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Effects of baclofen on operant performance for food pellets and vegetable shortening after a history of binge-type behavior in non-food deprived rats

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Abstract

Operant performance of non-food deprived rats ($n=8$) was assessed under progressive ratio (PR) and concurrent PR-fixed ratio schedules of food pellet and/or vegetable shortening reinforcement. Post operant baselines, rats were matched and divided into 2 groups based upon the schedule of shortening availability: High restriction binge group (H, 1-hr home cage shortening access each week on Monday, Wednesday, and Friday) and Low restriction (L, 1-hr shortening access daily). Chow and water were continuously available; only access to the shortening was restricted. After 8 weeks, operant performance was reassessed. Lever pressing for shortening increased in the H rats for all schedules, but was either unaffected or decreased in the L rats. Pellet responding under the concurrent schedules increased for both groups. The effects of four dosages of (*R*)-baclofen (0.3–1.8 mg/kg, i.p.) on operant performance were also assessed. For both groups, 1.0 mg/kg baclofen significantly reduced shortening responding relative to saline for all schedules except one, but had no or minimal effect on pellet responding. This suggests a specific effect of baclofen on responding maintained by fat. These results indicate that intermittent episodes of bingeing on fat can increase the reinforcing efficacy of fat and that $GABA_B$ receptor activation can attenuate this effect.

Keywords: Baclofen; Binge eating; Dietary fat; Progressive ratio; Reinforcing efficacy

1. Introduction

Intermittent episodes of behavioral excess characterize several disorders, including substance abuse and the bingeing-related eating disorders. These disorders often share co-morbidity and are difficult to treat. Modeling this kind of behavior in animals would facilitate the elucidation of basic mechanisms and the screening of potential therapeutics. Our laboratory has developed a rat protocol for examining intermittent excessive food intake in which limited access to a preferred food is provided to non-food deprived rats (Corwin, 2004; Corwin et al., 1998; Dimitriou et al., 2000; Thomas et al., 2002). Under this protocol non-food deprived rats given 2 hr of access to vegetable shortening three times per week (high restriction) consume significantly more shortening per period of access than non-food deprived rats provided with daily two-hr access (low restriction). This differential amount of shortening consumption raises the question of whether shortening has become more reinforcing to the high-restriction group than to the low-restriction group. Stated otherwise, does the schedule of access to shortening change the reinforcing efficacy of shortening in non-food deprived rats?

One method of investigating the reinforcing efficacy of a stimulus is to use a progressive ratio schedule of reinforcement. In a progressive ratio schedule the value of the ratio requirement increases with each subsequent reinforcer delivery according to some mathematical formula. The highest ratio that the animal completes is defined as the "breakpoint", which is used as an index of reinforcer efficacy or reinforcer value, i.e. it serves as a measure of "how hard the animal is willing to work" or "how motivated the animal is" to obtain different reinforcers.

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Breakpoints can be compared to one another with various independent variable manipulations, and have been used extensively in the study of substance abuse (Richardson and Roberts, 1996; Deroche-Gamonet et al., 2004). Progressive ratio schedules also have been used to assess the reinforcing efficacy of food and have been shown to be sensitive to a variety of independent variable manipulations including reinforcer concentration (Cheeta et al., 1995; Hodos, 1961; Reilly, 1999; Sclafani and Ackroff, 2003), reinforcer magnitude (Spear and Katz, 1991), and the deprivation state of the animal (Cheeta et al., 1995; Hodos and Kalman, 1963).

Progressive ratio schedules in conjunction with agonist and/or antagonist injections have also been used to examine drug self-administration in animals to elucidate the neurochemical system(s) mediating drug mechanism(s) of action. Recent research has indicated that $GABA_B$ receptors may be involved in substance abuse disorders. Baclofen, a $GABA_B$ agonist, has been shown to reduce cocaine, *d*- and meth-amphetamine, apomorphine, nicotine, ethanol and heroin self-administration in animals (Brebner et al., 1999, 2000a,b, 2005; Campbell et al., 1999; Corrigall et al., 2001; Di Ciano and Everitt, 2003; Loh and Roberts, 1990; Paterson et al., 2004; Ranaldi and Poeggel, 2002; Roberts, 1989; Roberts et al., 1996; Stromberg, 2004). The majority of these studies used progressive ratio schedules of reinforcement alone or in combination with other schedules of reinforcement. Of relevance to the present study is research showing that baclofen reduced progressive ratio responding for cocaine at lower dosages than was required to reduce fixed ratio responding for cocaine or for food (Brebner et al., 2000a).

While the above studies have reported that baclofen reduced drug self-administration, numerous other studies have reported that baclofen had either no significant effect on or increased food intake and/or food-maintained responding whether given either peripherally (Brebner et al., 2000a; Ebenezer, 1995, 1996; Ebenezer and Patel, 2004; Ebenezer and Pringle, 1992; Higgs and Barber, 2004; Shoaib et al., 1998) or centrally (Brebner et al., 2000b; Ebenezer, 1990; Echo et al., 2002; Jonaidi et al., 2002; McFarland and Kalivas, 2001; Minano et al., 1992; Stratford and Kelley, 1997; Ward et al., 2000; Wirtshafter et al., 1993; Znamensky et al., 2001). In contrast, our lab has recently reported that baclofen reduced shortening intake under both high and low restriction access conditions at dosages that either had no effect on or stimulated chow intake (Buda-Levin et al., 2005). While this suggests that consumption of shortening under limited access conditions may be similar in some ways to drug self-administration, the behavioral requirements are quite different in the two types of studies. Furthermore, food intake measurements are confounded by satiation that can occur during the test sessions. Therefore, intake is not a sensitive assay for assessing reinforcing efficacy, nor for assessing potential receptors that may modulate reinforcing efficacy.

In order to assess the effects of the shortening access schedule on reinforcing efficacy, the present study examined operant responding for solid vegetable shortening and for food pellets alone under a progressive ratio schedule, and for shortening and food pellets under concurrent progressive ratio fixed ratio, and concurrent fixed ratio schedules of reinforcement. Pre-binge and post-binge responding for solid vegetable shortening and for food pellets was compared in non-food deprived rats maintained on our high and low restriction protocols (Corwin et al., 1998). In order to compare the effects of baclofen more directly to those reported for drug self-administration, the effects of baclofen were assessed during the post-binge behavioral assessment of operant performance.

2. Materials and methods

2.1. Animals

Eighteen male Sprague Dawley rats, 60 days of age and weighing 275–301 g (Harlan, Indianapolis, IN) at the start of the study, were individually housed in hanging stainless steel wire cages in a temperature- and humidity-controlled environment with a 12:12 light:dark cycle. All rats were maintained on a nutritionally complete commercial laboratory rodent diet (Laboratory Rodent Diet 5001, PMI Feeds, Richmond IN; percent of calories as protein: 28.05%, fat: 12.14%, carbohydrate: 59.81%; 3.3 kcal/g) placed in hanging metal food hoppers at the front of the cage. Tap water was freely available. All procedures were approved by the Pennsylvania State University Institutional Animal Care and Use Committee.

2.2. Apparatus

The animals were tested in three identical operant chambers (30 × 30 × 30 cm) located in a room adjacent to the vivarium. Each chamber contained a food magazine (Gerbrands model D-1) that delivered 45 mg food pellets (Noyes Precisions Pellets™, PJAI-0045 Research Diets, Inc., New Brunswick, NJ; percent of calories as protein: 25%, fat:11%, carbohydrate:64%; 3.2 kcal/g) into a receptacle located on the right side of the front chamber wall. The nutrient composition of the pellets was based upon the same formulation as the maintenance rodent diet, but the pellets also contained corn syrup (~12% of energy). A solid-fat pump (Razel model A, Razel Scientific Instruments, Inc., Stamford, CN) located outside the operant chamber delivered solid vegetable shortening (Crisco® All-Vegetable shortening, J.M. Smucker Co., Orrville, OH, 9.17 kcal/g) packed into a 30 cc syringe (Becton Dickinson, Franklin Lakes, NJ) through a hole located on the left side of the front chamber wall. A lever (BRS/LVE model CRL-005) located in the middle of the right side of the chamber served as the "food lever", and an identical lever located in the middle of the front panel of the chamber served as the "shortening lever". Each lever was present in the chamber only when there was a reinforcement contingency in effect for that lever.

2.3. Operant training

Animals were randomly assigned to two groups and 1-hr experimental training sessions were conducted on Mondays, Wednesdays and Fridays for one group, and on Tuesdays, Thursdays and Saturdays for the other group. During these training sessions only, all rats were food-deprived Mondays