Drug and Alcohol Dependence 178 (2017) 87–93

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Heroin and saccharin demand and preference in rats

Lindsay P. Schwartz, Jung S. Kim, Alan Silberberg, David N. Kearns*

Psychology Department, American University, Washington, DC, United States

ARTICLE INFO

Keywords:
Heroin self-administration
Demand
Essential value
Choice
Saccharin
Rats

ABSTRACT

Background: Several recent studies have investigated the choice between heroin and a non-drug alternative reinforcer in rats. A common finding in these studies is that there are large individual differences in preference, with some rats preferring heroin and some preferring the non-drug alternative. The primary goal of the present study was to determine whether individual differences in how heroin or saccharin is valued, based on demand analysis, predicts choice.

Methods: Rats lever-pressed for heroin infusions and saccharin reinforcers on fixed-ratio schedules. The essential value of each reinforcer was obtained from resulting demand curves. Rats were then trained on a mutually exclusive choice procedure where pressing one lever resulted in heroin and pressing another resulted in saccharin. After seven sessions of increased access to heroin or saccharin, rats were reexposed to the demand and choice procedures.

Results: Demand for heroin was more elastic than demand for saccharin (i.e., heroin had lower essential value than saccharin). When allowed to choose, most rats preferred saccharin. The essential value of heroin, but not saccharin, predicted preference. The essential value of both heroin and saccharin increased following a week of increased access to heroin, but similar saccharin exposure had no effect on essential value. Preference was unchanged after increased access to either reinforcer.

Conclusion: Heroin-preferring rats differed from saccharin-preferring rats in how they valued heroin, but not saccharin. To the extent that choice models addiction-related behavior, these results suggest that overvaluation of opioids specifically, rather than undervaluation of non-drug alternatives, could identify susceptible individuals.

1. Introduction

Recently, a number of studies have investigated choice between heroin and non-drug reinforcers in rats (Lenoir et al., 2013; Madsen and Ahmed, 2015; Tunstall et al., 2014; Vandaele et al., 2015). This interest has been stimulated by the observation that preference for drugs over non-drug alternatives may model aspects of addiction (Ahmed, 2010). A common finding in studies with rats is that there are large individual differences in preference, with some rats consistently choosing heroin while others prefer the non-drug alternative.

The factors responsible for these individual differences are not well understood. The present study was designed to investigate whether differences in the ways that rats value heroin or a non-drug alternative (saccharin, in this case) account for the choices they make. In a mutually exclusive choice situation, heroin preference could result from either high heroin valuation or low saccharin valuation. That is, heroin-preferring rats could differ from saccharin-preferring rats in terms of how they value heroin, with there being no difference in how these subsets of rats value saccharin. Alternatively, heroin- and saccharin-preferring rats may value heroin comparably, but saccharin-preferring rats may value saccharin more highly than do heroin-preferring rats. Either of these possibilities, or a combination of the two, would be expected to lead to heroin preference.

Essential value (EV), a behavioral economic measure that covaries with inelasticity of demand (Hursh and Silberberg, 2008), was used to index reinforcer value. EV quantifies how hard subjects work to defend baseline consumption levels of a reinforcer as the price of that reinforcer increases. EV is especially useful in a study such as the present one because EV is independent of reinforcer magnitude (Hursh and Silberberg, 2008), thus facilitating comparisons of different reinforcers. A growing number of recent studies investigating drugs as reinforcers have used EV to quantify reinforcer value (e.g., Bentzley et al., 2013, 2014; Grebenstein et al., 2015; Hofford et al., 2016; Huskinson et al., 2017; Lamb and Daws, 2013; Lemley et al., 2016).

The primary goal of the present study was to investigate how the EVs of heroin and saccharin relate to the choice between these

* Corresponding author at: Psychology Department, American University, 4400 Massachusetts Ave. NW, Washington, DC 20016, United States.
E-mail address: kearns@american.edu (D.N. Kearns).

http://dx.doi.org/10.1016/j.drugalcdep.2017.04.031
Received 21 December 2016; Received in revised form 6 April 2017; Accepted 30 April 2017
Available online 13 June 2017
0376-8716/

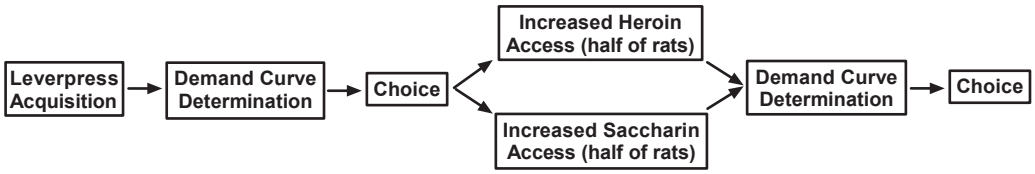

Fig. 1. Schematic diagram of sequence of phases.

reinforcers. The design of this study also allowed for a comparison of the EVs of heroin and a non-drug reinforcer in rats. This information adds to the results of research comparing the EVs of other drugs and non-drug alternatives in rats. Previous studies found that, when directly compared, food (in hungry rats) had higher EV than cocaine (Christensen et al., 2008a, 2009; Kearns et al., 2016) or methamphetamine (Galuska et al., 2011), whereas saccharin (in non-fluid-deprived rats) and cocaine had similar EVs (Kearns et al., 2016). The present study extends this research, which has focused on psychostimulants thus far, to another drug class by using the opioid heroin as the drug reinforcer.

An additional goal of the present study was to investigate how increased access to heroin or saccharin alters demand for these reinforcers and the choice between them. In an earlier study, Christensen et al. (2008b) found that just seven additional two-h cocaine self-administration sessions made demand for cocaine less elastic (i.e., the EV of cocaine increased). In contrast, similar exposure to a schedule of food reinforcement did not alter the elasticity of demand for food. The present study used a design similar to that of Christensen et al. (2008b) to determine whether the elasticity of demand for heroin or saccharin, as well as preference between them, changes as a result of increased access to these reinforcers.

2. Materials and methods

2.1. Subjects

Twenty naïve adult male Long-Evans rats, weighing approximately 450 g at the start of the experiment, served as subjects. Rats were individually housed in plastic cages with wood-chip bedding and had unlimited access to rat chow and water in their home cages. The colony room where the rats were housed had a 12-h light:dark cycle with lights on at 08:00 h. Training sessions were conducted five days per week during the light phase of the light:dark cycle. Throughout the experiment, rats were treated in accordance with the Guide for the Care and Use of Laboratory Animals (National Academy of Sciences, 2011) and all procedures were approved by American University's Institutional Animal Care and Use Committee.

2.2. Apparatus

Training took place in 10 standard operant test chambers described in detail elsewhere (Tunstall and Kearns, 2014). The essential features of each chamber were two retractable levers, a retractable sipper tube and bottle, cue lights above each lever, and a speaker used to provide a tone (4000 Hz and 70 dB) stimulus. Heroin (provided by the Drug Supply Program, National Institute on Drug Abuse, Bethesda, MD) in a saline solution at a concentration of 0.0512 mg/ml was infused at a rate of 3.19 ml/minute by 10-ml syringes driven by Med-Associates (St. Albans, VT) syringe pumps. Tygon tubing extended from the 10-ml syringes to a 22-gauge rodent single-channel fluid swivel (Instech Laboratories, Plymouth Meeting, PA) and tether apparatus (Plastics One, Roanoke, VA) that descended through the ceiling of the chamber. Heroin was delivered to the subject through Tygon tubing that passed through the metal spring of the tether apparatus

2.3. Surgery

Before training, all rats were surgically prepared with chronic indwelling jugular vein catheters, using procedures described in detail elsewhere (Thomsen and Caine, 2005; Tunstall and Kearns, 2014). In brief, approximately 3.5 cm of Silastic tubing was inserted into the right jugular vein. From this insertion site, an additional 8 cm of Silastic tubing passed under the skin to the midscapular region where it connected to the 22-guage stainless steel tubing of a backmount catheter port (Plastics One, Roanoke, VA) that was implanted subcutaneously. The spring tether in the chamber was attached to the threaded plastic cylindrical shaft of the port that protruded through an opening in the skin. All surgery was conducted under ketamine (60 mg/kg) and xylazine (10 mg/kg) anesthesia. Rats were given 7–10 days to recover from surgery. Catheters were flushed daily with 0.1 ml of a saline solution containing 1.25 μg/ml heparin and 0.08 mg/ml gentamicin.

2.4. Procedure

See Fig. 1 for a schematic diagram showing an overview of the procedure.

2.4.1. Phase 1: demand for heroin and saccharin

The demand procedure used here was similar to that in Christensen et al. (2008a). Rats were first trained to lever press for heroin and for saccharin on a fixed-ratio (FR)-1 schedule. During sessions lasting 3 h, there were eight 15-min components where one of the two retractable levers was inserted. There were four presentations each of the heroin and saccharin levers, with the order of presentation randomized with the restriction that there were no more than two consecutive components of the same type. Each component was followed by a 7.5-min period where both levers were retracted. Thus, over the course of the 3-h session, rats had access to each of the levers for a total of 60 min. The position (left vs. right) of the heroin and saccharin levers was counterbalanced over rats. During heroin-lever components, a lever press resulted in a 0.02-mg/kg heroin infusion, simultaneous illumination of the cue light above the lever, and a 10-s tone presentation. During saccharin-lever components, pressing the lever resulted in the saccharin sipper tube being inserted into the chamber for 20 s, allowing rats to drink the 0.2% (w/v) saccharin solution. The 0.02-mg/kg/infusion dose was used because previous studies have found that this dose supports maximal responding in rats (Martin et al., 1998). Our goal was to try to make the baseline numbers of heroin and saccharin reinforcers obtained as comparable as possible because a previous study (Kearns et al., 2016) found that essential value is most useful as a predictor of preference between reinforcers when they maintain similar baseline consumption levels.

Rats were trained on this procedure with an FR-1 schedule for a minimum of eight sessions and until the consumption of each reinforcer stabilized. Stability was defined as three consecutive sessions where the total number of reinforcers earned of each type did not vary from the rolling three-session mean by more than 20%. Once this stability criterion was reached, the FR increased over blocks of two sessions according the following sequence: 3, 10, 32, 100, 320. The progression of the sequence ended early if a rat's consumption of both reinforcers at a particular FR declined to less than 10% of consumption observed at FR 1.