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

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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.

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Contributors

Borland designed and participated in conducting all experiments, analyzed the data, and also wrote the first draft of this manuscript. Aiani and Grantham participated in conducting the experiments and scored behavior. Dr. Frantz and Dr. Albers supervised data analyses and also contributed significantly in the experimental design, and preparation and editing of the manuscript. Dr. Albers also supervised all the experiments. Dr. Song made significant contributions to the experimental design.

Conflict of interest

The authors declare no conflicts of interest.

Ethical standards agreement

I, H. Elliott Albers have read and have abided by the statement of ethical standards for manuscripts submitted to the Journal of Neuroscience Methods

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jneumeth.2017.06.003>.

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.

Keywords

Place preference; Social motivation; Hamsters; Apparatus; Dopamine; Food reward

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). 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 ($43 \times 22 \times 20$ 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 ($50.8 \times 33 \times 30.5$ cm, $l \times w \times h$) and two smaller adjacent chambers ($25.4 \times 17.8 \times 30.5$ 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), 227g(8oz), 340 g (12oz), 454 g (16oz), 634 g (22oz), 794g (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 after each entry, if consumed by a subject). Otherwise, all conditions were the same

2.4. Behavior scoring

All behavior tests were recorded and analyzed using the Noldus Observer system. A scorer blind to treatments and groups scored each videotape. In addition to chamber entries and latency to chamber entry, the following mutually exclusive behaviors were scored: duration of aggression, social investigation, submission (e.g. fleeing, avoidance), grooming and non-social behavior. The frequency of attacks was scored as a point event during displays of aggression, and frequency of flank marks was scored as a point event during non-social behavior. For operational definitions of these behaviors, please see (Drickamer et al., 1973; Gray et al., 2015). Flank marking was scored due to its strong link to dominance status and territoriality in rodents (Ferris et al., 1987; Albers and Rowland, 1989). Generally these behaviors were measured to enable description of how time was spent in the small chamber, ultimately aiding conclusions about their ability to reinforce the chamber entry behavior. Time spent pushing door open was measured by scoring duration in which subject hamster displaces either door from normal resting position. Locomotor activity was also scored: the OSP apparatus was subdivided into 6 equal-sized squares (16.9×16.5 cm) and the number of square entries was counted.

2.4.1. Experimental design and statistical analysis—Data were analyzed using SPSS software (SAS Institute, 1990) 23.0 for Windows. All data were examined to determine if the assumptions of parametric statistical tests were met. When assumptions were violated, data were square root transformed (number of chamber entries and grooming duration in exp. 1 and time spent pushing door open in exp. 2) or cube root transformed (frequency of flank marks in exp. 1). All tests were two-tailed, and results considered statistically significant if $p < 0.05$. All data are presented as mean $\pm$ standard error of the mean.

2.5. Experiment 1: effects of social interaction on chamber preference

Male Syrian hamsters were assigned to either the social exposure group ($n = 8$) or the no social exposure control group ($n = 8$). In the social exposure group, hamsters were tested with a stimulus hamster in one of the small chambers for 7 consecutive days (acquisition training, social days: SD), followed by three days with both chambers empty (extinction, extinction days: ED), followed by a final day on which a stimulus hamster was reintroduced into one of the small chambers (reinstatement test). In the no social exposure control group, both small chambers were empty for all 11 sessions. Body weights of hamsters were counter-balanced between groups.

In Experiment 1, data were averaged over the last 3 acquisition days and the 3 extinction days. Mixed or repeated measures ANOVAs were performed to examine effects of treatment condition (between subjects: social versus no-social), chamber condition (within subjects: stimulus hamster versus empty), and training condition (within subjects: acquisition versus extinction, or separately over each of the 11 test days) on number of entries and latency to enter chambers, grooming duration, frequency of flank marks, aggression duration and duration of social investigation. Post-hoc comparisons were carried out as appropriate using paired and independent sample t -tests. Correlations were carried out to investigate potential relationships between social behaviors and number of social entries or social preference scores (number of entries into social chambers– number of entries into empty chambers) on test days 1, 4, 6, 7, and 11. To control for experiment-wise error, alpha levels were adjusted according to the Holm-Bonferroni method.

2.6. Experiment 2: comparison of effects of social interaction and sunflower seeds on chamber preference

First in Experiment 2 male hamsters were assigned to either the social exposure group ($n = 10$) in which one of the small chambers contained a stimulus hamsters, or a food exposure (sunflower seed) group ($n = 8$) in which one of the chambers contained sunflower seeds. Acquisition of a preference for the chamber containing the stimulus hamster or sunflower seeds, over an empty chamber, was tested over 4 consecutive days. Second in Experiment 2, after stable acquisition of door entries for social or sunflower preference at 0 g and 113 g, door weights were increased daily from 227 g, to 340 g, 454 g, 634 g and 794 g. On the final day of testing, door weights were returned to 113 g. Two social condition subjects were excluded for not meeting acquisition criteria, or displaying submissive behavior when in the presence of a conspecific. Body weights of hamsters were counter-balanced between groups.

For experiment 2, data for 0g and 113 g were averaged across multiple test days. Mixed measures ANOVAs were used to examine effects of treatment condition (between-subjects: social versus sunflower), chamber condition (within subjects: stimulus versus empty), and acquisition day (within-subjects: days 1–4) or weights (within-subjects: PWs 113g–794g) on number of entries and latency to enter chambers, social or sunflower preference scores and time spent pushing doors open. Post hoc comparisons were carried out using paired and independent sample *t*-tests.

3. Results

3.1. Experiment 1: effects of social interaction on chamber preference

To determine whether social interactions were rewarding based on their ability to reinforce chamber entry behavior, the number of entries into the chambers was analyzed in the social versus no-social group by averaging the last 3 acquisition and 3 extinction days and factoring them into a 2×2 mixed measures ANOVA. There was a main effect of treatment (social exposure versus no-social exposure: $p < 0.001$, $F(1,14) = 117.830$) on entries into chambers. There was also an effect of training condition (acquisition versus extinction: $p = 0.001$, $F(1,14) = 15.653$), and an interaction of treatment group and training condition ($p = 0.001$, $F(1,14) = 19.635$) on entries into chambers (Fig. 2a inset). Fewer entries into chambers were observed during extinction training than acquisition training for social exposure ($p = 0.003$, $t(7) = 4.350$), but not for the no-social exposure treatment groups ($p = 0.402$, $t(7) = -0.585$). A 2×11 mixed measures ANOVA on entries into chambers on individual sessions revealed a main effect of social treatment ($p < 0.001$, $F(1,14) = 103.447$), an effect of test session (11 test days: $p < 0.001$, $F(10,140) = 3.578$), and a significant interaction ($p < 0.001$, $F(10,140) = 3.958$; Fig. 2a) on the number of entries into chambers. Independent sample *t*-tests with Holm-Bonferroni corrections revealed that social exposure increased the number of chamber entries on social acquisition days 2 ($p = 0.006$), 3 ($p = 0.009$), 4 ($p = 0.001$), 5 ($p < 0.001$), 6 ($p < 0.001$), 7 ($p = 0.001$), extinction days 1 ($p < 0.001$), 2 ($p = 0.005$) and social reinstatement day ($p < 0.001$), but not extinction day 3 ($p = 0.161$), compared to chamber entries in the no-social exposure treatment group.

With regard to latency to enter the first (or stimulus) chamber, a main effect of treatment group ($p = 0.002$, $F(1,14) = 13.521$), test session ($p < 0.001$, $F(10,140) = 11.395$) and interaction of treatment group and test session ($p < 0.001$, $F(10,140) = 5.940$) were all significant (Fig. 2b). Social exposure decreases latency to enter chambers. The latency to enter chambers also decreased from the first test session to all subsequent test sessions ($p < 0.001$). Independent *t*-tests revealed that social exposure decreased the latency to enter chambers on social acquisition days 5 ($p = 0.003$, $t(14) = -3.894$), 6 ($p = 0.003$, $t(14) = -3.763$), 7 ($p = 0.006$, $t(14) = -3.274$), and the second extinction day ($p = 0.001$, $t(14) = -3.958$), compared to no-social exposure group (Fig. 2b).

To determine the effect of social interaction on chamber preference in the social exposure treatment group only, the number of entries into the chamber containing a stimulus hamster versus the empty chamber was averaged for the last 3 acquisition and 3 extinction days. A 2×2 repeated measures ANOVA revealed a main effect of within-subjects chamber stimulus (social vs. empty: $p < 0.001$, $F(1,7) = 65.790$), a main effect of training condition ($p < 0.001$,

$F(1,7) = 38.769$), and an interaction ($p = 0.021$, $F(1,7) = 8.773$; Fig. 2c inset). Paired t -tests revealed that there were more entries into chambers containing stimulus hamsters compared to empty chambers during acquisition ($p < 0.001$, $t(7) = 6.440$) and extinction training ($p = 0.003$, $t(7) = 4.338$). Paired t -tests also revealed that extinction training decreased entries into chambers containing stimulus hamsters ($p = 0.003$, $t(7) = 4.350$), but not empty chambers ($p = 0.577$, $t(7) = 0.577$). A 2×11 repeated measures ANOVA revealed that there was a main effect of within-subjects chamber stimulus ($p < 0.001$, $F(1,7) = 59.316$) and a main effect of test session ($p = 0.007$, $F(10,70) = 2.723$) on number of entries into chambers for social exposure treatment group. There was no interaction of test session and within-subjects chamber stimulus on number of entries into chambers ($p = 0.466$, $F(10,70) = 0.984$). There were fewer entries into chambers on the third extinction day compared to all other test days ($p < 0.05$), except for the second and third acquisition days and second extinction day ($p > 0.05$; Fig. 2c).

With regard to latency to enter the stimulus chamber, a main effect of within-subjects chamber stimulus (social versus empty: $p = 0.004$, $F(1,7) = 18.140$) was revealed in a 2×11 repeated measures ANOVA, with a shorter latency to enter chambers containing a stimulus hamster versus empty chambers (Fig. 2d). There was also a main effect of test session ($p < 0.001$, $F(10,70) = 29.818$) on the latency to enter chambers in social exposure treatment group, such that the latency was longer on the first day compared with all other days ($p < 0.001$).

For scored social behaviors there was no main effect of treatment group ($p = 0.090$, $F(1,14) = 3.313$) on number of flank marks as revealed by a 2×11 mixed measures ANOVA nor significant interaction ($p = 0.344$, $F(10,140) = 1.138$; Fig. 3a). There was a main effect of test session ($p = 0.033$, $F(10,140) = 3.248$), with more flank marking on day 1 compared to days 8 ($p = 0.020$), 10 ($p = 0.036$) and 11 ($p = 0.020$). For grooming, there was a main effect of treatment ($p = 0.020$, $F(1,14) = 6.841$) and an interaction of treatment condition and test session ($p = 0.020$, $F(10,140) = 2.217$), but no main effect of test session ($p = 0.441$, $F(10,140) = 1.006$; Fig. 3b). Independent t -tests revealed more grooming in the no-social exposure group on days 4 ($p = 0.034$), 5 ($p = 0.009$), 6 ($p = 0.040$), 8 ($p = 0.012$) and 11 ($p = 0.019$), compared to the social exposure group (Fig. 3b). One-way ANOVAs revealed that neither the duration of social investigation ($p = 0.911$, $F(7,49) = 0.158$; Fig. 3c) nor the duration of aggression ($p = 0.355$, $F(7,49) = 1.142$; Fig. 3d), differed over the 8 days of social interaction testing in the social exposure treatment group.

Neither the number of entries into the chambers containing stimulus hamsters, nor social preference score (entries into social chamber – entries into empty chamber) correlated with the duration of aggression, duration of grooming, nor the number of flank marks on test days 1, 4, 6, 7 and 11 ($p > 0.05$; data not shown). There was a trend for the duration of aggression to be positively correlated with number of entries into chamber containing stimulus hamsters on day 1 ($p = 0.056$, $r = 0.694$). However, as expected, the number of entries into chambers containing stimulus hamsters and social preference scores were correlated with the duration of social investigation on test sessions 1, 4, 6, 7 and 11 ($p < 0.05$).

3.2. Experiment 2: comparison of the rewarding properties of social interactions and sunflower seeds

To compare the rewarding properties of social interactions and sunflower seeds during acquisition, one group of hamsters was allowed access to a chamber containing a stimulus hamster or an empty chamber, while another group was allowed access to either a chamber containing sunflower seeds or an empty chamber. The placement of the stimulus hamster or sunflower seeds in either the left or right chamber was counter-balanced between subjects. Number of entries into chambers containing either stimulus hamsters or sunflower seeds was greater than the number of entries into empty chambers ($p < 0.001$, $F(1,14) = 48.744$) as revealed by a $2 \times 2 \times 4$ mixed measures ANOVA. There was no main effect of test session on number of entries into chambers ($p = 0.090$, $F(3,42) = 2.312$), nor were there between group differences on number of entries into the chambers (social versus sunflower seed condition: $p = 0.890$, $F(1,14) = 0.020$; Fig. 4a).

The latency to enter chambers containing a stimulus hamster or chamber containing sunflower seeds was shorter than the latency to enter empty chambers ($p < 0.001$, $F(1,10) = 28.338$) as revealed by a $2 \times 2 \times 4$ mixed measures ANOVA (Fig. 4b). There was a main effect of test session on the latency to enter chambers ($p < 0.001$, $F(3,30) = 20.935$), such that the latency to enter chambers decreased after the first day in comparison with days 2, 3 and 4 ($p < 0.002$). There were no between group differences on the latency to enter chambers ($p = 0.859$, $F(1,10) = 0.033$).

There were no between group differences on social or sunflower seed preference score ($p = 0.445$, $F(1,14) = 0.616$), as revealed by a 2×4 mixed measures ANOVA (data not shown). There was also no main effect of test session on social or sunflower seed preference score ($p = 0.489$, $F(3,42) = 0.822$).

To compare the rewarding properties of social interactions and sunflower seeds as the door weight was progressively increased; the same groups of hamsters from Experiment 2 were trained until the hamsters consistently chose the chamber containing the stimulus hamster over the empty chamber, or they chose the chamber containing sunflower seeds over the empty chamber, at 113 g door weights. On subsequent trials the weights on both doors were progressively increased from 113 g up to 794 g over 5 consecutive days (227g–794g). On the final day of the experiment, the door weight was returned to the standard 113 g. Door weights had a significant effect on number of entries into chambers ($p < 0.001$, $F(7,98) = 34.062$), as revealed by a $2 \times 2 \times 8$ mixed measures ANOVA (Fig. 4c). Specifically, as the weight of the door increased, the number of entries decreased ($p < 0.05$). There were also significantly more ($p < 0.001$, $F(1,14) = 53.937$) entries into chambers containing stimulus hamsters or sunflower seeds than into empty chambers. There was an interaction of weights and within-subjects chamber stimulus on number of entries into chambers ($p < 0.001$, $F(7,98) = 13.267$). Subjects made more entries into chambers containing stimulus hamsters or sunflower seeds, compared to empty chambers at 0 g, 113 g, 227 g, 340 g, 454 g, and reinstatement at 133 g door weights as revealed by paired t -tests ($p < 0.05$). There were no between group differences ($p = 0.653$, $F(1,14) = 0.211$; Fig. 4c) in number of entries into all chambers.

Door weights had an effect on the latency to enter chambers ($p < 0.001$, $F(7,77) = 17.364$) as revealed by a $2 \times 2 \times 8$ mixed measures ANOVA (Fig. 4d). There was also a main effect of within-subjects chamber stimulus on the latency to enter chambers ($p < 0.001$, $F(1,11) = 25.110$), with a shorter latency to enter chambers containing a stimulus hamster or sunflower seeds than empty chambers. There was an interaction of within-subjects chamber stimulus and door weights on the latency to enter chambers ($p = 0.050$, $F(7,77) = 2.128$). Subjects showed a shorter latency to enter chambers containing stimulus hamsters or sunflower seeds at 113 g, 227 g, 340 g and reinstatement at 113 g door weights, compared to empty chambers, as revealed by paired t -tests ($p < 0.05$). There were no between group differences in the latency to enter chambers between social and sunflower seed conditions ($p = 0.899$, $F(1,11) = 0.017$).

Door weights had an effect on social or sunflower seed preference score ($p < 0.001$, $F(7,98) = 13.267$; Fig. 5e) as revealed by a 2×8 mixed measures ANOVA. As weights increased, preference scores decreased ($p < 0.05$; data not shown). There were no significant between group differences in social or sunflower seed preference score ($p = 0.174$, $F(1,14) = 2.052$).

Door weights had an effect on time spent pushing the doors open ($p < 0.001$, $F(5,55) = 10.895$), as revealed by a $2 \times 2 \times 6$ mixed measures ANOVA (Fig. 5). There was also a main effect of door condition (doors leading to stimulus hamsters or sunflower seeds versus doors leading to empty chambers) on time spent pushing doors open ($p < 0.001$, $F(1,11) = 80.109$). Yet there was no significant between group differences in the time spent pushing the doors open ($p = 0.490$, $F(1,11) = 0.510$). There was an interaction of door condition and door weights on time spent pushing the doors open ($p = 0.033$, $F(5,55) = 2.640$). Subjects spent more time pushing the doors open at 340 g, 454 g, 634 g and 794 g compared to 113 g weights as revealed by pairwise comparisons ($p < 0.05$).

4. Discussion

These data indicate that this novel operant social preference task is a valid measure of social reward and social motivation. Opportunity for social interaction reinforces movement through a vertical-swing door. Hamsters rapidly acquired a preference for the chamber that provided social interaction over an empty chamber, in most cases requiring only 1–2 test sessions. Subjects also dramatically reduced their latency for performing the operant task of entry through a weighted chamber door by the second test session. Furthermore, a conventional rewarding stimulus of presumably palatable food (sunflower seeds) also reinforced chamber entries in a manner similar to social interaction. Finally, progressively increasing the weight of the chamber door decreased the number of chamber entries, as expected, while increasing the time spent pushing the door open. In summary, this task provides a new approach for assessing reward and motivation.

The present operant task is independent of memory, as the doors allow visual, auditory and olfactory communication, and the task allows for the assessment of motivation under varying energy expenditure conditions. This method also allows for estimation of energy expenditure (cost) for rewarding stimuli by measuring the work required to push the door (potential energy of the door). Although still controversial and often debated, motivation can be

operationally defined as the set of energetic forces that initiates work-related behaviors, determining the form, direction, intensity, onset and duration of emitted behaviors (Lorenz, 1950; Hogan, 1997; Graham and Weiner, 2006; Walton et al., 2006; Elliot, 2008; Pinder, 2008; Caldwell and Albers, 2015; Kim et al., 2017). Thus, with this OSP task, social motivation can be calculated using a set of dependent measures including latency to enter chamber, number of chamber entries, chamber preference score, the time spent pushing doors open and energy expenditure. These measures provide the opportunity to estimate reward value by measuring the relationship between rewards acquired and cost requirements (door weights). Additional highlights of this novel behavioral task are notable. 1) Social preference and social behavior are stable across consecutive days of testing (maintenance). 2) Removal of stimulus hamster results in a steady decrease in entries into chambers containing stimulus hamsters but not empty chambers (extinction), and reintroduction of stimulus hamster reinstates entries into social chamber and social preference (reinstatement). 3) Similar to Bailey et al. (2015) progressive hold-down task, the OSP task can dissociate between the goal-directed components of motivation vs. general arousal (Bailey et al., 2015). At heavy door weights, rewards are accessed only through prolonged and continuous periods of goal-directed effort. Increases in goal-directed motivation are easily measured as increased time spent pushing doors to loaded stimulus chambers, but not doors to empty chambers. In contrast, increases in general arousal may increase time spent pushing any doors. 4) Finally, sunflower seeds reinforced entries into chambers in the absence of prior food deprivation, suggesting that the seeds have high hedonic value, although nutritional value may also contribute. Observation of hamsters during the testing revealed that they often retained the seeds in their mouth pouches as well as consuming the sunflower seeds immediately.

As with any experimental procedure, this one does have limitations. First, the interval between completion of operandum and presentation of the resultant stimulus is not and cannot be varied. Second, the number of entries through chamber doors (rewards acquired) particularly under high weights may depend on the subject's body weight and strength (although time spent attempting to push the door open serves as a complementary measure for motivation that should be less dependent on subject strength). Third, this apparatus is not automated. An experimenter must be present at all times to return subjects to the main chamber after entry into small chambers. Finally, in the present conditions, hamsters were socially deprived prior to testing, but were not food restricted. Future experiments can address at least this last caveat.

Due to the critical role of social motivation in the development and maintenance of beneficial social relationships, understanding the neural mechanisms controlling social reward and social motivation remains a high priority. The novel operant task reported here is a more direct measure of social reward and social motivation compared to the more traditional CPP paradigm because it is independent of social memory, directly quantifies consumption of reward, and subjects have the choice to access or not access the social stimulus. This is the first operant task to use progressively weighted doors to assess social motivation, and the first to systematically quantify an operational definition of energy expenditure for reward (e.g. time spent pushing the door open). In summary, this operant task allows for a detailed assessment of social reward and social motivation, and presents

great potential for use in identifying the neural mechanisms for these phenomena, as well as for studies of the rewarding properties of non-social stimuli.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

CPP	conditioned place preference
OSP	operant social preference

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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.

Fig. 1.

Operant Social Preference Apparatus: schematic (left) and vertical view (right). The main chamber contains an experimental subject and a stimulus hamster occupies one of the side chambers, separated by the vertical-swing door. The door allows visual, auditory and olfactory cues to enter the small chambers through the open top and holes in the door. Drop zone rectangular box is to the immediate left of subject hamster.

Fig. 2.

Comparison of the preference for chambers containing a stimulus hamster versus an empty chamber (video 1 attachment). Panel a: Comparison between the group that had stimulus hamsters present in one chamber (social exposure) and the group that had only empty chambers (no-social exposure group) on chamber entries. Social exposure results in more chamber entries than no-social exposure group on all days except first day of testing and third extinction day (* indicates significant difference between groups, $p < 0.05$). Inset is comparing averages of last 3 acquisition days and 3 extinction days for each group. Removal of social stimulus decreases chamber entries in social exposure group. Panel b: Shorter latency to enter the chambers in the social exposure group developed to significant difference by day 5 compared to the latency to enter the chambers in the no-social control group. There was a shorter latency to enter the chambers from the first session compared to all subsequent sessions independent of treatment group (# indicates significant difference compared to all other test sessions). Panel c: In the social exposure group hamsters preferred the social chamber over the empty chamber (* indicates significant difference between chambers). Inset is comparing averages of last 3 acquisition days and 3 extinction days for

each within-subjects chamber stimulus. Removal of social stimulus decreases entries in chambers containing a stimulus hamster, but not entries into empty chambers. Panel d: Similarly, the social exposure group showed shorter latency to enter the social chambers compared to empty chambers. There was a shorter latency to enter the chambers from the first session compared to all subsequent sessions independent of treatment group (# indicates significant difference compared to all other test sessions).

Fig. 3.

Effect of social exposure (one chamber containing a stimulus hamster) vs. no-social exposure (both chambers empty) on the number of flank marks expressed and the duration of grooming. Panel a: Number of flank marks increases over the days of testing (* indicates main effect of test session). Panel b: More grooming was observed in no-social exposure group compared to social exposure group on test days 4, 5, 6, extinction test day 1 and reinstatement test day (* indicates difference in treatment group). Panel c: No significant difference in the duration of social investigation across all social test days in the social exposure group. Panel d: No significant difference in the duration of aggression across all social testing days in social exposure group.

Fig. 4.

Chamber preferences of a group of hamsters that selected between a chamber containing a stimulus hamster or an empty chamber (Social Condition: $n = 8$) or a group of hamsters that selected between a chamber containing sunflower seeds or an empty chamber (Sunflower Condition: $n = 8$) during the acquisition of chamber preference (a,b) and under progressively increasing weight of doors (c,d). Panel a: More entries were observed into chambers containing stimulus hamsters or sunflower seeds compared to empty chambers (* indicates significant difference in within-subjects chamber stimulus). Panel b: Shorter latency to enter chambers containing stimulus hamsters or sunflower seeds compared to empty chambers. There was a longer latency to enter chambers on the first testing session compared to all subsequent testing sessions (# indicates significant difference compared to all other test sessions). Panel c: More entries were observed into chambers containing stimulus hamsters or sunflower seeds compared to empty chambers at 0g, 113 g, 227 g, 340 g, 454g and reinstatement of 113 g door weights. Panel d: There was a shorter latency to enter chambers

containing stimulus hamsters or sunflower seeds compared to empty chambers at 113 g, 227 g, 340g and reinstatement of 113 g door weights.

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Fig. 5.

Effect of door weights on the time spent pushing the doors open (video 2 attachment). As door weights increased the time spent pushing the doors for entry into stimulus chambers increased, but not doors for entry into empty chambers (* indicates difference in within-subjects door weights on time spent pushing the door open).