABSTRACT

Background: Social reward plays a critical role in the development of beneficial social relationships, and disorders of the mechanisms controlling social reward are involved in the etiology of many psychiatric diseases.
New method: We present a novel operant social preference task to quantify social reward in rodents using an apparatus with three chambers separated by one-way vertical-swing doors. The experimental animal is placed in the larger chamber while the two smaller chambers either remain empty or contain a stimulus animal or other potential reward stimulus. Adding weights to the door can alter effort required for rewards.
Results: Hamsters (Mesocricetus auratus) entered the chamber containing a stimulus hamster significantly more frequently than an empty chamber. When the reinforcing effects of social interactions were compared to food reward under progressive cost requirements, the reinforcing effects of social interaction and sunflower seeds were similar. Progressively increasing the door weight decreased number of entries, but increased time spent attempting to open the doors.
Comparison with existing methods: The quantification of the rewarding properties of social interactions has almost exclusively used the conditioned place preference (CPP) paradigm. Although robust and reliable, CPP includes a memory component, because it relies on the association of place with the social interaction while the operant task presented here does not.
Conclusions: This task allows for detailed and direct assessment of social and non-social rewards that may serve as effective behavioral reinforcers in this operant conditioning model, and it can be used to investigate the neural mechanisms regulating motivation.

1. Introduction

The rewarding properties of social interactions are critical for the expression of adaptive social behaviors, including the development of social relationships in most species (Darwin, 1859; Thorndike, 1905; Skinner, 1938; Lorenz and Leyhausen, 1973; Oliveira et al., 1998; Pettinger et al., 2011; Pusey and Packer, 1997; Krach et al., 2010). In humans, deficits in the rewarding properties of social stimuli likely contribute to many psychiatric disorders (Dichter et al., 2012; Stavropoulos and Carver, 2013; Foulkes et al., 2015; Novacek et al., 2016). The basic neural mechanisms regulating social reward have been investigated in rodent models almost exclusively with the conditioned place preference (CPP) paradigm (Calcagnetti and Schechter, 1992; Meisel and Joppa, 1994; Peartree et al., 2012; Dolen et al., 2013; Gil et al., 2013; Song et al., 2016).

Abbreviations: CPP, conditioned place preference; OSP, operant social preference.

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Although robust and reliable, CPP includes a memory component, because it relies on the association of place with the social interaction (Trezza et al., 2011). In other words, reward value is operationalized as time spent in the area associated with the memory of the rewarding stimulus, even though the presumed reward is not present at the time of testing. Here, we present a novel operant social preference (OSP) task that more directly quantifies social reward; as an operant task that tests the reinforcing effects of a visible social stimulus, it does not rely on memory.

Other operant conditioning tasks investigate the rewarding properties of opportunities to interact with a conspecific using lever-pressing or nose-pokes (Martin and Iceberg, 2015; Achterberg et al., 2016). For the first time here, movement through one-way vertical-swing doors is the operandum used to assess motivation to interact with a conspecific (Olsson and Keeling, 2002; Wirth et al., 2003; Seaman et al., 2006; Tilly et al., 2010). This new operant task allows investigation of whether social interaction reinforces entries into a separate chamber. As with other operant tasks, if placing a stimulus in the chamber increases chamber entry behavior (the operandum), then that stimulus is likely to be serving as positive reinforcement with some reward value. This task is less dependent on memory than other tasks, because holes in the doors allow visual, auditory and olfactory stimuli to be detected throughout the test session. Reward value can be quantified by directly measuring number of rewards "consumed" and allowing subjects the choice to access reward or not. In addition, progressively increasing the weight of the door allows assessment of reward value via its relationship with energy expenditure (Beeler et al., 2012). Syrian hamsters were used to validate this novel task, because hamsters have been successfully employed in studies of social motivation (Ferris et al., 1984; Solomon et al., 2007; Morrison et al., 2014; Song et al., 2014; Gray et al., 2015) and social reward (Meisel and Joppa, 1994; Gil et al., 2013; Song et al., 2016). They also provide an excellent model for pre-clinical studies of psychiatric disorders (Terranova et al., 2016).

To validate this novel task, we tested whether same-sex social interactions would reinforce the acquisition of an operant task, followed by testing its extinction in the absence of the social stimulus, and its reinstatement by re-introducing the social stimulus (Suomi et al., 1971; Phillips and Fibiger, 1990; Ranaldi and Roberts, 1996; Sapolsky, 2015). We also compared the reinforcing effects of social interaction with a more conventional food reward, sunflower seeds, in both acquisition conditions and under progressive increases in door weights (Rickard et al., 2009). If this novel OSP task is a valid measure of reward, then the presentation of rewarding stimuli should decrease latency and increase frequency of entries into chambers containing rewarding stimuli compared to empty chambers. Further we examined whether social and food rewards have similar reinforcing properties.

2. Materials and methods

2.1. Subjects

Male Syrian hamsters (n = 34, 120–140 g) arrived from Charles River Laboratory (Wilmington, MA) at 11 weeks old and were housed singly in a humidity and temperature controlled (22 °C) vivarium. All animals were housed in solid-bottom Plexiglas cages (43 × 22 × 20 cm) containing corncob bedding and cotton nesting material (Neslets; Ancare, Bellmore, NY) in a reverse light-dark (LD) cycle (14L:10D; lights off at 13:00). Food and water were available *ad libitum*. Hamsters acclimated for 4 weeks before experiments. Hamsters were weighed just prior to their first behavioral test and again at the end of their last behavior test. All behavioral tests were performed under red light during the first 3 h of the dark phase of the LD cycle. All procedures were carried out in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and approved by the Georgia State University Institutional Animal Care and Use Committee.

2.2. Operant social preference apparatus

The OSP apparatus was constructed of clear acrylic (Custom Plastics, Decatur, GA, USA) (Fig. 1). The apparatus consisted of three chambers: a main chamber (50.8 × 33 × 30.5 cm, $l \times w \times h$) and two smaller adjacent chambers (25.4 × 17.8 × 30.5 cm, $l \times w \times h$). Each small chamber is separated from the main chamber by a one-way vertical-swing door (10.2 × 7.6 cm, $l \times h$); smaller chambers can only be accessed from main chamber. Chamber doors were brushed with steel wool to achieve coarse texture, distinct from rest of apparatus, and doors were perforated by circular holes to allow airflow. Buckets that served to hold weights [85 g (3oz), 113 g (4oz) and 170 g (6oz)] were attached to each door on the small chamber side.

2.3. Operant social preference conditioning

Operant conditioning sessions began with hamsters placed in a designated drop zone (10.2 × 7.6 cm, $l \times h$) against the far wall of the main chamber in the OSP apparatus, equidistant from both small chambers. A smaller (100–120 g) non-aggressive (group housed), same-sex stimulus hamster was confined to either the left or right smaller chamber. Assignment of the stimulus hamsters to the right or left chamber was counter-balanced across experimental subjects. Subjects never interacted with the same stimulus hamster across testing days: a new stimulus hamster was provided for each subject on each test day. Subjects were allowed to move throughout the apparatus, while stimulus hamsters were confined to one of the small chambers. Twenty seconds after entry into either small chamber, the subject was returned to the drop zone in the main chamber. An initial acquisition session lasted between 10 and 30 min; each subject was required to enter the chamber holding the stimulus animal at least 3 times. Time spent in the apparatus for controls without social interaction (both chambers empty) was yoked with subjects that were experiencing social interaction. All hamsters received at least two more acquisition sessions on two consecutive days. Additional sessions were conducted if criteria for acquisition were not met (at least 2 social entries for 2 consecutive days). No extra acquisition sessions were needed in these experiments. All test sessions except for the first acquisition session were 10 min in duration. Hamsters progressed from no weights in the door buckets during the first 2 days to 113 g for the next 2 days during acquisition testing. Only subjects that met the acquisition criterion of least 2 social entries into the chamber holding the stimulus hamsters during the 10-min session for two consecutive days were included in subsequent experiments. Displays of submissive behavior in the presence of conspecifics were also grounds for exclusion (two in experiment 2).

2.3.1. Progressive weights schedule

To assess motivation under higher cost requirements, test sessions began under the same procedure as described above except door weights were progressively increased over consecutive days starting at 113 g (4oz), 227 g (8oz), 340 g (12oz), 454 g (16oz), 634 g (22oz), 794 g (28oz)].

2.3.2. Food reinforcer

To compare reward-related behavior between social stimulus and food stimulus, 10–15 sunflower seeds were placed in one of the small chambers, rather than a stimulus hamster. Ten to fifteen unsalted shell-less seeds were maintained in the chamber throughout the test session. (Sunflower seeds were replenished to 10–15